Omega-3 Fatty Acids for Maternal and Infant Health and Development
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Abbreviations

AA .............. arachidonic acid 20:4 (long chain omega-6)
AI .............. Adequate Intake
ALA .............. alpha-linolenic acid 18:3 (omega-3)
CNS .......... central nervous system
DHA ............ docosahexaenoic acid 22:6 (long chain omega-3)
DPA ............ docosapentaenoic acid 22:5 (long chain omega-3)
EPA ............ eicosapentaenoic acid 20:5 (long chain omega-3)
GLA ............ gamma-linolenic acid 18:3 (omega-6)
LCPUFA .... long chain polyunsaturated fatty acids
NHMRC...... National Health & Medical Research Council
Omega-3...... omega-3 polyunsaturated fatty acids
Omega-6...... omega-6 polyunsaturated fatty acids
PUFA ........ polyunsaturated fatty acids
SDT .......... Suggested Dietary Target
Contents

Recommendations.................................................................................................................................................. 4

Summary of evidence
  Summary of evidence for long chain omega-3s in pregnancy, lactation and early infancy................................. 6

Introduction.......................................................................................................................................................... 7

Role of omega-3s in infant development
  Long chain polyunsaturated fatty acids (LCPUFA) for term infants ................................................................. 8
  Ms Suzanne Meldrum and Professor Karen Simmer
  Benefits of omega-3s in neurodevelopmental outcomes of preterm infants....................................................... 10
  Professor Robert Gibson

Omega-3s and immune development in infancy ................................................................................................. 13
  The role of omega-3 fatty acids in allergy prevention
  Ms Nina D’Vaz and Professor Susan Prescott

Omega-3s and maternal health (during and after pregnancy)
  Long chain omega-3 polyunsaturated fatty acids and maternal health (during and after pregnancy) ................ 17
  Professor Maria Makrides

International perspective
  The role of long-chain omega-3 fatty acids in pregnancy, lactation and infancy – European recommendations. ... 21
  Professor Bert Koletzko

Public Health recommendations and implications
  Current guidelines for pregnancy, lactation and infant feeding ........................................................................... 24
  Ms Wendy Morgan
  How much fish and omega-3s do Australian women and young children consume? ....................................... 27
  Professor Lynne Cobiac

Participant details .................................................................................................................................................. 30
Omega-3 Intakes for Infants, Pregnancy and Lactation

1. Long chain omega-3s are important for neurological development and are derived from the mother during gestation and from breastfeeding. However, dietary intakes of long chain omega-3s in Australian women of childbearing age are well below guidelines designed to achieve optimal health outcomes.

2. The long chain omega-3 fatty acid, DHA, must be deposited in adequate amounts in the brain, eye and other tissues during fetal and early postnatal life. Unlike DHA, other long chain omega-3 fatty acids (e.g. EPA and DPA) do not accumulate to any appreciable extent in the growing brain and eye. Therefore, recommendations for pregnancy and lactation need to be based on meeting adequate DHA status.

3. Consistent with the European consensus statement, pregnant and breastfeeding women should aim to achieve a DHA intake of at least 200mg per day. This translates into 1 to 2 oily fish meals per week or a wide variety of fish meals per week that do not unduly focus on large predatory fish, is safe in pregnancy and when breastfeeding. The potentially positive effects of high amounts of long chain omega-3s from sea fish on child development outcomes outweigh potential disadvantages. Current recommendations to pregnant and lactating women regarding warning messages about fish and mercury/contaminants can lead to limitation or avoidance of fish and seafood.

4. Breastfeeding should be actively encouraged as the preferred method of feeding healthy infants. An adequate supply of DHA (an average daily intake of 200mg per day) is recommended for breastfeeding women to meet the growing infant’s needs as breast-milk content is dependent on maternal intake. When breastfeeding is not possible, a DHA-fortified infant formula is recommended for healthy infants.

5. There is a need for consumer-tested public health messages that communicate the benefits of fish and long chain omega-3s. Recommending 1 to 2 oily fish meals per week or a wide variety of fish meals per week that do not unduly focus on large predatory fish, is safe in pregnancy and when breastfeeding. The potentially positive effects of high amounts of long chain omega-3s from sea fish on child development outcomes outweigh potential disadvantages. Current recommendations to pregnant and lactating women regarding warning messages about fish and mercury/contaminants can lead to limitation or avoidance of fish and seafood.

6. Breastfeeding should be actively encouraged as the preferred method of feeding healthy infants. An adequate supply of DHA (an average daily intake of 200mg per day) is recommended for breastfeeding women to meet the growing infant’s needs as breast-milk content is dependent on maternal intake. When breastfeeding is not possible, a DHA-fortified infant formula is recommended for healthy infants.

Communication to Health Professionals

7. Inform health professionals of:
   a) New European consensus statement regarding long chain omega-3 intakes for pregnant and breastfeeding women.
   b) Safety of recommended intakes of 500mg long chain omega-3s or 200mg DHA per day in pregnancy and lactation.
   c) Wide variety of dietary sources are recommended - whole foods (e.g. fish, seafood), enriched foods and beverages and marine or algal supplements.

8. Consult with health professional organisations and health professionals on:
   a) Guideline development for pregnant and breastfeeding women that are consistent with the new European consensus statement and national Dietary Guidelines.
   b) Dietary sources of long chain omega-3s that are suitable in pregnancy and lactation. Develop specific information on amount and type of appropriate food sources, including non-oily fish, enriched foods and beverages and role of supplements.
9. There is a key role for government:
   a) To update dietary guidelines and relevant nutrition policy to take into account the current evidence on the important role of long chain omega-3s in infant neurodevelopment.
   b) To include long chain omega-3 dietary advice for pregnancy and lactation in relevant diet and nutrition communications to encourage adequate intake.
   c) To review and research dietary implications of current communications on mercury in fish for women who are pregnant or breastfeeding, women planning pregnancy, infants and children to ensure communications are also supportive of long chain omega-3 intakes.

10. The Omega-3 Centre recommends that the planned National Health Survey includes an adequate sample of pregnant women and women planning a pregnancy to ascertain current long chain omega-3 intakes and dietary sources.

11. Messages to government:
   a) The European consensus statement for long chain omega-3 intakes for pregnant and lactating women provides a useful evidence-based guideline to achieve an average daily DHA intake of at least 200mg. These guidelines are consistent with the Australian Dietary Guidelines (2 to 3 fish meals per week) and NHFA’s guidelines for all Australians to consume 500mg per day of long chain omega-3s (EPA + DHA) which equates to 2 or 3 serves of oily fish (150g) per week.

12. As part of the planned National Health Survey, assess the long chain omega-3 status of an adequate sample of pregnant women and women planning a pregnancy to ascertain current long chain omega-3 intakes and dietary sources.

13. Current data on long chain omega-3 nutritional status are needed on children less than 2 years of age (recent Children’s Nutrition & Physical Activity Survey did not include children < 2 years of age).


15. Ongoing development and maintenance of an updated high quality food and supplement long chain omega-3 database, e.g. as part of the FSANZ Food Composition Program.

16. Development of practical consumer-friendly guidelines on how to meet recommended long chain omega-3 intakes from a variety of sources. It is recommended that the Omega-3 Centre collaborate with the Seafood Co-operative Research Centre on this project.

17. Further research is needed to establish the relationship between long chain omega-3 intake and the impact on specific aspects of CNS structure and function including mechanisms of action with a particular focus on docosanoids.

18. Studies exploring the short- and long-term effects of long chain omega-3 status in pregnancy, lactation and infancy according to inter-individual differences, including genetic variation in fatty acid desaturase gene cluster, sex, birth weight and gestational age.

19. Further research to determine the optimal dietary level of DHA for preterm infants that addresses sex, birth weight, gestational age and genetic differences.

20. Dose-response studies to determine the Nutrient Reference Values for DHA intake and total long chain omega-3 intake in infants (< 6 months and > 6 - 12 months).
At the consensus meeting the panel discussed relevant areas and ranked them according to the level of evidence available at the current time.

There is no evidence that long chain omega-3s cause harm and are therefore safe to consume in pregnancy, lactation and early infancy. The evidence is rated from positive indication of benefit to conclusive for effects on pregnancy outcomes, maternal health (during and post-pregnancy) and infant development.

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**Table 1: Summary of evidence for long chain omega-3s in pregnancy, lactation and early infancy**

<table>
<thead>
<tr>
<th>Area</th>
<th>Level of Benefit</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pregnancy Outcomes</strong></td>
<td>Conclusive evidence of benefit</td>
<td>Long chain omega-3s are safe. There is no evidence of increased risk of bleeding in pregnancy.</td>
</tr>
<tr>
<td></td>
<td>Good evidence of benefit</td>
<td>In high risk pregnancies, there is evidence of reduced risk of early premature births. The clinical benefit of long chain omega-3 intake/supplementation requires further investigation.</td>
</tr>
<tr>
<td></td>
<td>Positive indication of benefit</td>
<td>Enhanced maternal dietary intakes of DHA particularly in the 3rd trimester increase fetal supply and are associated with beneficial effects on the development of visual acuity, motor activity and various cognitive functions in term infants after birth. Greater benefits are seen in infants of mothers with low baseline intake.</td>
</tr>
<tr>
<td>Evidence of harm</td>
<td></td>
<td>No areas showed evidence of harm.</td>
</tr>
<tr>
<td>No evidence</td>
<td></td>
<td>There is no evidence either way of the effect of long chain omega-3s on pre-eclampsia.</td>
</tr>
<tr>
<td><strong>Maternal Health (during and post-pregnancy)</strong></td>
<td>Conclusive evidence of benefit</td>
<td>Long chain omega-3s are safe to consume in pregnancy and lactation. There is no evidence of adverse effects on maternal health when consumed in recommended amounts – 1 to 2 oily fish meals per week, enriched foods and fish oil supplements.</td>
</tr>
<tr>
<td></td>
<td>Positive indication of benefit</td>
<td>Low dietary intake of long chain omega-3s in pregnancy and after birth has been associated with postnatal depression. It is important to encourage adequate intakes (an average daily intake of at least 200mg DHA), however there is a need for large scale clinical trial evidence before definitive guidelines can be made.</td>
</tr>
<tr>
<td>Evidence of harm</td>
<td></td>
<td>No areas showed evidence of harm.</td>
</tr>
<tr>
<td><strong>Infant Development</strong></td>
<td>Conclusive evidence of benefit</td>
<td>In pre-term infants, there is a convincing effect of high dose DHA-supplementation in the maternal diet when breastfeeding (3g of fish oil = 900mg DHA) on neurodevelopment and visual acuity. There is a gender effect, with evidence that girls benefit from this dose. Long chain omega-3 supplementation is safe in pre-term and term infants with no evidence of a detrimental effect on growth and development.</td>
</tr>
<tr>
<td></td>
<td>Good evidence of benefit</td>
<td>There is a beneficial effect of long chain omega-3s on visual acuity in term infants. Promote a healthy maternal diet with adequate DHA (an average daily intake of at least 200mg) when breastfeeding or encourage use of DHA-fortified formula.</td>
</tr>
<tr>
<td></td>
<td>Positive indication of benefit</td>
<td>Enhanced maternal dietary intakes of DHA particularly in the 3rd trimester increase fetal supply and are associated with beneficial effects on the development of visual acuity, motor activity and various cognitive functions in term infants after birth. Greater benefits are seen in infants of mothers with low baseline intake. There is a possible role for long chain omega-3 supplementation during pregnancy or early infancy as a preventative measure against allergic disease. Large scale clinical trials are underway that will provide evidence on the role of omega-3 supplementation and optimal timing, duration and form of supplementation.</td>
</tr>
<tr>
<td>Evidence of harm</td>
<td></td>
<td>No areas showed evidence of harm.</td>
</tr>
</tbody>
</table>
Introduction

