

Potential benefits of fish for maternal, foetal and neonatal nutrition: a review of the literature

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he health of many poor populations is affected by deficiencies in essential n-3 fatty acids and amino acids, as well as minerals and vitamins. A particular focus of research is the potential impact of including essential fatty acids (EFAs) derived from fish in the diets of women of childbearing age. However, the evidence to justify such an intervention is conflicting. While some studies show fish or fish oil consumption significantly improving the outcome of pregnancy and infant development, other studies do not find any associations.

Lipids in nutrition

An adequate amount of dietary fat is essential for health. In adults, it is

recommended that at least 15 percent of energy intake is met by dietary fats. An adequate intake of dietary fat is particularly important prior to and during pregnancy and lactation, and it is recommended that women of childbearing age consume at least 20 percent of their energy intake in the form of fat. The consumption of EFAs is important for normal growth and development in infants, and breastmilk is a good source of both EFAs and their elongated and desaturated metabolites, as well as long-chain polyunsaturated fatty acids (LC-PUFAs) (FAO/WHO, 1994).

Essential fatty acids

EFAs are long carbon molecules that contain their first double bond at either the n-3 or the n-6 position. The parent fatty acids, linoleic acid (LA, 18:2, n-6) and alpha

Polyunsaturated fatty acids (PUFAs)

Common or trivial name	Abbreviation	Family
Linoleic acid	LA	18:2 n-6
Gamma linolenic acid	GLA	18:3 n-6
Alpha linolenic acid	ALA	18:3 n-3
Arachidonic acid	AA	20:4 n-6
Eicosapentaenoic acid	EPA	20:5 n-3
Docosahexaenoic acid	DHA	22:6 n-3

linolenic acid (ALA, 18:3, n-3) are present in vegetables and plants. These EFAs are metabolized by chain elongation and desaturation to LC-PUFAs containing 20 or more carbon atoms of the n-6 family, arachidonic acid (AA, 20:4, n-6) and n-3-family eicosapentaenoic acid (EPA, 20:5, n-3) or docosahexaenoic acid (DHA, 22:6, n-3). LC-PUFAs are also available directly from the diet. AA is found in plants, eggs or the dietary fats from grain-fed animals. EPA and DHA are found in the lipids from marine sources, where they are ten to 100 times more concentrated than in fats of terrestrial origin.

The recommended essential fatty acid balance (n-6/n-3) – the ratio of LA to ALA acid in the diet – should be between 5:1 and 10:1. The 1993 FAO/World Health Organization (WHO) Expert Consultation on Fats and Oils in Human Nutrition (FAO/WHO, 1994) recommended that individuals with a ratio in excess of 10:1 should be encouraged to consume, if possible, more n-3-rich foods such as green leafy vegetables, legumes, fish and other seafood.

DHA and foetal growth

EFAs, especially DHA, are among the materials required for foetal brain, central nervous system (CNS) and retinal growth in late pregnancy. The parent fatty acid, ALA, is used partly as a source of energy and partly as a precursor of metabolites, but the degree of conversion appears to be unreliable and restricted. More specifically, most human studies have shown that, whereas conversion

of high doses of ALA to EPA occurs, conversion to DHA is restricted. The use of labelled isotopic ALA has shown that, with a diet high in saturated fat, conversion to metabolites is 6 percent for EPA and 3.8 percent for DHA (Gerster, 1998).

Restricted conversion to DHA may be critical since there is increasing evidence that this metabolite has an autonomous function in the brain, retina and spermatozoa, where it is the most

prominent fatty acid. A diet rich in n-6 PUFA will reduce the conversion of ALA to EPA and DHA by 40 to 50 percent. In pre-term and low-birth-weight (LBW) babies, DHA deficiency has been associated with visual impairment and delayed cognitive development. Brain growth utilizes 70 percent of foetal energy, and 80 to 90 percent of cognitive function is determined before birth.

The interest in whether nutrition in early infancy, with emphasis on LC-PUFAs, affects subsequent neurodevelopment and function was renewed by studies of the LC-PUFA composition of the cerebral cortex grey matter in infants who had died from sudden infant death syndrome (SIDS) (Farquharson et al., 1992). The hypothesis was: "if there is an effect of nutrition, it seems likely that the EFAs and their metabolites, the major constituents of the brain structure, will be the most susceptible to dietary influence". The authors found that formula-fed babies had a significantly lower DHA content (7.6 percent) than agecomparable breastfed infants (9.7 percent).



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Maternal nutrition, foetal and neonatal growth and development

The most vulnerable period of neural development is during embryonic and foetal growth. Both retrospective and prospective studies provide evidence that maternal nutrition prior to conception is most important to the pregnancy outcome. Studies on nutrition in pregnancy illustrate its relationship to birth weight and head circumference (Crawford et al., 1993). The best correlation with the diet of the mother was found at or about the time of conception rather than later in the pregnancy. The nutrient intakes of mothers with LBW babies were well below those of mothers whose babies were in a less risky range.1 Nutrient intakes were positively correlated with birth weight until the weight reached 3.3 kg.