Omega-3 Fatty Acids for Maternal and Infant Health and Development was the third Scientific Consensus Meeting convened by The Omega-3 Centre. It was a full day meeting held in Sydney on 11 June 2009. The format of the meeting was a facilitated discussion between the nine expert participants, who each presented current evidence in their area of expertise.

The Centre’s objective was to produce a scientific consensus report on omega-3s for maternal and infant health and development based on the meeting’s outcomes to help raise community and government awareness and understanding of this key nutritional issue. The aim is to encourage a supportive environment for an optimal intake of long chain omega-3 fatty acids by these population groups.

It is well known that long chain omega-3s play a vital role in the development of the brain, central nervous system and eyes. Scientific experts have proposed long chain omega-3 supplementation of the mother and infant may improve brain function, vision and prevent the development of allergies in infants. The Centre identified a need to better understand the strength of evidence for omega-3s and maternal and infant health and development.

Dietary intakes of long chain omega-3s in Australia and New Zealand are considered low when compared to recommended intakes. Recommendations for intakes of omega-3s were released by the NHMRC in 2006 but did not include specific values for infants. The expert participants were asked to consider recommended intakes for this population group.

Government nutrition policy currently pays little attention to the need for long chain omega-3 fatty acids in the health of Australians. There is a need to understand the role of omega-3s in maternal and infant health and ensure recommendations and advice on omega-3s are communicated effectively to improve their intakes.

Previous scientific consensus meetings convened by The Omega-3 Centre focused on omega-3s for children (April 2007) and omega-3s for Baby Boomers (July 2008). Copies of these reports are available from The Omega-3 Centre (www.omega-3centre.com).
LCPUFAs are essential for optimal neurological development (Lauritzen et al. 2001) and are derived from the mother during gestation and from breastfeeding. Dietary intake of long chain omega-3s is low in the modern western world and, theoretically, there are numerous mechanisms whereby LCPUFA supplementation could improve brain function especially the rate of visual maturation. Many studies have assessed whether omega-3 supplementation results in improved central nervous system (CNS) development but meta-analysis of randomised clinical trials has not demonstrated a consistent effect (Simmer et al. 2008). Earlier trials with small sample sizes were more likely to show a benefit but the majority of trials with adequate sample sizes did not. In addition, recent publications with large sample size (n=1160) also conclude that there is no demonstrable effect of DHA supplementation on later motor milestones of term infants (Agostini et al. 2009).

A number of reasons for a lack of conclusive findings in this area have been proposed, and the evaluation of such factors may reveal a clearer method to achieve more consistent results. Such factors include the sample population, the supplement dosage, the test selection period and duration of supplementation, and composition and source of supplement.

An interesting new field of research is genetic differences and how they may moderate the effects of LCPUFAs. This research examines the FADS 1 and FADS 2 candidate genes which have a role in the modification of dietary fatty acids, by encoding the delta-5 desaturase and delta-6 desaturase enzymes, the rate-limiting steps when docosahexaenoic acid (DHA) and arachidonic acid (AA) are metabolized. It is possible that genetic differences may partly explain the reason for the inconclusive findings from previous research.

Strong associations have been observed between polymorphisms of FADS 1 and FADS 2 and the serum phospholipid levels of AA (Schaeffer et al. 2006). Erythrocyte membrane levels of AA and additionally levels of dihomo-gamma-linolenic acid have also been observed to correlate with FADS1 and FADS2 polymorphisms (Rzehak et al. 2009). These polymorphisms may be of particular importance to infants as the genetic variants affect not only maternal blood lipid composition during pregnancy but also the fatty acid composition of breastmilk (Xie & Innis 2008).

Caspi and colleagues (2007) published results indicating that the genetic variation in fatty acid metabolism (FADS 2) moderated the effects of breastfeeding upon cognitive development, the original link between LCPUFA and CNS development (Figure 1). The authors also concluded that genetic heterogeneity in fatty acid metabolism may be diluting supplementation effects, and that if genetically responsive subgroups can be identified for analysis, modest benefits may be revealed as stronger than previously thought for a proportion of children.

A dose-response relationship has been proposed and may explain the lack of effect seen in many trials (Lauritzen 2001, Uauy et al. 2003, Simmer et al. 2008). An optimal dosage of long chain omega-3s has been estimated by analysing the rate of deposition of DHA within brain tissue during pregnancy and early infancy. Autopsy studies in infants whose cause of death was not neurologically related showed the DHA in the forebrain increases from ~650mg at birth to ~2 grams at 2 years of age, and most of the accumulation happens during the first 12 months of life. DHA accretion into the brain and nervous system is greatest during the last trimester of pregnancy and postmortem studies indicated that average whole-body accretion of DHA during this time is in excess of 50mg/kg/day and is equivalent to a dietary DHA content of approximately 1% of total fatty acids. The proposed requirement of DHA at
1% of total fatty acids is higher than that used in most trials and with the preliminary evidence consisting of a dose-response relationship for DHA and neurodevelopmental outcomes, it is conceivable that a high dose DHA, may result in more convincing evidence.

Our trial using high dose supplementation (2.2g DHA/day) during the second half of pregnancy resulted in improved hand-eye coordination of term infants at 2.5 years of age (Dunstan et al 2008). In preterm infants, a large randomised trial of high (1%) v low (0.3%) DHA supplementation suggested some improvement in Bayley scores in subgroup analyses and a reduction in the percentage of children with disability at 18 months of age (Makrides et al 2009). The current randomised clinical trial in Perth uses high dose DHA (280mg/day) in term infants (which approximately equates to 1% DHA in 6kg infant receiving 120ml milk/kg/day) whereas the recent randomised trial in Italy reported no effect of LCPUFA supplementation used low dose DHA (20mg /day) (Agostoni et al 2009).

Assessments used in randomised trials of LCPUFAs include the Bayley Scales of Infant Toddler Development, the Fagan Test of Infant Intelligence, The Knobloch, Passamanik and S ierrards Developmental Screening Inventory and the Macarthur-Bates Communicative Development Inventory. Most of these tests were designed to select abnormal populations not to discriminate between groups within the normal range. Further research is needed to establish the exact relationship between proposed benefits of supplementation and the role of LCPUFA in CNS structure and function. Tests should be selected that are specific to facets of the CNS for which DHA has particular importance such as was done in the trials of Birch et al (2005) in which a benefit of LCPUFA supplementation on visual acuity was demonstrated.

In summary, we need to better understand why some infants respond to omega-3 supplementation and others do not. The issue of population subgroups including genetic differences is important, as is baseline omega-3 status. An appropriate dose, long duration of study, large sample size and relevant assessments must also be considered when designing an appropriate trial which examines the potential benefits of long chain omega-3 supplementation in infancy.

References


Makrides M et al. Neurodevelopmental outcomes of preterm infants fed high dose DHA; a randomised controlled trial. JAMA. 2009; 301: 175-82.


Overview of the Science

It had been known for many years that DHA was a major constituent of visual and neural tissues and some early animal experiments had hinted at compromised learning abilities in rats raised on omega-3 deficient diets. These studies reached a climax when the seminal study by Martha Neuringer in the early nineties (Neuringer et al 1984) rang alarm bells in regard to omega-3 PUFA requirements for infants. In that study she fed rhesus monkeys two infant formulas that reflected the infant formulas of the day. One was extremely rich in LA but contained little or no ALA and the other, based on soy oil, contained adequate ALA. When the infants were assessed at later times the infants fed the omega-3 deficient milk were found to have lower levels of retinal and neural DHA and had poorer retinal and visual responses. Although subsequent treatment with DHA improved status, it did not reinstate visual performance which hinted at a possible optimal window for visual and possibly neural development.

These experiments were essentially duplicated in preterm infants by the Dallas group led by Ricardo Uauy and Eileen Birch (Uauy et al 1990, Birch et al 1992). Their results confirmed the need for omega-3 fatty acids (preferentially preformed LCPUFA) in infants who, by being born very premature, were denied the normal flow of omega-3 fatty acids from the mother via the placenta during their brain growth spurt. Their results prompted several studies of varying size and quality. In general they have confirmed the need for preformed long chain omega-3 for preterm infants to optimise visual responses but there has been confusion and some uncertainty regarding the effects of dietary LCPUFA, particularly DHA, on more global measures of neurodevelopment.

Our recent systematic review and meta-analysis examining the effects of LCPUFA-supplemented versus control formulas on neurodevelopment of preterm infants identified 7 trials with relevant outcomes, 5 of which assessed a combination of DHA and AA (Smithers et al 2008). In the meta-analysis of all 7 trials, infants fed LCPUFA-supplemented formula and tested with the Bayley Scales of Infant Development Version II (BSID-II) had a Mental Development Index (MDI) that was 3 points higher than infants fed control formula (WMD 3.44, 95% CI 0.56, 6.31, n=879, p=0.02). Fewer MDI data were available for infants tested with BSID-I and the control and treatment groups did not differ (WMD -4.09, 95% CI -9.85, 1.67, n=97, p=0.16). Overall no significant difference in MDI was observed between infants fed control or LCPUFA-supplemented formula when MDI data from both BSID-I and BSID-II assessments were combined (WMD 2.13, 95% CI -0.87, 5.14, n=976, p=0.16). In our meta-
analyses, the incongruence observed between the MDI scores and version of the BSID added to the heterogeneity between trials and contributed to the need to apply random effects models. It was not possible to combine the BSID-I and II data in a meaningful way because the differences between trials contributed to a greater diversity in responses than expected. The differences between trials may arise from the sample population studied, the way the intervention was applied, the types of outcomes or trial methodology. We have limited confidence in the BSID-I outcome as these data were generated from two trials with small sample sizes and methodological limitations. It is therefore not surprising that other meta-analyses, which combine all forms of the BSID suggest that LCPUFA supplementation of infant formula for preterm infants has no clear effect of neurodevelopmental outcomes (Simmer et al 2008, Simmer et al 2008).