The mother's intake of fats is of special interest. The mother's fat store will be relevant to the maternal hormonal responses and to the nourishment of the embryo, and provides the basis for subsequent fat storage

Maternal depletion syndrome

The term "maternal depletion syndrome" has been used to describe the consequences of frequent childbearing under difficult living conditions. Short birth intervals are associated with increased child mortality in several populations, and maternal nutritional depletion has been postulated as a possible mechanism for this relationship. Not only infant mortality, but also LBW, growth retardation and increased morbidity have been associated with the effects of maternal nutritional depletion. Women in less developed countries experience repeated pregnancies followed by long periods of lactation. As much as 60 percent of their reproductive period is spent either pregnant or lactating. In the past, much attention was paid to the effects of this on pregnancy outcome and the infant's health. Only recently have the nutritional demands of mothers been included.

Dietary enhancement, or fortification of the diets of women of childbearing age (and their families), before and during pregnancy, rather than after the child is born, is more likely to lead to sustainable good health than any other policy.

accumulation is a placental function. However, if DHA is not available in the maternal diet, the placenta depletes the mother of DHA (Al et al., 1995), a situation that is exacerbated by multiple pregnancies (Zeijdner et al., 1997; Prentice et al., 1989).

The role of the placenta in controlling the supply of fatty acids to the foetus has been studied. It was shown that the the infants of control mothers (7.92 percent compared with 5.86 percent). DHA concentrations were 35.2 percent higher than in control infants in red blood cells and 45.5 percent higher in plasma. It is notable that the increase in DHA concentration in maternal red blood cells and plasma is higher than the difference between the infant groups. This is in line

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and utilization during pregnancy. The intake of fat is also the vehicle for dietary fat-soluble vitamins. The composition of fats in breastmilk, which is essential for early neonatal growth, brain development and retinal function, varies according to the mother's dietary fat intake, the length of gestation and the period of lactation.

Foetal supply of fatty acids

Deficiency of dietary n-3 PUFA has been associated with biochemical changes in the brain and with disturbances in vision and other neurological parameters. Under normal nutritional conditions, foetal brain DHA accumulation is substantial and a "DHA accretion spurt" is seen in the last period of gestation. This accumulation is supported by the maternal supply of DHA or ALA, but the selectivity of DHA

placental selectivity for ALA and DHA appears to be relatively unresponsive to changes in the mixture of fatty acids in the maternal circulation, but the selectivity for AA increases with a rise in maternal AA concentration (Haggarty et al., 1999). In a study by Connor, Lowensohn and Hatcher (1996), healthy pregnant women received supplements of n-3 fatty acids during the third trimester. The fatty supplementation consisted of sardines and additional fish oil that provided a total of 2.6 g of n-3 fatty acids per day. This included 1.01 g of DHA per day. The concentration of DHA in maternal red blood cells increased from 4.6 to 7.15 percent, and maternal plasma showed a similar change. Levels of DHA in blood differed greatly in infants whose mothers received n-3 supplements compared with with the results of Haggarty et al. (1999) in studies of placental selectivity for ALA and DHA.

Other mechanisms designed to ensure the optimal use of EFAs during the last trimester of pregnancy have been outlined by Green and Yavin (1998). As well as the foetal gastrointestinal tract, the foetal brain may also be instrumental in supplying DHA under certain conditions, thus contributing to the accumulation of its own DHA during one of the most crucial periods of its development. These results suggest that the maternal concentration of individual fatty acids, and hence the composition of the maternal diet, may have

¹WHO estimates that, worldwide, 17.4 percent of babies are born with LBW (i.e. weighing less than 2.5kg), which can have negative consequences for health and development (FAO/WHO, 1994).

large effects on LC-PUFA delivery to the foetus. Since concentrations of DHA and AA in foetal circulation increase around mid-term and at the end of gestation, babies who are born prematurely miss this DHA accretion spurt.

were given a supplement containing vitamins, minerals and halibut liver oil. Reductions were seen in the risk of delivering before 40 weeks of gestation (20.4 percent) and pre-eclampsia (31.5 percent). Later studies of vitamin and mineral fortification that a high n-3 fatty acid intake, derived from marine fat, would prolong pregnancy by shifting the balance of the prostaglandins production involved in parturition. Increases in the length of gestation (four days) and birth weight (107 g) were achieved without

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Pre-term and intrauterine growthretarded babies are born with deficits of LC-PUFAs (AA, DHA). Deficits of brain DHA have been found to impair visual and cognitive development in pre-term and LBW babies.

Fish oils, foetal growth and pregnancy complications

The renewed interest in EFA intake in relation to pregnancy stemmed from epidemiological observations of longer gestation, larger babies and, in some cases, reduced numbers of pregnancy complications in areas of high fish intake (Olsen and Joensen, 1985). The first controlled trial of fish oil supplementation in the diets of pregnant women was conducted as early as 1938-1939 in London (Olsen and Secher, 1990). Pregnant women

(in the same amounts) of the diets of pregnant women failed to show similar results. The evidence in support of using fish oil to supplement the diets of pregnant women at risk of pregnancy complications is conflicting. Studies aimed at demonstrating the impact of n-3 fatty acids on intrauterine growth restriction, pregnancy-induced hypertension, preeclampsia or pre-delivery have failed to demonstrate any effect (Salvig, Olsen and Secher, 1996; Bulstra-Ramakers, Huisjes and Visser, 1994; Onwude et al., 1994).

Olsen et al. (1995) conducted a controlled study of the relation between fish oil supplementation and pregnancy duration, birth weight and birth length. The high birth weights and the long duration of pregnancy in the Faroe Islands led the group to suggest

detrimental effects to the course of labour. In contrast to this, Olsen et al. (1995) could not detect any association between the length of gestation, birth weight and birth length and the intake of n-3 fatty acids in the second trimester of pregnancy, when intake was quantified by a validated questionnaire or biochemical measurements. As there is evidence to suggest that it is the mother's preconception diet or nutritional status that is most strongly associated with the outcome of the infant (Crawford et al., 1993; Beal, 1971), in future studies attention should be focused on the diets of women of childbearing age and, if necessary, the optimal timing of supplementation. Eating fish twice or three times a week can be encouraged as part of a healthy balanced diet (Wasantwisut, 1997) during pregnancy and for all the family.



Maternal diet and breastfeeding

Human milk is the best source of fat and dietary EFAs in infant feeding (Gartner and Stone, 1994). Maternal dietary intake significantly affects milk composition.

EFA requirements in neonates and infants

Research has shown that both pre-term and full-term infants can actively convert the EFAs LA and ALA to LC-PUFAs. However, the amounts of LC-PUFAs being produced, particularly DHA, may not be sufficient to meet the developmental requirements of the infant. Rapid synthesis of brain tissue, involving the formation of complex lipids, occurs during the last trimester of development of the human brain and the early postnatal weeks. Specific deficits in n-3 fatty acids influence neural integrity and, more selectively,

(1992a). This compromised the level of AA and was found to affect growth adversely. The concern that poor growth was linked to depressed AA status has lately been removed by using low-EPA marine oil with an EPA/DHA ratio of 1:10. This did not compromise weight gain and resulted in higher mental development scores (in pre-term babies) at 12 months (Carlson *et al.*, 1993b).

For pre-term and LBW infants, there is a consensus that if formula feeding is necessary the concentration of DHA and AA should be the same as in human breastmilk (0.2 to 0.8 percent DHA, and 0.3 to 1.1 percent AA) (Clandinin *et al.*, 1997) for optimal development of the neonate. It should, however, be kept in mind that the concentrations of DHA and AA in breastmilk vary according to the time since birth and the maternal diet.

differences have been questioned, particularly the methods used to assess cognitive function and development of infants (Clandinin, 1999). Other researchers (Innis et al., 1997; Scott et al., 1998; Auestad et al., 1997; Horby Jorgensen et al., 1998; Gibson, Neumann and Makrides, 1997; Gibson and Makrides, 1998) found no differences in visual acuity, visual function or growth that could be correlated with DHA or AA availability. Scott et al. (1998) even found significant negative correlation between DHA levels and vocabulary outcomes and Makrides et al. (1999) found no difference between formula groups for weight, length or head circumference, and concluded that dietary LC-PUFAs do not influence the growth of healthy term infants to a clinically significant degree. Lucas et al. (1999) also found no effect on long-term

In pre-term and low-birth-weight babies DHA deficiency has been associated with visual impairment and delayed cognitive development

affect learning and visual abilities (Galli and Socini, 1983; Wheeler, Benolken and Anderson, 1975; Lamptey and Walker, 1976 and 1978; Bourre *et al.*, 1989; Yamamoto *et al.*, 1987).

Controlled randomized trials with preterm infants have indicated how essential n-3 fatty acids are and the need to include DHA in pre-term infants' food (Birch et al., 1992b; Hoffman et al., 1993; Carlson et al., 1993b; Uauy et al., 1990). Deficiency in AA has been associated with low prenatal and post-natal growth in pre-term infants (Crawford et al., 1989; Leaf et al., 1992). AA, along with DHA, is generally considered to be an essential nutrient in early development, taking into account the balance between the n-3 and n-6 families, the special function of AA in neural and vascular function and the importance of its eicosanoids in cell regulation.

A marine oil supplement (EPA/DHA; 2:1) was used in a study by Carlson *et al.*

Recently, a number of controlled randomized studies have been initiated to test the effect of dietary LC-PUFA on neural outcomes in full-term infants. Attention has been focused on the effect of n-3 and n-6 LC-PUFAs on normal postnatal development, and the extent to which early dietary intake of preformed DHA and AA appears necessary for optimal development of the brain and eye of the human infant. These studies have largely involved a comparison of neural responses from infants fed standard infant formula (without LC-PUFAs) with infants receiving LC-PUFAs from either supplemented formula or breastmilk.