The new phase of LCPUFA research is focusing on dose. Post-mortem tissue analyses of stillbirths suggested that in utero whole body accumulation of DHA was in the order of 60mg/kg/day (Clandinin et al 1981, Martinez 1992). We tested whether increasing the amount of dietary DHA, from ~20 mg/kg/day to levels that we calculated to provide the fetal accumulation rate (~60 mg/kg/day), would improve neurodevelopment in infants born <33 weeks gestation (Makrides et al 2009). DHA enrichment of breastmilk fed to infants was achieved through maternal supplementation with tuna oil or direct addition to infant formula. In this large and inclusive trial we showed that infants fed the DHA-enriched diet had better visual development in infancy (Smithers et al 2008). We also demonstrated an improvement in mean MDI at 18 months corrected age that did not reach statistical significance (p=0.2), although there were 50% (5.2% vs. 10.5%, p=0.03) fewer children with significant cognitive delay in the high-DHA (60mg/kg/day) group (Makrides et al 2009). Furthermore, DHA-supplemented girls (Figure 2) and infants born weighing <1250g (Figure 3) had a 5-point improvement in mental development scores compared with control (Makrides et al 2009). The efficacy of about 90 mg/kg/d of DHA in infants born <1500g has also recently been reported, showing improved problem solving and better recognition memory at six months corrected age (Henriksen et al 2008), indicating that higher DHA doses than currently found in infant formulas or the breastmilk of women with Westernized diets may be needed at least for infants born preterm.

What don’t we know?

DHA: How does it work and how much is needed?

Essentially we have very little knowledge about how the brain works and the role of DHA in this process or how much DHA is required in the diet of preterm infants. New animal data suggest that high-dose DHA is neuroprotective. Huang and co-workers, using an animal model of thoracic spinal cord compression, have established that axonal injury was reduced and locomotor recovery improved when animals received DHA compared with the saline treated control group (Huang et al 2007). In contrast, animals treated with AA had a significantly worse outcome than controls indicating specificity of effect to DHA (King et al 2006). Two conditions were necessary to achieve the best outcomes – a high DHA dose [8-10 times the treatment dose in our trial with preterm infants (Makrides et al 2009)] and the absence of a delay between injury and DHA administration. Two mechanisms have been suggested from these animal studies – increase in neurite growth and axonal injury was reduced and locomotor recovery improved when animals received DHA compared with the saline treated control group (Huang et al 2007). In contrast, animals treated with AA had a significantly worse outcome than controls indicating specificity of effect to DHA (King et al 2006). Two conditions were necessary to achieve the best outcomes – a high DHA dose [8-10 times the treatment dose in our trial with preterm infants (Makrides et al 2009)] and the absence of a delay between injury and DHA administration. Two mechanisms have been suggested from these animal studies – increase in neurite growth and return of homeostasis. A complex series of E and D resolvins along with neuroprotective D1 are now known to work in concert to overcome neural damage from the inflammatory response when DHA was around 2% dietary fats. In this regard, there are a number of case studies in which high-dose DHA has been infused intravenously to patients with major brain or spinal cord injury and resulted in dramatic recovery of function (Bailes et al 2008). It is possible that high-dose DHA is not only an important building block for the preterm brain but may be neuroprotective in the critical first days and weeks following preterm delivery. These data have raised new questions about DHA dose as well as its timing. Although we have answered many questions in LCPUFA nutrition, many still remain.

AA: What is its role?

AA is also found in high levels in the brain and although AA has been included in infant formulas there has been no large scale RCT to establish a clear role for AA. Huang and co-workers (Huang et al 2007) have also found that AA can give rise to neuron-protective metabolites but given the capacity for infants to make their own AA from LA much work remains to be done to elicit the requirement for dietary AA for preterm infants.

What should we know?

A huge effort has gone into the scientific investigation of the role of omega-3 fatty acids in infant nutrition, more than for any other nutrient. It is thus surprising that we have so many questions. Until we can elucidate the actual role of DHA in the brain and other organs it seems that we will continue to be conducting ‘black box’ science.

Conclusions and Recommendations

As always, there is a need for further research in this important area. The results of the DINO trial (Makrides et al 2009) have told us that if we are to address complex clinical outcomes we need well designed studies that are sufficiently powered to detect a clinically important effect if it is there. DINO has also shown us that levels of DHA in the diet of preterm infants as high as that found in the breastmilk of Japanese mothers is not harmful and nor does it compromise growth. Finally DINO tells us that we may not have determined the optimal dietary level of DHA for preterm infants since we failed to benefit some girls or any of the boys. Finally, the concept that there should be a fixed ratio of DHA to AA in the diet of preterm infants has very little support.


Omega-3s and immune development in infancy

The role of omega-3 fatty acids in allergy prevention

Nina D’Vaz and Susan L Prescott, University of Western Australia

The prevalence of allergic diseases has risen by epidemic proportions in Westernized countries over the past decades and the same concerning trend is now evident in many developing countries. Australia is currently one of the worst affected countries with more than 40% of school aged children showing evidence of allergic sensitization. These children commonly develop associated allergic diseases such as asthma, eczema, food allergy and allergic rhinitis. Rates of asthma are now among the highest in the world, affecting more than 20% of children. Although levels appear to have reached a plateau, rates of food allergy and eczema are continuing to rise at alarming rates (Mullins 2007) with enormous personal, social and economic cost. It is clear that this “allergy epidemic” is driven by complex environmental changes, although the precise candidates and mechanisms are still unclear.

The continuing objective of research in this area is to identify environmental changes with plausible biological mechanisms for promoting allergic disease, in the hope that these can be favourably modified for the primary prevention of these disorders.

Complex dietary changes have occurred with progressive industrialization. One of the most significant changes has been a decrease in dietary consumption of omega-3 polyunsaturated fatty acids (PUFA) in favor of omega-6 PUFA. Given the well recognized biological effects of these fatty acids, this relative change in composition could plausibly have effects on immune development and predisposition to allergic disease. As summarized below, omega-3 PUFAs have less inflammatory properties than omega-6 PUFAs. This has logically led to interest in the role of omega-3 PUFA supplementation (using fish oil) in the treatment and prevention of allergic diseases such as asthma and other inflammatory diseases.

What do we know:

A number of observational studies show a protective relationship between fish consumption and/or long chain omega-3 levels in pregnancy and childhood and the development of allergic disease. As with other aspects of development, any beneficial effects are likely to be greatest in early life when the immune system is developing (Prescott & Clifton 2009). The potential mechanisms have been attributed to the broad ranging anti-inflammatory properties of the omega-3 fatty acids (recently reviewed by Calder 2008) including:

- **Effects on eicosanoid metabolism, which may influence immune function:**
  Omega-3 PUFA and omega-6 PUFA compete for the same metabolic pathways to produce metabolites with very different properties. The omega-6 PUFA favour the production of the 2-series prostaglandins (such as PGE2) and the 4-series leukotriennes (LTB4), which are highly inflammatory and may promote allergic “Th2” immune differentiation. In contrast, omega-3 PUFA derived products (PGE3 and LTB5) are significantly less inflammatory. This may influence the milieu during antigen presentation and the propensity for inflammatory responses.

- **Effects on antigen presentation:**
  Increasing omega-3 PUFA levels has been associated with reduced expression of MHC class II and adhesive molecule ICAM-1 on antigen presenting cells (APC), which may influence the level and pattern of T cell activation.

- **Effects on T cell function:**
  Supplementation with omega-3 PUFA has been shown to reduce T cell lymphoproliferation and cytokine production. This has been associated with changes in intracellular signaling.

- **Propensity for inflammatory cytokine production:**
  Omega-3 PUFA inhibit the production of inflammatory cytokines IL-1, IL-6 and TNFalpha, possibly through an interaction with nuclear lipid activated transcription factors (peroxisome proliferator-activated receptors [PPARs]), which also regulate cellular responses including inflammation.

- **Emerging pathways of additional influence:**
  A newly described family of EPA- and DHA-derived lipid mediators called resolvins (E- and D-series) appear to have potent anti-inflammatory and inflammation resolving properties (reviewed in Calder 2009).

The apparently protective relationship between long chain omega-3 (fish) intake and allergic disease seen in observational studies has prompted researchers to explore the role of fish oil supplementation in allergic disease. While the effects of fish oil in established disease has been disappointing in the treatment of established asthma and allergic disease, the role in primary prevention is still being explored with some optimism. One of the first studies to use fish oil supplementation in infants reported no allergy preventative effect of supplementing children at high risk of allergic disease from around 6 months of age onwards with tuna oil (or placebo). Although there was a reduction in wheezing at 18 months of age (Mihrshahi et al 2003), there were no long term benefits for the reduction of allergic sensitisation or any diagnosed allergic disease, as assessed at 5 years of age (Marks et al 2006).

As the increased expression of T helper type 2 (Th2) allergic responses is frequently already established by 6 months of age in subsequently allergic children (even though this may be asymptomatic) (Prescott et al 2008) it is possible that earlier intervention could be more effective. There has subsequently
been more interest in PUFA status in pregnancy as a ‘window of opportunity’ before the allergic immune phenotype is established and when there may be more inherent plasticity. This notion is supported by a number of observational studies that have shown a protective relationship between omega-3 PUFA consumption in pregnancy and allergic symptoms in early childhood (Table 2).

So far there are relatively few randomised controlled trials of fish oil supplementation in pregnancy (summarised in Table 3), although there are several currently in progress. These have shown some promise in altering infant immune parameters (not shown) (Dunstan et al. 2003 and some clinical measures of subsequent allergic disease (Dunstan et al. 2003, Olsen et al. 2008, Furuhielm et al. 2009) although not all of these were originally designed for this purpose.

Additional studies are currently underway to assess the role of fish oil in allergy prevention more definitively.

**What we don’t know:**
- It is not yet known whether the changes in immune function that have been observed after fish oil supplementation in pregnancy translate to a consistent reduction in clinical symptoms in infancy. There are a number of studies addressing this.
- The effect of fish oil supplementation of infants between birth and 6 months of age is not known, but is also currently investigated.
- It is not clear if fish oil supplementation is more effective in some individuals than others and whether these differences are attributable to genetic variation. For example, genetic variants in the fatty acid desaturase 1 fatty acid desaturase 2 (FADS1 FADS2) gene cluster are associated with variations in the PUFA in cell membrane (Rzezhak et al. 2009), and the relationship with allergic disease and with the relative effectiveness of fish oil need to be further investigated.
- While fish oil supplements are intended to favourably modify n-6/omega-3 ratios, it is important to consider the essential nature of omega-6 fatty acids in immune function (particularly thymus development), neurodevelopment.

**Table 2: Observational studies to examine the relationship between fish oil in pregnancy and infant allergic disease**

<table>
<thead>
<tr>
<th>Year</th>
<th>Participants</th>
<th>Study design</th>
<th>Conclusion</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004</td>
<td>5144 pregnant women</td>
<td>Late pregnancy maternal and cord blood red blood cells were analysed for total n-6 and omega-3 fatty acid content, which was correlated to early childhood wheezing as well as occurrence of eczema</td>
<td>A reduction of childhood wheeze and eczema with increased cord blood Red blood cell omega-3/ n-6. Not significant after adjustments for multiple comparisons</td>
<td>(Newson et al. 2004)</td>
</tr>
<tr>
<td>2005</td>
<td>5 year old children and their mothers</td>
<td>Grouped by asthmatic status of children, maternal fish consumption during pregnancy was assessed through questionnaires</td>
<td>A protective effect of consumption of oily fish during pregnancy against development of asthma by the age of 5 in children to asthmatic mothers</td>
<td>(Salam et al. 2005)</td>
</tr>
<tr>
<td>2006</td>
<td>295 children born to allergic mothers and 693 children born to non-allergic mothers</td>
<td>SPT of the children were correlated to maternal intake of fish, butter and margarine during pregnancy</td>
<td>Fish consumption in non-allergic mothers correlate with a decreased risk of SPT positivity to foods in offspring</td>
<td>(Calvani et al. 2006)</td>
</tr>
<tr>
<td>2007</td>
<td>1212 5 year old children</td>
<td>Allergic and asthmatic status of children was assessed through questionnaires and correlated to maternal diet during pregnancy</td>
<td>Maternal consumption of fish during pregnancy was inversely correlated to the occurrence of eczema in offspring at 5yrs</td>
<td>(Willers et al. 2007)</td>
</tr>
<tr>
<td>2007</td>
<td>631 3 year old children</td>
<td>Doctor diagnosed asthma by age 3 was correlated to maternal diet during pregnancy</td>
<td>Higher maternal intake of oily fish was associated with a reduced risk of asthma in offspring</td>
<td>(Fitzsimon et al. 2007)</td>
</tr>
<tr>
<td>2007</td>
<td>462 children</td>
<td>Prevalence of atopy and asthma in offspring followed up till 6 years of age was correlated to maternal fish consumption during pregnancy</td>
<td>Fish intake during pregnancy was inversely correlated to occurrence of allergic disease in children</td>
<td>(Romieu et al. 2007)</td>
</tr>
<tr>
<td>2007</td>
<td>2641 2 year old children and their mothers</td>
<td>Maternal diet during final 4 weeks of pregnancy was assessed through questionnaires and correlated to infant eczema and allergic sensitization</td>
<td>A negative correlation between fish intake during final 4 weeks of pregnancy and occurrence of eczema in offspring in the first 2 years of life</td>
<td>(Sausenthaler et al. 2007)</td>
</tr>
</tbody>
</table>
and many other aspects of infant development. It has also been observed that atopy is not only associated with omega-3 status but, at least in some cases, also associated with low arachidonic acid (AA) levels. It is therefore important that fish oil supplementation does not compromise appropriate omega-6 levels necessary for normal infant development and immune function.

**What do we need to know?**

- Many experts have emphasised the need for large scale well controlled intervention studies to obtain statistically sound clinical data on the effect of fish oil supplementation in allergy prevention.
- If fish oil supplementation is ultimately shown to be effective against the development of allergic symptoms, the optimal timing (i.e. during pregnancy or infancy) duration and form of supplementation need to be determined.
- Mechanisms of effect and interactions with other early environmental exposures need to be more fully understood.

**How are we going to find out?**

- Several clinical trials are currently being undertaken in Australia and Europe to assess the effects of fish oil supplementation on infant allergic outcomes. These trials are exploring different methods of fetal/infant supplementation: a) including actual fish intake during pregnancy (Calder et al personal communication), b) fish oil supplementation during pregnancy (Makrides et al personal communication, Biegaard et al personal communication) and c) supplementation to infants from birth to 6 months (Prescott et al personal communication). The results of the current trials are awaited with great interest and expected to significantly improve our understanding of the role of fatty acid supplementation in the prevention of allergic disease.

**Recommendations:**

- Diet is a critical influence on early immune development and this should remain a research priority.
- At present it is considered premature to recommend fish oil supplementation during pregnancy or early infancy as a preventative measure against allergic disease.

**References:**


Marks GB, Mihrshahi S, Kemp AS, Tovey ER, Webb K, Almqvist C, et al. Prevention of asthma during the first 5 years of life: a

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**Table 3: Intervention studies using fish oil in pregnancy: effects on allergy prevention**

<table>
<thead>
<tr>
<th>Year</th>
<th>Participants</th>
<th>Study design</th>
<th>Conclusion</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>83 women with confirmed allergic disease</td>
<td>Participants received fish oil (3.7 gram omega-3/day) or placebo (olive oil) from 20 weeks pregnancy till time of delivery. (Study not initially designed to assess clinical outcomes)</td>
<td>Allergen specific responses as well as clinical outcomes altered in infants born to mothers supplemented with fish oil</td>
<td>(Dunstan et al 2003)</td>
</tr>
<tr>
<td>2008</td>
<td>533 healthy pregnant women</td>
<td>Participants received fish oil (2.7g omega-3/ day), olive oil or no oil from 30 wks pregnancy till time of delivery</td>
<td>Children born to women receiving fish oil were significantly less likely to have developed doctor diagnosed asthma by the age of 16 years</td>
<td>(Olsen et al 2008)</td>
</tr>
<tr>
<td>2009</td>
<td>145 pregnant women, with families at high risk of allergic disease</td>
<td>Participants received 9 capsules of fish oil (1.6g EPA and 1.1g DHA) or soybean placebo daily from 25 weeks pregnancy through the third month of nursing</td>
<td>Lowered prevalence of food allergy and atopic eczema in children born to mothers supplemented with fish oil</td>
<td>(Furuhjelm et al 2009)</td>
</tr>
</tbody>
</table>


This paper considers the rationale for increasing the intakes and status of long chain omega-3s and discusses the functional and clinical outcomes for mothers (and their off-spring). Clinically, eicosapentaenoic acid (EPA, 20:5omega-3) and docosahexaenoic acid (DHA, 22:6omega-3) have been shown to modulate inflammatory and vascular effects. Since pre-eclampsia and gestational hypertension are associated with vasoconstriction and endothelial damage, it is plausible that marine oil fatty acids may ameliorate their effects. Alternatively, marine oil fatty acids could delay initiation of labour and cervical ripening by inhibiting the production of prostaglandins F2α and E2. This biochemical plausibility taken together with the observational studies showing an association between high fish consumption and increased duration of pregnancy, higher birth weight and a lower incidence of pre-eclampsia (Olsen et al 1986, Olsen & Joensen 1985) resulted in a number of randomised controlled trials to assess the cause and effect relationship between fish oil supplementation in pregnancy and improved major pregnancy outcomes.

Marine oils to prevent pre-eclampsia, preterm birth, low birth weight and small-for-gestational age?

Three systematic reviews have recently aggregated the results of the relevant randomised controlled trials (Makrides et al 2006, Horvath et al 2007, Szaiejewska et al 2006). The meta-analyses showed remarkably consistent results despite the fact that these reviews had differing inclusion criteria. In brief, supplementation with marine oil in the second half of pregnancy resulted in a modest increase in the length of gestation (approximately 2.5 days) compared with no marine oil treatment. This was not reflected in a clear difference between the two groups in the risk of preterm birth (<37 weeks gestation), although women allocated marine oil did have a lower risk of giving birth before 34 weeks gestation (Makrides et al 2006, Horvath et al 2007). Birth weight was slightly greater in infants born to women in the marine oil group compared with control, and this difference was commensurate with the small increase in gestation length. There were no overall differences between the groups in the proportion of low birth weight or small-for-gestational age babies (Makrides et al 2006). There was also no clear difference in the relative risk of pre-eclampsia between the two groups (Makrides et al 2006). Collectively these data suggest that routine use of marine oil supplements in pregnancy is likely to have limited benefit in preventing pre-eclampsia, preterm birth and low birth weight.

Although many of the trials assessing the effects of long chain omega-3 supplementation on pregnancy outcomes have taken a pharmacological approach, they have been useful in providing information about safe intakes of long chain omega-3s. For example, supplementation with the commonly used dose of 3g EPA+DHA per day (20 times the average intake of most pregnant women in Westernized countries) was not associated with increased risk of bleeding complications such as nasal bleeding, antepartum vaginal bleeding, maternal anaemia, vaginal blood loss after birth and blood loss at birth, a concern that has commonly been raised in relation to fish oil supplements in pregnancy because of their anti-coagulant properties (Makrides et al 2006). There were also no clear differences between the groups in the mean length of infant hospital stay or the relative risks of admission to neonatal care, congenital malformation, neonatal bleeding disorders and neonatal non-bleeding disorders (Makrides et al 2006).