LC-PUFA (DHA, AA) supplementation after birth has been shown to improve vision and cognition (Carlson, Werkman and Tolley, 1996; Birch *et al.*, 1998; Willats *et al.*, 1998; Morley, 1998). It should, however, be noted that both the methods and the impact of the measured

cognitive or motor development following the addition of n-3 and n-6 LC-PUFAs to the formula of full-term infants during their first six months.

While some randomized studies of DHA supplementation of infant formula for full-term infants demonstrated that the visual function of formula-fed infants could be increased to breastfed levels by adding DHA to their formula, others failed to demonstrate an effect. Recommendations on the extent to which full-term babies benefit from LC-PUFA supplements (from well-nourished mothers on a "Western" diet) have been equivocal. The most frequent conclusions are either that additional research should be undertaken before these supplements are introduced into standard infant formulas or that full-term infants may benefit from LC-PUFA supplementation, and the effects persist beyond the period of supplementation.

Application in populations with maize-based diets

The staple food of people in many of the sub-Saharan African countries is maize. The nutritional value of maize is similar to that of other cereal grains, somewhat superior to wheat flour and only a little below rice. Up to 45 percent (aggregated figures) of the daily energy intake is obtained from maize products (mainly flour). Higher intakes (up to 66 percent) have been reported in the lower socio-economic groups. Deficiencies of EFAs, micronutrients and amino acids may be present among groups who rely on maize. While deficiencies in essential amino acids, vitamins, minerals and calories in maizebased diets have been widely studied, the unbalanced and deficient content of EFAs or, in other terms, deficiency of n-3 fatty acids has not attracted the same interest. A complete food consumption survey would be needed in order to understand the potential of supplementing the maize-based diet with EFAs from fish and with the consumption of n-3-rich foods, such as green leafy vegetables, legumes, fish and other seafood.



n-3 PUFA-rich foods such as green leafy vegetables, legumes, fish and other seafood.

In addition, populations consuming degermed maize (4 to 6 percent fat) will often suffer from a lack of dietary fat. In the last decade, according to WHO reports, there has been a dramatic deficiency of dietary fat intake (less than 10 percent of deficiencies of micronutrients, associated with reliance on maize are vitamins (A, B [thiamine, niacin, riboflavin, folate] and C) and minerals (calcium, zinc, iron, iodine and, to some extent, magnesium) (Rosado, Camacho-Solis and Bourges, 1999; Jukes, 1989; Wasantwisut, 1997; Contreras, Elias and Bressani, 1981; Soldenhoff and van der

Deficiencies of EFAs, micronutrients and amino acids may be present among groups who rely on maize

In populations that consume maize oil as their main source of dietary fat an unbalanced EFA status with a deficiency in n-3 fatty acids can develop. The recommended EFA balance (n-6/n-3 PUFAs) - the ratio of LA to ALA in the diet should be between 5:1 and 10:1 (FAO/ WHO, 1994), while maize oil, at best, represents an EFA balance of 80: 1; i.e. a severely unbalanced diet in terms of EFAs. This imbalance will be exaggerated, as a large amount of LA will restrict the conversion of ALA to elongated and desaturated metabolites. In a diet rich in n-6 PUFA, the conversion of ALA to n-3 PUFAs is reduced by 40 to 50 percent. The FAO/WHO expert consultation recommended that individuals with a ratio in excess of 10:1 should be encouraged, if possible, to consume more total caloric amounts) in the majority of developing countries, while the EFA requirements of normal-nourished women during pregnancy are evaluated at 6 percent of total caloric amounts. A mild deficiency in dietary EFA may be a limiting factor in foetal growth processes in humans, as has been shown in rats (Menon, Moore and Dhopeshwarkar, 1981).

Micronutrients

Micronutrient deficiency is widespread and affects the health status and function of populations with a maize-based diet. An intervention study might aim to supplement the maize diet with n-3 fatty acids and other nutrients known to be lacking in these diets. Common Westhuyzen, 1988; Garcia-Casal *et al.*, 1998; Layrisse *et al.*, 1996; Malfait *et al.*, 1993; Huddle, Gibson and Cullinan, 1998; Richter *et al.*, 1984; Fitzgerald *et al.*, 1993).

Defining the supplement formula for maize-based diets

Deficiency in essential n-3 fatty acids and amino acids, as well as in minerals and vitamins, will affect the health and function of many sub-Saharan populations with maize-based diets. In addition to correcting general deficiencies resulting from an unbalanced diet, supplementation may restore the nutrients that are lost during cereal processing to obtain flour or use new technologies in order to protect the nutrients during processing (Ojofeitimi and Abiose, 1996). Furthermore, a range of safety issues

for eliminating the risk of adverse effects on health, even at the highest level of food intake, have to be analysed. Finally, product-specific attributes, such as the reactivity of each supplemented compound and possible impacts on the stability of the supplement, as well as market availability and costs, have to be analysed.