The role of long chain omega-3s beyond major pregnancy outcomes

The metabolic demand for DHA during pregnancy is higher than for the non-pregnant state. The last trimester of pregnancy is the time when DHA accretion into the fetal brain and nervous system is at its greatest velocity. The fetus is supplied with its DHA from the maternal circulation and post-mortem studies indicate that the fetus accumulates an average of 67mg of omega-3 fatty acids, mostly as DHA, per day during the last trimester of pregnancy (Innis 2003). In addition the mother has increased requirements to support the expanded red cell mass and placenta as well as her own base needs. This increased metabolic need for DHA in pregnancy may be furnished by maternal DHA intake, adaptive metabolic mechanisms in pregnancy such as an increased synthetic capacity to metabolise ALA to DHA (Burdge & Calder 2005) and a preferential use of the DHA stored in adipose tissue (Makrides & Gibson 2000), and the DHA saved from pregnancy amenorrhea. It has not been possible to quantify the positive and negative sides of the DHA balance equation during pregnancy to ascertain whether there is a “true” increased requirement. However, we do know that the DHA intake of women in industrialized countries is generally low and there is little evidence that women change their dietary habits to enhance their DHA intakes in pregnancy. Mean DHA in Western countries is 70-200mg/day (Denomme et al 2005, Innis & Elias 2003, Meyer et al 2003, Otto et al 1997, Stark et al 2005) but in some cases median intake is lower (30-50mg/day) highlighting a skewed distribution of intakes (Meyer et al 2003) so that many women have intakes less than the estimated daily accretion of DHA into the fetus during the last trimester of pregnancy. These observations highlight a potential dietary insufficiency of DHA for both mother and baby.
Dietary insufficiency of long chain omega-3s in pregnancy and maternal depression

A pooled analysis of cross country data showed a negative association between the prevalence of postnatal depression and either seafood consumption or breastmilk DHA concentration (Hibbeln 2002). This led to further investigation of the association between long chain omega-3s intake during pregnancy and symptoms of postnatal depression using the data available from the Avon Longitudinal Study of Parents and Children (ALSPAC). This report, with data from approximately 14,000 women, suggests that a negligible intake of seafood at 32 weeks gestation was associated with a doubling in depressive symptoms in the perinatal period compared with a high to moderate intake seafood intake supplying at least 320mg of long chain omega-3s per day (Hibbeln et al 2003). These observations together with the association between omega-3 fatty acid deficiency and reduced brain serotonin in animal studies highlight the plausibility of the hypothesis that dietary DHA insufficiency may be associated with symptoms of postnatal depression, and clearly highlight the need for well designed randomised controlled trials to establish a cause and effect relationship between increased dietary intake of long chain omega-3s and reduced postnatal depression. Although two of the three available trials indicate that long chain omega-3s may ameliorate depressive symptoms in the perinatal period, all three trials suffer from methodological limitations (small numbers and/or open label design) that cannot exclude bias and random error (Llorente et al 2003, Freeman et al 2006, Freeman et al 2006). To the best of our knowledge at least two large scale trials are in progress that will report on the cause and effect relationship between long chain omega-3 intake in pregnancy and postnatal depression (Makrides, Australia and Ramakrishnan, Mexico).

Long Chain Omega-3s During Pregnancy and Neurodevelopmental Outcome of the Offspring

It is almost impossible to consider dietary intakes of long chain omega-3s during pregnancy without some consideration of childhood outcome. Indeed there has been renewed interest regarding the intake of long chain omega-3s, fish and seafood during pregnancy and the developmental outcome of children. Data from large cohort studies in the USA and the UK, in which dietary intake was measured in pregnancy and development of the offspring assessed, demonstrate that maternal fish intake during pregnancy was positively associated with developmental and behavioral outcomes. Interestingly the data from both cohorts indicate that there may be a threshold (minimum intake) to achieve the beneficial associations between fish intake in pregnancy and child development. For example in the cohort from the USA the developmental advantage was noted when fish intake in pregnancy was greater than 2 fish meals per week (Oken et al 2008), while in the cohort from the UK, seafood intake greater than 340g per week was associated with improved childhood cognition and behavior (Hibbeln et al 2007). These data add to the debate regarding the relative risks and benefits of fish and seafood intake during pregnancy especially with regard to neurotoxicity from methyl mercury. Hibbeln et al modeled their analyses to test the US Federal Government advisories for pregnant women to limit their intake of seafood to <340g per week (Hibbeln et al 2007). Oken et al specifically assessed maternal mercury levels and found that higher mercury concentrations in maternal red cells were independently adversely associated with developmental outcome. Inclusion of both fish and mercury in their statistical model strengthened the positive association between maternal fish intake and early childhood development as well as strengthening the negative associate between maternal mercury concentration and developmental outcome (Oken et al 2008). Collectively these data highlight an independence of fish and seafood intake from mercury. Interestingly, only 23% of the mothers who consumed fish more than twice per week were likely to have the highest concentrations of red cell mercury (Oken et al 2008) indicating that either these women ate fish low in mercury or that there were other sources of mercury exposure.

Fish and seafood are good dietary sources of long chain omega-3s as well as other nutrients that may impact on...
progress that should soon provide more
a number of trials internationally are in
cognitive development of the offspring,
omega-3s during pregnancy and the
increased dietary supply of long chain
cause and effect relationship of an
any robust conclusions regarding the
and hence increase the likelihood of
or selective loss can both interfere with
or selective loss from the fish oil
in childhood. Furthermore, most trials
studying global cognitive outcomes
and were thus underpowered for
all of the trials had methodological
limitations – all had small sample sizes
and hence it is not possible to draw
any robust conclusions regarding the
cause and effect relationship of an
increased dietary supply of long chain
omega-3s during pregnancy and the
cognitive development of the offspring,
a number of trials internationally are in
progress that should soon provide more
robust answers.

The need for conclusive evidence
Pregnant women are presented with
conflicting advice over fish intake, dietary
DHA intake and DHA supplement use.
There is variation in the DHA intake
recommended for pregnancy made by
learned societies. Most organizations
agree there is enough evidence to
encourage women to increase their DHA
take to meet the needs of pregnancy,
but the lack of high quality evidence has
prevented most societies from assigning
a specific recommended dietary intake
for DHA during pregnancy (Koletzko
et al 2007, European Food Safety Authority
& Allen 2008). Similarly, Australians
have adopted an Adequate Intake for
omega-3 fatty acids in pregnancy (115
mg/day) due to the paucity of evidence
to support a specific Recommended
Dietary Intake for DHA (NHMRC 2006).
Meanwhile the Royal Australian and New
Zealand College of Obstetricians and
Gynaecologists advise that pregnant
women avoid consuming nutritional
supplements containing omega-3 fatty
acids because of the absence of high
quality evidence (Royal Australian and
New Zealand College of Obstetricians
and Gynaecologists). There is an obvious
need for clarity in the advice presented
to pregnant women and this will only
come once high quality RCTs with long-
term follow up are available.

Acknowledgment
The information contained in this paper
is a synthesis of information reviewed
in the following three publications.
Makrides M, Gibson RA. Marine oil
supplements for pregnant women: good
for mum, good for baby? NeoReviews
2007;8:152-158
Makrides M. Outcomes for mothers
and their babies: do omega-3 long
chain polyunsaturated fatty acids and
seafoods make a difference? J Am Diet
Assoc 2008;108:1622-6
Makrides M. Is there a dietary
requirement for DHA in pregnancy?
Prostaglandins Leukotrienes EFA 2009
(in press)

References
Burdge GC, Calder PC. Conversion of alpha-
linolenic acid to longer-chain polyunsaturated
fatty acids in human adults. Reprod Nutr Dev
Denome J, Stark KD, Holub BJ. Directly
quantitated dietary omega-3 fatty acid
intakes of pregnant Canadian women are
lower than current dietary recommendations.
Department of Health & Ageing. Nutrient
reference values for Australia and New
Zealand including recommended dietary
Dunstan JA et al. Cognitive assessment at 2
1/2 years following fish oil supplementation
in pregnancy: a randomised controlled trial. Arch
European Food Safety Authority. Opinion of
the Scientific Panel on contaminants in the
food chain related to the safety assessment of
wild and farmed fish 2005.
Freeman MP, Hibbeln JR, Wisner KL,
Brumbach BH, Watchman M, Gelenberg
AJ. Randomised dose-ranging pilot trial of
omega-3 fatty acids for postpartum depression.
Freeman MP, Hibbeln JR, Wisner KL,
Watchman M, Gelenberg AJ. An Open
Trial of omega-3 fatty acids for depression
in pregnancy. Acta Neuropsychiatrica
Helland IB et al. Similar effects on infants of
omega-3 and n-6 fatty acids supplementation
to pregnant and lactating women. Pediatrics
Helland IB et al. Effect of supplementing
pregnant and lactating mothers with omega-3
very-long-chain fatty acids on children’s
IQ and body mass index at 7 years of age.
Helland IB et al. Maternal supplementation
with very-long-chain omega-3 fatty acids
during pregnancy and lactation augments
children’s IQ at 4 years of age. Pediatrics
2003;111:e39-e44.
Hibbeln JR. Seafood consumption, the DHA
content of mothers’ milk and prevalence
rates of postpartum depression: a cross-
national, ecological analysis. J Affect Disord
Hibbeln JR, Davis JM, Heron J, Evans J,
Wolke DH, Golding J. ALSPAC study
team. Low dietary omega-3s and increased
depression risk in 14,541 pregnancies.
Abstract [NR418] - American Psychiatric
Association 2003 Annual Meeting.


Intrauterine and postnatal growth requires a high supply of essential substrates that cannot be synthesized endogenously, which includes polyunsaturated fatty acids (PUFA) of both the omega-6 and omega-3 series (Koletzko, Cetin et al 2007, Koletzko et al 2008, Cetin & Koletzko 2008). The essential PUFA linoleic acid (18:2n-6, an omega-6 fatty acid) and alpha-linolenic acid (18:3n-3, an omega-3 fatty acid) are the precursors of long-chain polyunsaturated fatty acids (LC-PUFA) with 20 and more carbon atoms. LC-PUFA, in particular docosahexaenoic acid (DHA, omega-3) are rapidly deposited in brain and retina during early growth.

The supply of omega-3 LC-PUFA to pregnant women affects pregnancy outcomes. Meta-analyses of randomised controlled trials providing pregnant women with placebo or with oils providing either DHA or a combination of DHA and eicosapentaenoic acid showed a reduction of premature births <34 weeks by 31 % in the total population, and by 61 % in at risk pregnancies (Szajewska et al 2006, Horvath et al 2007, Makrides & Olsen 2006). This was associated with a slightly longer mean pregnancy duration and slightly larger infant size at birth. Of importance, no relevant adverse effects were found in RCTs providing to pregnant women up to 1 g DHA/day, 2.7 g omega-3 LC-PUFA/day or 5 g fish oil/day (Koletzko, Cetin et al 2007). This strong preventive effect on early premature birth is expected to have major benefits with respect to associated infant morbidity and mortality.

In addition to the effects on pregnancy outcome, perinatal DHA supply was also shown to affect infant development. In utero, the human fetus is supplied with preformed LC-PUFA by selective placental transfer that our group demonstrated in vivo with stable isotope studies (Koletzko, Larque et al 2007, Larque et al 2003). This preferential transfer is mediated by specific fatty acid transfer proteins that we detected in human placenta (Larque, Krauss-Etschmann et al 2006, Larque, Demmelmaier et al 2006). This materno-fetal LC-PUFA appears to secure fetal needs for tissue growth (Hanebutt et al 2008), Maternal DHA supply is reflected in DHA contents of infant cord blood at birth (Krauss-Etschmann et al 2007, Klingler et al 2003) and in human milk DHA levels (Koletzko et al 2001, Fidler et al 2000, Demmelmaier et al 2001). Since the infant’s ability to synthesize LC-PUFA is very limited (Demmelmaier et al 1995, Sztanyi et al 1999), the supply through plaenenta and human milk is important for DHA accretion in infant brain and other tissues, and for functional outcomes.

Several observational and controlled intervention studies indicate that the degree of DHA supply to pregnant and lactating women, and to infants, improves the child’s visual development, fine motor function, social skill scores, language discrimination, and verbal IQ up to school age. Results from studies in Arctic Inuit, with a very high habitual consumption of seafood, demonstrate a dose response relationship between DHA status at birth and later child development even at very high DHA intake levels (Jacobson et al 2008). Maternal DHA supply during pregnancy also modulates the infant’s immune response at birth, yielding a pattern compatible with lower allergy risk (Krauss-Etschmann et al 2008, Susaenthaler et al 2007). Recently, evidence based consensus recommendations on dietary fat supply for pregnant and lactating women were developed with support from the European Commission (Koletzko, Cetin et al 2007). These recommendations are supported by ESPGHAN as well as the Child Health Foundation, the Diabetic Pregnancy Study Group, the Early Nutrition Academy, the European Association of Perinatal Medicine, the European Society for Clinical Nutrition and Metabolism, the International Federation of Placenta Associations, the International Society for the Study of Fatty Acids and Lipids, and the World Association of Perinatal Medicine (Koletzko, Cetin et al 2007, Koletzko et al 2008). Based on a systematic
evaluation of the available evidence, it was concluded that pregnant and lactating women should aim to achieve an average DHA intake of at least 200 mg DHA/day, which can usually be reached by 1-2 meals of oily fish per week (e.g. herring, mackerel, salmon). Women who do not achieve this level of regular fish consumption should consider using DHA supplements.

Numerous studies in both preterm and term infants have evaluated the effect of DHA status on the developing visual system, and a positive correlation between visual development and dietary omega-3 fatty acid intake was demonstrated, and it has been concluded that a supply providing at least 0.2-0.3 % of fatty acids as DHA enhances infant visual acuity development (Koletzko et al 2008, European Food Safety Authority 2009). In the assessment of infant DHA status effects on infant development, a variety of tests of general developmental (e.g. Bayley Scales of Infant Development), psychomotor development (e.g. Brunet-Lezine test), and more specific evaluations such as problem solving and language development tests as well as measures of motor development have been used. Several but not all studies reported beneficial effects of a supply of preformed DHA to infants, in most of these studies along with a supply of arachidonic acid (AA), on infant development (Koletzko et al 2008). In addition, possible benefits of a preformed supply of DHA and AA to infants on development of immune phenotypes and on blood pressure regulation have been reported. Based on an assessment of the available information, an international expert group recently recommended and fully endorse breastfeeding, which supplies preformed LC-PUFA, as the preferred method of feeding for healthy infants (Koletzko et al 2008). When breastfeeding is not possible, the use of an infant formula providing DHA at levels between 0.2 and 0.5 weight percent of total fat, and with the minimum amount of AA equivalent to the contents of DHA was supported (Koletzko et al 2008). It was also concluded that dietary LC-PUFA supply should continue after the first six months of life, but that currently there is not sufficient information for quantitative recommendations beyond the first six months of life. Further research was encouraged to strengthen our understanding of the relationship between perinatal dietary lipid intake and health and developmental outcomes.

References


**Figure 7:** The capacity for DHA synthesis remains limited throughout the first year of life in infants born at term.

Plasma phospholipid DHA levels in infants with phenylketonuria not provided with preformed DHA (open circles) remain significantly lower throughout the first year of life than in infants randomised to an LC-PUFA supply. Modified from (Koletzko, Sauerwald et al. 2007).


Public Health Recommendations and Implications

Current guidelines for pregnancy/lactation and infant feeding

Wendy Morgan, innovations & solutions

The National Health and Medical Research Council (NHMRC) stated in 1992 that in pregnancy and early infancy adequate omega-3 fatty acids (omega-3s) are needed to provide DHA which is a major fatty acid in the phospholipids of cerebral tissue and the retina. They recommended that consideration be given to providing more omega-3s, some as DHA, to infant formulas based on cows’ milk (NHMRC, 1992).

Food Regulatory Developments

Since that time developments have included changes to the Food Standards Code so that omega-3s are specifically included in the standard for infant formula (FSANZ, 2009). Currently the fats in infant formula and follow-on formula must meet certain conditions including:

- have a ratio of linoleic acid to α-linolenic acid of no less than 5 to 1 and no more than 15 to 1; and

- if specified in column 1 of Table 4 below, must comply with the limits, if any, specified in columns 2 and 3 of the Table; and

- have a ratio of total long chain omega-6 fatty acids (C≥20) to total long chain omega-3s (C≥20) that is not less than 1 in an infant formula or follow-on formula which contains those fatty acids; and

- where long chain polyunsaturated fatty acids are present in an infant formula or follow-on formula, an EPA content of no more than the DHA content.

These requirements permit long chain omega-3s in infant formula up to 1% of total fatty acids. If EPA is present in equal quantities to DHA, the maximum DHA is then 0.5% of total fatty acids. There is no mandatory addition of long chain omega-3s to infant formula.

Infant formula products formulated for premature or low birth weight infants may be specifically formulated provided that in all other respects they comply with the Standard.

Nutrient Reference Values and their Basis

The Nutrient Reference Values for Australia and New Zealand (NRVs) (NHMRC 2006) provide guidance for pregnancy, lactation and infant feeding. However there is no specific recommendation for long chain omega-3 intake for infants up to 12 months (Table 5).

The Adequate Intakes (AIs) for young children are based on median intakes. The AIs for pregnant women are based on non-pregnant women’s AI plus 25% to take account of the increase in body weight. The AIs for breast feeding women are based on those for non-pregnant, non-lactating women plus that of the infant. As the infant AIs are for total omega-3s, ALA and long chain omega-3s were apportioned in the same ratio as in the maternal AI.

The Dietary Guidelines – Australia

Guidelines published in 2003 refers to the recommendation for 1.5 serves a day of meat, fish, poultry or alternatives in pregnancy and 2 serves during lactation (NHMRC(a) 2003). A serve of fish is described as 80–120g of cooked fish fillet. Whilst 2 – 3 serves per week of fish high in omega-3s are recommended, there is no specific reference to the needs of pregnant or lactating women for long chain omega-3s.

The benefits of breast feeding are described due to a number of factors including the presence of long chain omega-3s (NHMRC(b) 2003). Improved visual acuity and psychomotor development are linked to polyunsaturated fatty acids in human milk, particularly DHA.

Food and Nutrition Guidelines – New Zealand

Pregnant women are given mixed messages. Intake of fish as a source of long chain polyunsaturated fatty acids

| Table 4: Food Standards Code, Standard 2.9.1, Table to clause 2 |
|-------------------|-------------------|-------------------|
| Column 1          | Column 2          | Column 3          |
| **Fatty acids**   | Minimum % total fatty acids | Maximum % total fatty acids |
| **Essential fatty acids** | Linoleic acid (18:2) | 9 | 26 |
|                   | α-Linolenic acid (18:3) | 1.1 | 4 |
| **Long chain polyunsaturated fatty acids** | Long chain omega-6 series fatty acids (C≥20) | 2 |
|                   | Arachidonic acid (20:4) | 1 |
|                   | Long chain omega-3 series fatty acids (C≥20) | 1 |
| **Total trans fatty acids** | | |
|                   | | 4 |
| **Eruccic acid (22:1)** | | 4 |

From: (FSANZ 2009)
Table 5: NRVs for fatty acids for Australia and New Zealand

<table>
<thead>
<tr>
<th>Population group</th>
<th>Omega-3s</th>
<th>Omega-6s</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>α-linolenic acid (g/day)</td>
<td>LC omega-3s DHA/EPA/DPA (mg/day)</td>
</tr>
<tr>
<td></td>
<td>AI</td>
<td>UL</td>
</tr>
<tr>
<td>Pregnancy 14–18 y</td>
<td>1.0</td>
<td>NP</td>
</tr>
<tr>
<td>19–30 y</td>
<td>1.0</td>
<td>NP</td>
</tr>
<tr>
<td>31–50 y</td>
<td>1.0</td>
<td>NP</td>
</tr>
<tr>
<td>Lactation 14–18 y</td>
<td>1.2</td>
<td>NP</td>
</tr>
<tr>
<td>19–30 y</td>
<td>1.2</td>
<td>NP</td>
</tr>
<tr>
<td>31–50 y</td>
<td>1.2</td>
<td>NP</td>
</tr>
<tr>
<td>Infants 0–6 m</td>
<td>0.5*</td>
<td>BM</td>
</tr>
<tr>
<td>7–12 m</td>
<td>0.5*</td>
<td>BM</td>
</tr>
<tr>
<td>Children 1–3 y</td>
<td>0.5</td>
<td>NP</td>
</tr>
</tbody>
</table>

* Recommendation for total omega-3s

Abbreviations
AI – Adequate Intake, BM – amount normally received from breast milk, NP – not possible to set, UL – upper level of intake, - may be insufficient evidence or no clear level for adverse effects. From: NHMRC, 2006

is recommended but mercury and cadmium concerns are described in more length (Ministry of Health(a) 2008). Breast feeding women are advised to choose foods rich in polyunsaturated fat and omega-3 under the heading “Prepare foods low in fat (especially saturated fat), salt and sugar” (Ministry of Health(b) 2008).

The background paper to the guidelines for healthy infants and toddlers (Ministry of Health(c), 2008) describes the ability of ALA to be converted to long chain omega-3s in several sections. Whilst the benefits of DHA for visual function are mentioned, reference is also made to the lack of evidence for benefits for cognition, vision and growth. Recommendations for intake are based on the NRVs (NHMRC 2006). The corresponding consumer booklet makes no reference to omega-3s or sources (Ministry of Health(d) 2008).