Fish oils should have a high content of DHA, while EPA has been shown to have the potential to interfere with the growth of infants (Carlson et al., 1992a). High-quality oils are needed, in order to avoid the risk of generating free radicals or of accumulating pesticides, and antioxidants should be added. Other safety issues (Lucas, 1997), such as the impact of increased bleeding time (Uauy et al., 1993) and possible disturbances of the immune system (Carlson, Werkman and Tolley, 1996; Carlson et al., 1996) must be considered when applying supplements to the diets of malnourished women of childbearing age. These women and their infants might be more prone to infections and already be deficient in iron. Supplements in the diets of women of childbearing age should not contain high doses of vitamin A, since it is potentially teratogenic at intakes of more than 10 000 IU.

references

Al, M.D.M., Houwelingen, A.C., Kester, A.D.M., Hasaart, T.H.M., De-Jong, A.E.T. & Hornstra, G. 1995. Maternal EFA patterns during normal pregnancy and relationship to neonatal EFA status. British Journal of Nutrition, 74: 55-68.

Auestad, N., Montalto, M.B., Hall, R.T., Fitzgerald, K.M., Wheeler, R.E., Connor, W.E., Neuringer, M., Connor, S.L., Taylor, J.A. & Hartmann, E.E. 1997. Visual acuity, erythrocyte fatty acid composition, and growth in term infants fed formulas with long chain polyunsaturated fatty acids for one year. Ross Paediatric Lipid Study. Paediatric Research, 41(1): 1-10.

Beal, V.A. 1971. Nutritional studies during pregnancy. Journal of the American Dietary Association, 58: 1655-1659.

Birch, D.G., Birch, E.E., Hoffman, D.R. & Uauy, R.D. 1992a. Retinal development in very low-birth-weight infants fed diets differing in n-3 fatty acids. Invest. Ophthalmol. Vis. Sci., 33(8); 2365-2376.

Birch, E.E., Birch, D.G., Hoffman, D.R. & Uauy, R.D. 1992b. Dietary essential fatty acid supply and visual acuity development. Invest. Ophthalmol. Vis. Sci., 33(11): 3242-3253.

Birch, E.E., Hoffman, D.R., Uauy, R., Birch, D.G. & Prestidge, C. 1998. Visual acuity and the essentiality of docosahexaenoic acid and arachidonic acid in the diet of term infants. Paediatric Research, 44(2): 201-209

Bourre, J.M., Francois, M., Youyou, A., Dumont, O., Piciotti, M., Pascal, G. & Durand, G. 1989. The effects of dietary alpha-linolenic acid on the composition of nerve membranes, enzymatic activity, amplitude of electrophysiological parameters, resistance to poisons and performance of learning tasks in rats. Journal of Nutrition, 119(12): 1880-1892.

Bulstra-Ramakers, M.T.E.W., Huisjes, H.J. & Visser, G.H.A. 1994. The effects of 3g eicosapentaenoic acid daily on recurrence of interuterine growth retardation and pregnancy induced hypertension. British Journal of Obstetrics and Gynaecology, 102: 123-126.

Calder, P.C. 1997. n-3 polyunsaturated fatty acids and cytokine production in health and disease. Ann. Nutr. Metab., 41(4): 203-234.

Cantarelle, P. & Leridon, H. 1971. Breastfeeding, mortality in childhood and fertility in a rural zone of Senegal. Population Studies, 25: 505-533.

Carlson, S.E., Cooke, R.J., Werkman, S.H. & Tolley, E.A. 1992a. First year growth of preterm infants fed standard compared to marine oil n-3 supplemented formula. Lipids, 27(11): 901-907.

Carlson, S.E., Cooke, R.J., Rhodes, P.G., Peeples, J.M. & Werkman, S.H. 1992b. Effect of vegetable and marine oils in pre-term infant formulas on blood arachidonic and docosahexaenoic acids. Journal of Paediatrics, 120: \$159-167.

Carlson, S.E., Werkman, S.H., Peeples, J.M., Cooke, R.J. & Tolley, E.A. 1993a. Arachidonic acid status correlates with first year growth in pre-term infants. Proceedings of the National Academy of Science, United States, 1, 90(3): 1073-1077.

Carlson, S.E., Werkman, S.H., Rhodes, P.G. & Tolley, E.A. 1993b. Visual-acuity development in healthy pre-term infants: effect of marine-oil supplementation. American Journal of Clinical Nutrition, 58(1): 35-42.

Carlson, S.E., Werkman, S.H. & Tolley, E.A. 1996. Effect of long-chain n-3 fatty acid supplementation on visual acuity and growth of preterm infants with and without bronchopulmonary dysplasia. American Journal of Clinical Nutrition, 63: 687-697.

Carlson, S.E., Ford, A.J., Werkman, S.H., Peeples, J.M. & Koo, W.W. 1996. Visual acuity and fatty acid status of term infants fed human milk and formulas with and without docosahexaenoate and arachidonate from egg yolk lecithin. Paediatric Research, 39(5): 882-888.

Clandinin, M.T. 1999. Brain development and assessing the supply of polyunsaturated fatty acid. Lipids, 34(2): 131-137.

Clandinin, M.T., Van Aerde, J.E., Parrott, A., Field, C.J., Euler, A.R. & Lien, E.L. 1997. Assessment of the efficacious dose of arachidonic and docosahexaenoic acids in pre-term infant formulas: fatty acid composition of erythrocyte membrane lipids. Paediatric Research, 42(6): 819-825.

Connor, W.E., Lowensohn, R. & Hatcher, L. 1996. Increased docosahexaenoic acid levels in human newborn infants by administration of sardines and fish oil during pregnancy. Lipids, 31(Suppl.): S183-187.

Contreras, G., Elias, L.G. & Bressani, R. 1981. Effect of vitamin and mineral supplements on the protein utilization of mixtures of corn and beans. Arch. Latinoam. Nutr., 31(4): 808-826.

Crawford, M.A., Doyle, W., Drury, P., Lennon, A., Costeloe, K. & Leighfield, M. 1989. n-6 and n-3 fatty acids during early human development. Journal of Intern. Med. Suppl., 225(731),159-169.

Crawford, M.A., Doyle, W., Leaf, A., Leighfield, M., Ghebremeskel, K. & Phylactos, A. 1993. Nutrition and neurodevelopmental disorders. Nutrition and Health, 9(2): 81-97.

Desai, M. & Hales, C.N. 1997. Role of foetal and infant growth in programming metabolism in later life. Biological Review of the Cambridge Philosophical Society, 72(2): 329-348.

FAO. 1992. Maize in human nutrition. Food and Nutrition Series No. 25. Rome, Food Policy and Nutrition Division. 166 pp.

FAO/WHO. 1994. Fats and oils in human nutrition. Report of a Joint FAO/WHO Expert Consultation, 19 to 26 October 1993, Rome. 168 pp.

Farquharson, J., Cockburn, F., Patrick, W.A., Jamieson, E.C. & Logan, R.W. 1992. Infant cerebral cortex phospholipid fattyacid composition and diet. Lancet, 340: 810-813.

Farguharson, J., Jamieson, E.C., Abbasi, K.A., Patrick, W.J., Logan, R.W. & Cockburn, F. 1995. Effect of diet on the fatty acid composition of the major phospholipids of infant cerebral cortex. Arch. Dis. Child., 72(3): 198-203.

Fitzgerald, S.L., Gibson, R.S., Quan de Serrano, J., Portocarrero, L., Vasquez, A., de Zepeda, E., Lopez-Palacios, C.Y., Thompson, L.U., Stephen, A.M. & Solomons, N.W. 1993. Trace element intakes and dietary phytate/Zn and Ca x phytate/Zn millimolar ratios of periurban Guatemalan women during the third trimester of pregnancy. American Journal of Clinical Nutrition, 57(2): 195-201.

Galli, C. & Socini, A. 1983. Dietary lipids in pre- and postnatal development. In E.G. Perkins and W.J. Visek, eds. Dietary fats and health. Proceedings of American Oil Chemists Society Conference. Chicago, United States, 16: 278-301.

Garcia-Casal, M.N., Layrisse, M., Solano, L., Baron, M.A., Arguello, F., Llovera, D., Ramirez, J., Leets, I. & Tropper, E. 1998. Vitamin A and beta-carotene can improve non-heme iron absorption from rice, wheat and corn by humans. Journal of Nutrition, 128(3): 646-650.

Gartner, L.M. & Stone, C. 1994. Two thousand years of medical advice on breastfeeding: comparison of Chinese and western texts. Semin. Perinatol., 18(6): 532-536.

Gerster, H. 1998. Can adults adequately convert alpha-linolenic acid (18:3n-3) to eicosapentaenoic acid (20:5n-3) and docosahexaenoic acid (22:6n-3)? European Journal of Clinical *Nutrition*, 53, Suppl. 1: S66-77.

Gibson, R.A. & Makrides, M. 1998. The role of long chain polyunsaturated fatty acids (LCPUFA) in neonatal nutrition. Acta Paediatr., 87(10): 1017-1022.

Gibson, R.A., Neumann, M.A. & Makrides, M. 1997. Effect of increasing breastmilk docosahexaenoic acid on plasma and erythrocyte phospholipid fatty acids and neural indices of exclusively breastfed infants. European Journal of Clinical Nutrition, 51(9): 578-584.

Green, P. & Yavin, E. 1998. Mechanisms of docosahexaenoic acid accretion in the foetal brain. Journal of Neuroscientific Research, 52(2): 129-136.

Grimsgaard, S., Bonaa, K.H., Hansen, J.B. & Myhre, E.S. 1998 Effects of highly purified eicosapentaenoic acid and docosahexaenoic acid on hemodynamics in humans. American Journal of Clinical Nutrition, 68(1): 52-59.

Haggarty, P., Ashton, J., Joynson, M., Abramovich, D.R. & Page, K. 1999. Effect of maternal polyunsaturated fatty acid

references

concentration on transport by the human placenta. *Biol. Neonate*, 75(6): 350-359.