Other Health Authorities
Many other authorities do not mention the importance of long chain omega-3s for pregnant and breast feeding women or provide advice on dietary or supplemental sources (for example: Queensland Health 2006, Children’s Hospital Westmead 2004, RACGP 2009, Department of Health & Ageing 2009, Dietitians Association of Australia 2008, The Royal Australian and New Zealand College of Obstetricians and Gynaecologists advise avoidance of supplements such as omega-3 fatty acids (2008).

Conflicting Messages about Omega-3s
Concerns regarding the mercury and contaminants’ content of fish have led organisations to communicate warning messages to the public and specifically to pregnant and lactating women (FSANZ 2004, NSW Food Authority 2008, Vic Health 2009, NSW Health 2006, Children’s, Youth & Women’s Health Service SA 2008 & 2009).

Whilst raising an important issue, communications must ensure that messages about long chain omega-3s are not conflicting or too complex, particularly during pregnancy and breast feeding when women may be more vulnerable to anxiety. Hibbeln (2007) suggests that advice to limit seafood consumption could actually be detrimental based on his studies.

Conclusions and Recommendations
Consumer nutritional advice to pregnant and lactating women and for infants takes little account of long chain omega-3s.

NRVs are required for DHA intake in infants and the actual amount of long chain omega-3s in pregnancy and during lactation required for optimal outcomes for mothers and their infants. More research may be required.

Nutrition policy advice from the Australian Commonwealth Department of Health should take account of the current science demonstrating the critical importance of long chain omega-3s in infant development before and after birth. This should then be reflected in recommendations and clear advice to the public. For example, the revised Dietary Guidelines should include practical advice on ensuring a desirable intake of long chain omega-3s, particularly DHA in pregnancy, during the period of lactation or formula feeding and in the continued diet of young children.

Greater priority should be given to long chain omega-3s in consumer publications from the NZ Ministry of Health to clearly state their roles and dietary sources. References to the conversion of ALA to EPA and DHA should be updated based on scientific evidence for minimal conversion.

Communications on the benefits and desirable intakes of long chain omega-3s should not be counteracted by warning messages regarding mercury and contaminants.
References


Children’s, Youth & Women’s Health Service SA. Eating well in pregnancy. 2009.

Children’s, Youth & Women’s Health Service SA. Fish for young children. 2008.


FSANZ. The Food Standards Code, Standard 2.9.1. 2009.


Scientific Consensus Workshop Omega-3 Fatty Acids for Maternal and Infant Health and Development - November 2009
Current and comprehensive intake data of both fish and total omega-3 fatty acid consumption of Australian women of childbearing age and young children (between the ages of 1 to 3 years) are limited. Methodologies used for estimating intakes will often vary in different surveys or studies ranging from general food frequencies (few questions on fish), more targeted food frequencies focusing on fish consumption (many questions on fish), food records (weighed/unweighed) and 24-hour recalls or records (single or multiple) and may or may not include specific questions relating to fish oil or omega-3 fatty acid supplement consumption. Whilst each of these methodologies has limitations, this paper has attempted to collate Australian-based intake data to provide indicative information on intakes. Estimates of intakes of omega-3s rely on representative compositional data for both fish and fish oil supplements which may not always be available. The most recent national survey of Australian adults was conducted in 1995 (McLennan W & Podger 1999) and of Australian children in 2007 (CSIRO & University of SA 2008).

### Intakes of Australian women of childbearing age

Whilst the 1995 National Nutrition Survey (1995NNS) is now over 14 years old, it still represents the most recent nationwide intake survey in Australia (McLennan W & Podger 1999).

#### Fish consumption

Estimates of fish intake from the 1995 NNS are presented for women aged 19 to 44 years to represent women of childbearing age (see Table 6). Based on these figures, women aged 19-44 years consumed approximately 1 serve of seafood per week in 1995. However, these values do not necessarily reflect intakes during pregnancy. Intakes for men are provided as a comparison. Approximately 17% of women of childbearing age consumed seafood on the day surveyed. When female consumers only were considered, the mean intake was 128g on the day of the survey and battered fish (takeaway) and fish fillets were eaten in the greatest amounts in women aged 19-29 years and 30-49 years respectively (FSANZ 2008).

#### Supplement consumption

No information was available in the 1995 NNS on the consumption of fish oil supplements.

#### Omega-3 fatty acid intakes

Estimates of intakes of omega-3 fatty acids in the 1995 NNS did not include omega-3 fatty acids from supplements. The median intake of total long chain omega-3s (DHA+EPA+DPA) averaged 90 mg/d for women, increasing to 430mg/d in the 90th percentile for all women (NHMRC 2006). The mean intakes of omega-3 fatty acids for all adult women are shown in Table 6 (Meyer et al 2003, Howe et al 2006). Seafood contributed 48% of total long chain omega-3 intake and was the major source of dietary DHA (70% of total DHA intake) and provided 50% of EPA and 15% of DPA. Meat, poultry, game products and dishes contributed 43% of total long chain omega-3s and provided 45%, 73% and 20% of total dietary intakes of EPA, DPA and DHA respectively.

For the average woman of childbearing age, intakes would appear to be well below the recommendations for pregnancy of around 200 mg/d of DHA.

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Lynne Cobiac, Flinders University

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**Table 6: Estimated mean daily intakes of fish in men and women aged 19-44 years and omega-3 fatty acid intakes in all adult women in the 1995 National Nutrition Survey, population weighted**

<table>
<thead>
<tr>
<th></th>
<th>Whole survey</th>
<th>Seafood consumers only</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean intake g/d</td>
<td>28</td>
<td>168</td>
</tr>
<tr>
<td>Fish &amp; Seafood Products &amp; Dishes</td>
<td>21.2</td>
<td>126</td>
</tr>
<tr>
<td>Percentage consuming</td>
<td>16.5%</td>
<td>-</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean intake g/d</td>
<td>28</td>
<td>168</td>
</tr>
<tr>
<td>Fish &amp; Seafood Products &amp; Dishes</td>
<td>21.2</td>
<td>126</td>
</tr>
<tr>
<td>Percentage consuming</td>
<td>17%</td>
<td>-</td>
</tr>
<tr>
<td>All adult women</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LC omega-3 fatty acids mg/d</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EPA</td>
<td>60</td>
<td>-</td>
</tr>
<tr>
<td>DPA</td>
<td>52</td>
<td>-</td>
</tr>
<tr>
<td>DHA</td>
<td>83</td>
<td>-</td>
</tr>
<tr>
<td>Total LC omega-3 fatty acids</td>
<td>195</td>
<td>-</td>
</tr>
</tbody>
</table>

n= 5585 for the 19-44 year age group; n=907 for consumers of fish and seafood products and dishes
Intakes of young Australian Children aged 1-3 years

The 2007 Australian National Children’s Nutrition and Physical Activity Survey (2007 Children’s Survey; 2007CS) collected intake data on 4,487 children aged 2-16 years across Australia, of which 1,071 were aged 2-3 years (CSIRO & University of SA 2008). Fish consumption (collected via 24-hour recall) and subsequent total long chain omega-3 fatty acids from dietary sources in children aged 2-3 years were very low across the total survey sample (Table 7).

As infant formula may be fortified with DHA, the mean intakes have also been included. There are limited data on intakes of children and infants aged 0-2 years although studies are currently underway.

Table 7: Estimated daily intakes of fish and omega-3 fatty acid intakes in children aged 2-3 years, 2007 Children’s Survey, population weighted

<table>
<thead>
<tr>
<th>Boys Mean intake</th>
<th>Whole survey</th>
<th>Consumers only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fish &amp; Seafood Products &amp; Dishes</td>
<td>10.6</td>
<td>73.3</td>
</tr>
<tr>
<td>Infant Formula &amp; Foods</td>
<td>10.2</td>
<td>158.0</td>
</tr>
<tr>
<td>Total LC omega-3 fatty acids (diet only)</td>
<td>98.9</td>
<td>389</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Girls Mean intake</th>
<th>Whole survey</th>
<th>Consumers only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fish &amp; Seafood Products &amp; Dishes</td>
<td>11.9</td>
<td>80</td>
</tr>
<tr>
<td>Infant Formula &amp; Foods</td>
<td>9.2</td>
<td>151</td>
</tr>
<tr>
<td>Total LC omega-3 fatty acids (diet only)</td>
<td>111.2</td>
<td>437</td>
</tr>
</tbody>
</table>

Fish consumption

Across all 2-3 year olds, the estimated mean intake of total long chain omega-3 fatty acids was 105 mg (99-111 mg) on the day surveyed, with a median of 42-47 mg/day. If we assume that approximately 30% of the total long chain omega-3s was DHA (Howe et al 2006), the estimated intake is 32 mg/day of DHA. Long chain omega-3 fatty acid intake was much higher in those young children who consumed fish (mean of 389-437 and median of 190-195 mg on the day of the survey). The intake of total long chain omega-3 fatty acids of the small number (n=37) of children taking oil supplements was 365-455 mg on the day of the survey.

Conclusion

Overall, 17% of women of childbearing age and 14-15% of children aged 2-3 years in Australia appeared to consume seafood on the day of the survey. Across the whole population, estimated intakes of both fish and total long chain omega-3 fatty acids are low – in part due to the low prevalence of consumers of fish and due to the low numbers of reported supplement users. When consumers of seafood only are considered, the estimated mean intakes of fish and other seafood were 126 g and 73-80 g on the day of the survey for women of childbearing age and for the 2-3 year olds respectively. Adult women consumed a mean of 195 mg/day of total long chain omega-3 fatty acids and 2-3 year old children consumed 105 mg/day from foods. Intakes on the day of the survey for total long chain omega-3 fatty acids were considerably higher than the population estimate. Children aged 2-3 years of age obtained only 1.3% and girls 1.6% of their estimated total energy intake per day from fish and seafood products and dishes. Other recent state based surveys did not include children <3 years of age (Glasson et al 2003, Abbott et al 2007, Booth et al 2006).
fatty acids were much higher in those children who consumed fish and fish oil supplements.

What else do we need?

Current data on usual intakes are needed on children <2 years of age, women during pregnancy and in young women contemplating becoming pregnant. Some of this much needed information for adult women should be provided with the proposed federally funded national adult survey but it is unknown if the intakes during pregnancy will be sufficiently captured in this survey.

A consensus is needed on actual requirements for individual fatty acids such as DHA for young children, during pregnancy and women wanting to become pregnant.

Finally, Australia needs to maintain an updated high quality food and supplement composition database.