Hamosh, M. 1996. Breastfeeding: unraveling the mysteries of mother's milk. *Medscape Women's Health*, 1(9): 4.

Hoffman, D.R., Birch, E.E., Birch, D.G. & Uauy, R.D. 1993. Effects of supplementation with omega 3 long-chain polyunsaturated fatty acids on retinal and cortical development in premature infants. *American Journal of Clinical Nutrition*, 57(5 Suppl.): 807S-812S.

Horby Jorgensen, M., Holmer, G., Lund, P., Hernell, O. & Michaelsen, K.F. 1998. Effect of formula supplemented with docosahexaenoic acid and gamma-linolenic acid on fatty acid status and visual acuity in term infants. *Journal of Pediatric Gastroenterology and Nutrition*, 26(4): 412-421.

Huddle, J.M., Gibson, R.S. & Cullinan, T.R. 1998. Is zinc a limiting nutrient in the diets of rural pregnant Malawian women? *British Journal of Nutrition*, 79(3): 257-265.

Innis, S.M., Akrabawi, S.S., Diersen-Schade, D.A., Dobson, M.V. & Guy, D.G. 1997. Visual acuity and blood lipids in term infants fed human milk or formulae. *Lipids*, 32(1): 63-72.

Jukes, T.H. 1989. The prevention and conquest of scurvy, beri-beri and pellagra. *Preventive Medicine*, 18(6): 877-883.

Kromhout, D., Bosschieter, E.B. & de Lezenne Coulander, C. 1985. The inverse relation between fish consumption and 20-year mortality from coronary heart disease. *New England Journal of Medicine*, 312(19): 1205-1209.

Lamptey, M.S. & Walker, B.L. 1976. A possible essential role for dietary linolenic acid in the development of the young rat. *Journal of Nutrition*, 106(1): 86-93.

Lamptey, M.S. & Walker, B.L. 1978. Learning behavior and brain lipid composition in rats subjected to essential fatty acid deficiency during gestation, lactation and growth. *Journal of Nutrition*, 108(3): 358-367.

Layrisse, M., Chaves, J.F., Mendez-Castellano, Bosch, V., Tropper, E., Bastardo, B. & Gonzalez, E. 1996. Early response to the effect of iron fortification in the Venezuelan population. *American Journal of Clinical Nutrition*, 64(6): 903-907.

Leaf, A.A., Leighfield, M.J., Costeloe, K.L. & Crawford, M.A. 1992. Factors affecting long-chain polyunsaturated fatty acid composition of plasma choline phosphoglycerides in pre-term infants. *Journal of Pediatric Gastroenterology and Nutrition*, 14(3): 300-308.

Lucas, A. 1997. Long chain polyunsaturated fatty acids, infant feeding and cognitive development. *In J. Dobbing, ed. Developing brain and behaviour.* London, Academic Press. p. 3-41.

Lucas, A., Stafford, M., Morley, R., Abbott, R., Stephenson, T., MacFadyen, U., Elias-Jones, A. & Clements, H. 1999 Efficacy and safety of long-chain polyunsaturated fatty acid supplementation of infant-formula milk: a randomised trial. *Lancet*, 354: 1948-1954.

Makrides, M., Neumann, M.A., Simmer, K. & Gibson, R.A. 1999. Dietary long-chain polyunsaturated fatty acids do not influence growth of term infants: a randomized clinical trial. *Pediatrics*, 104(3, 1): 468-475.

Malfait, P., Moren, A., Dillon, J.C., Brodel, A., Begkoyian, G., Etchegorry, M.G., Malenga, G. & Hakewill, P. 1993. An outbreak of pellagra related to changes in dietary niacin among Mozambican refugees in Malawi. *International Journal of Epidemiology*, 22(3): 504-511.

Martorell, R. & Merchant, K. 1992. Nutrition and population links: breastfeeding, family planning and child health. Reproductive stress and women's nutrition. *Papers from the ACC/SCN 18th Session Symposium*, May 1992. Nutrition policy paper (UN/ACC) No.11, p. 23-32. New York, UN/ACC.

Mathews, F., Yudkin, P. & Neil, A. 1999. Influence of maternal nutrition on outcome of pregnancy: prospective cohort study. *British Medical Journal*, 319: 339-343.

Menon, N.K., Moore, C. & Dhopeshwarkar, G.A. 1981. Effect of essential fatty acid deficiency on maternal, placental, and fetal rat tissues. *Journal of Nutrition*, 111(9): 1602-1610.

Menotti, A., Kromhout, D., Blackburn, H., Fidanza, F., Buzina, R. & Nissinen, A. 1999. Food intake patterns and 25-year mortality from coronary heart disease: cross-cultural correlations in the Seven Countries Study. The Seven Countries Study Research Group. *European Journal of Epidemiology*, 15(6): 507-515.

Morley, R. 1998. Nutrition and cognitive development. *Nutrition*, 14(10): 752-754.