References

FSANZ (2008) 22nd Total Diet Study FSANZ, Canberra
National Health and Medical Research Council (NHMRC) (2006). Nutrient Reference Values for Australia and New Zealand, AGPS, Canberra
Participant details

Professor Karen Simmer PhD, FRCPCH, FRACP
Professor of Newborn Medicine and Chair of the Academic Board, The University of Western Australia. Director of Neonatology, Princess Margaret Hospital and King Edward Memorial Hospital, Perth WA

Karen Simmer is Professor of Newborn Medicine and Chair of the Academic Board at the University of Western Australia. She is Director of the Neonatal Intensive Care Units at King Edward Hospital for Women and Princess Margaret Hospital for Children in Perth. She is Director of the Human Milk Bank in Western Australia which was recently awarded the Premier’s prize for outstanding contribution to the community of Western Australia. She has paediatric specialist qualifications from the Australasian and British Colleges and was awarded a PhD in perinatal nutrition from London University.

Prof Simmer is the Co-Lead of the WA Women’s and Newborns’ Network. She is Chair of the Nutrition Reference Group for the Royal Australasian College of Physicians. Her current research interests are in neonatal nutrition and infection. In 2009, she has been invited to lecture at scientific meetings in China, England, Japan and India. Prof Simmer is also a Board member of numerous research and educational institutions including Presbyterian Ladies College and Bonnie Babies Foundation.

Professor Robert A Gibson PhD FNSA
Senior NHMRC Research Fellow and Professor, Food Science and Nutrition, University of Adelaide.

Prof Gibson is a biochemist/nutritionist who has published over 200 peer reviewed papers in a variety of paediatric, nutrition and biochemical journals.

Prof Gibson has been actively involved in fatty acid research in cells, animals and humans for 30 years and has published numerous papers in this area. He has pioneered investigations into the functional role of early diet on visual and global development in term infants and was the first to demonstrate an effect of dietary LCPUFA on visual acuity in groups of otherwise healthy term infants. He has designed and conducted many randomised clinical trials involving nutrition interventions in the perinatal period. The trials were designed to test the effects of interventions with iron, selenium, probiotics, nucleotides and long chain polyunsaturated fatty acids (PUFA) on infant biochemistry, growth, physiology and developmental outcome. These findings have resulted in major changes in the fat composition of infant formulas world-wide. Recently, the results of DINO: a National DHA-dose response study on mental development in 650 preterm infants were published in JAMA. The results confirm the need for DHA in these infants but set new targets for the dose required for them to reach their full genetic potential.

Bob Gibson was awarded the Nutrition Society of Australia Research Medal in 2003 and made a Fellow of the Nutrition Society of Australia in 2004. When not analysing fats he can be found sampling the wide variety products available from the wineries of McLaren Vale where he lives.

Ms Nina D’Vaz BSc Honours, PhD Candidate
School of Paediatrics and Child Health, University of Western Australia

Originally from Denmark, Nina studied Biological Science at Copenhagen University and Murdoch University and completed a first class Honours (cand.Scient) degree in 2001 with a specialization in human immunology. In Denmark, her Honours project was carried out at The Department of Clinical Immunology, University Hospital of Copenhagen under supervision of Professors Torben Barington and Arne Sveigaard. This project involved the development of an assay for the investigation of polyreactivity in unmutated antibodies versus somatically mutated human antibodies.

After moving to Perth in 2001 and starting a family, in 2005 Nina undertook work as a research assistant at Ozgene and developed strong skills in genetic manipulation of mouse embryonic stem cells used to generate genetically modified mice for researchers and industry around the world.

In late 2007, after 2.5 years in the private sector, Nina enrolled in a PhD program under the supervision of Professor Susan Prescott at the University of Western Australia where she is currently investigating the effect of fish oil supplementation in infancy on the development of allergic disease.

Professor Maria Makrides PhD BND
Child Nutrition Research Centre, Women’s and Children’s Health Research Institute, North Adelaide

Maria Makrides is a NHMRC Senior Research Fellow and Deputy Director of the Women’s & Children’s Health Research Institute. She is also the Professor of Human Nutrition at the University of Adelaide. As a research dietitian, Maria is committed to improving the nutrition and health of mothers and their babies through the translation of high quality research. She has published widely and her work has been recognised nationally and internationally with a number of prestigious awards and appointments. She currently serves on the Board of Directors of the International Society for the Study of Fatty Acids and Lipids (ISSFAL) and is a member of the Nutrition Committee, Australian Academy of Science. Maria currently leads 4 national large-scale trials in the area of perinatal fatty acid nutrition funded by the NHMRC.

Professor Berthold Koletzko MD PhD [Dr med, Dr med habit]
Professor of Paediatrics, Dr. von Hauner Children’s Hospital, Univ. of Munich Medical Centre, Lindwurmstr

Berthold Koletzko is Professor of Paediatrics and Head of the Div. Metabolic Diseases and Nutritional Medicine at the Dr. Von Hauner Children’s Hospital, University of Munich, Germany. His research is on metabolism.
and nutrition in childhood, pregnancy & lactation, metabolic diseases, and clinical nutrition, with a particular focus on lipid and fatty acid metabolism. Bert has co-authored more than 650 publications and received numerous scientific awards and honors, including the 2009 Infant and Toddler Nutrition Research Award from the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN). He coordinates a number of research networks including the Early Nutrition Programming Project, he is the Chair of the Committee on Nutrition for the German Society for Paediatrics and is currently the Expert advisor to the Federal Minister of Families, Women and Health.

Ms Wendy Morgan BSc, Grad Dip Nutr & Diet, Grad Dip Com Mt, RNutr

Nutrition Advisor, The Omega-3 Centre; Director, innovations & solutions, Australia

Wendy Morgan is Director of innovations & solutions, a company which provides advice to research organisations, government departments and food companies. She is a Registered Nutritionist and was the inaugural Executive Director of The Omega-3 Centre. Her expertise is in assisting clients in the application of nutritional science and consumer understandings to new product development and consumer communications. Functional foods, food regulatory issues and nutrition policy are special areas of interest and raising the profile of Omega-3s is a passion.

Wendy has degrees in science, nutrition and communication management.

Professor Lynne Cobiac PhD, MBA (Adv), Post Grad Dip Nut Diet

Head, Department of Nutrition and Dietetics in the School of Medicine, Flinders University

Professor Cobiac is Associate Dean, Flinders Clinical and Molecular Medicine in the School of Medicine, Flinders University and is the Foundation Chair of Nutrition and Dietetics at Flinders University (2007 – now). Her current research interests include the development of a high Australian seafood diet suitable for women of childbearing age; nutrigenomics and colon cancer risk; dietary intake assessment; elderly and childhood nutrition. Prior to commencing at Flinders, Lynne held a senior position in Research, Business and Business Development Management in CSIRO. Professor Cobiac was the lead investigator responsible for collecting nutrition data in the Australian 2007 National Children’s Nutrition and Physical Activity and is currently undertaking analysis of these data for a range of food industry clients. She is currently also the lead investigator for the Department of Health and Ageing funded National Healthy Schools Canteen Project, and a chief investigator undertaking the development of the new Core Food Groups which will inform the development of the proposed new national food selection guide.

Professor Cobiac was invited to become a FSANZ fellow for 3 years commencing November 2007 and is a member of the FSANZ Food Composition Advisory Group.

Professor Andrew J Sinclair B Agric Sci, PhD

Scientific Advisor, The Omega-3 Centre; School of Exercise and Nutrition Sciences, Deakin University, Victoria, Australia

Andrew Sinclair is currently Professor of Human Nutrition and Director of the Metabolic Research Unit at Deakin University. He previously held the position of Professor of Food Science at RMIT University. He is a Fellow of the Australian Institute of Food Science & Technology and the Nutrition Society of Australia where he currently holds the position of President. He is also the President of ILSI Australasia and a Senior Associate Editor the journal Lipids and on the Editorial Board of Prostaglandins, Leukotrienes & Essential Fatty Acids.

His current research interests include food science (composition of food), nutrition (fatty acid metabolism in man and animals), functional foods (omega-3s, lycopene, olive oil, polyphenols, stearic acid), effect of omega-3s, meat-containing and vegetarian diets on cardiovascular health in humans, neuroscience (the role of omega-3s in brain and retina on neural function including blood pressure regulation, zinc transporters and Alzheimer’s disease in mammals). Professor Sinclair has more than 200 publications in peer-reviewed journals. He has consultancies with many of the major food companies on project by project bases over the past 15 years, providing expert advice to companies on issues relating to patent defence, functional foods, and nutrition. He has had significant interaction with agricultural organisations such as Dairy Australia, and Meat & Livestock Australia.

Dr Tony Helman MB, BS, D Obst.RCOG, MastMed, Grad D HumNutr, MRACGP

Managing Director, Arbor Communications

Dr Tony Helman is a physician-nutritionist, with graduate and post-graduate medical and nutrition qualifications from Australia and the US. His main focus is clinical nutrition education for health professionals. He was a senior medical educator with the Royal Australian College of General Practitioners for 10 years and is now the Editor-in-Chief of the electronic nutrition journal the Arbor Clinical Nutrition Updates.
About the Omega-3 Centre

The Omega-3 Centre Inc was established in 2006 and is dedicated to improving the health status of Australians and New Zealanders by:

• Effectively communicating the health benefits of omega-3s and where to find them
• De-mystifying omega-3s by translating the scientific evidence for these important nutrients
• Identifying barriers to optimal intakes of omega-3s and helping to address solutions
• Working with regulators and scientists to encourage a conducive environment for communications on omega-3s
• Differentiating between different types of omega-3s with a focus on the long chain omega-3s (EPA and DHA) which are of most potential benefit
• Facilitating and promoting research and development in this area
• Ensuring that sound science underpins all communications from the Centre

Full members of the Omega-3 Centre include:
Nu-Mega Ingredients | Ocean Nutrition Canada | DSM Nutritional Products Australia
BASF Human Nutrition | Nutricia Australia | Simplot Australia Pty Ltd
New Zealand King Salmon | Fisheries Research and Development Corporation (FRDC)
George Weston Foods | CSIRO Food Futures National Research Flagship
Meat and Livestock Australia (MLA)
The Omega-3 Centre appreciates the support from the following sponsors for the publication of the Report:

New research suggests that the health of Australian children is at risk from low intakes of long chain omega-3 fatty acids. A healthy balanced diet is particularly important during early childhood to support a toddler’s developing immune system and general health. When the diet is inadequate, a supplement may be considered.

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