Ojofeitimi, E.O. & Abiose, S. 1996. Prevention of nutrient loss during preparation of the most popular weaning diet in Nigeria: practical considerations. *Nutrition and Health*, 11(2): 127-132.

Olsen, S.F. & Joensen, H.D. 1985. High live-born birth-weights in the Faroes: comparison between birth-weights in the Faroes and in Denmark. *Journal of Epidemiology and Community Health*, 39: 27-32.

Olsen, S.F. & Secher, N.J. 1990. A possible preventive effect of low-dose fish oil on early delivery and pre-eclampsia: indications

from a 50-year-old controlled trial. British Journal of Nutrition, 64(3): 599-609.

Olsen, S.F., Sorensen, J.D., Secher, N.J., Hedegaard, M., Henriksen, T.B., Hansen, H.S. & Grant, A. 1992. Randomised controlled trial of effect of fish-oil supplementation on pregnancy duration. Lancet, 339: 1003-1007.

Olsen, S.F., Hansen, H.S., Secher, N.J., Jensen, B. & Sandstrom, B. 1995. Gestational length, and birth weight in relation to intake of marine n-3 fatty acids. British Journal of Nutrition, 73: 397-404.

Onwude, J.L., Lilford, R.J., Hjartardottir, H., Staines, A. & Tuffnel, D.A. 1994. A randomised double blind placebo controlled trial of fish oil supplementation in high risk pregnancy. British Journal of Obstetrics and Gynaecology, 102: 95-100.

Østerud, B., Elvevoll, E.O., Barstad, H., Brox, J., Halvorsen, H., Lia, K., Olsen, J.O., Olsen, R.L., Sissener, C., Rekdal, Ø. & Vognild, E. 1995. Effect of marine oils supplementation on coagulation and cellular activation in whole blood. Lipids, 30(12): 1111-1118.

Prentice, A., Landing, M.A.J., Drury, P.J., Dewit, O. & Crawford, M.A. 1989. Breastmilk fatty acids of rural Gambian mothers: effects of diet and maternal parity. Journal of Pediatric Gastroenterology and Nutrition, 8: 486-490.

Richter, M.J., Langenhoven, M.L., Du Plessis, J.P., Ferreira, J.J., Swanepoel, A.S. & Jordaan, P.C. 1984. Nutritional value of diets of blacks in Ciskei. South African Medical Journal, 65(9): 338-345.

Rosado, J.L., Camacho-Solis, R. & Bourges, H. 1999. Addition of vitamins and minerals to corn and wheat flour in Mexico. Salud Publica Mex., 41(2): 130-137. (in Spanish)

Salvig, J.D., Olsen, S.F. & Secher, N.J. 1996. Effects of fish oil in late pregnancy on blood pressure: a randomized trial. British Journal of Obstetrics and Gynaecology, 103: 529-523.

Sammon, A.M. 1999. Dietary linoleic acid, immune inhibition and disease. Postgraduate Medical Journal, 75: 129-132.

Scott, D.T., Janowsky, J.S., Carroll, R.E., Taylor, J.A., Auestad, N. & Montalto, M.B. 1998. Formula supplementation with long-chain polyunsaturated fatty acids, are there developmental benefits? Pediatrics, 102(5): E59.

Soldenhoff, M. & van der Westhuyzen, J. 1988. Niacin status of schoolchildren in Transvaal Province, South Africa. International Journal of Vitamins and Nutritional Research, 58(2): 208-212.

Thurnham, D.I. & Northrop-Clewes, C.A. 1999. Optimal nutrition: vitamin A and the carotenoids. Proceedings of the Nutrition Society, 58(2): 449-457.

Uauy, R.D., Birch, D.G., Birch, E.E., Tyson, J.E. & Hoffman, D.R. 1990. Effect of dietary omega-3 fatty acids on retinal function of very low-birth-weight neonates. Pediatric Research, 28(5): 485-492.

Uauy, R.D., Birch, D.G., Birch, E.E., Hoffman, D.R. & Tyson, J.E. 1993. Visual and brain developments in infants as a function of essential fatty acid supply provided by the early diet. In Lipids, learning and the brain: fats in infant formulas. Report of the 103rd Ross Conference on Pediatric Research, p. 215-230.

Wasantwisut, E. 1997. Nutrition and development: other micronutrients' effect on growth and cognition. Southeast Asian Journal of Tropical Medicine and Public Health, 28(Suppl. 2): 78-82.

Wheeler, T.G., Benolken, R.M. & Anderson, R.E. 1975. Visual membranes: specificity of fatty acid precursors for the electrical response to illumination. Science, 188(4195): 1312-1314.

Willats, P., Forsyth, J.S., Di Modugno, M.K., Varma, S. & Colvin, M. 1998. Effect of long chain polyunsaturated fatty acids in infant formula on problem solving at 10 months of age. Lancet, 352: 688-691.

Yamamoto, N., Saitoh, M., Moriuchi, A., Nomura, M. & Okuyama, H. 1987. Effect of dietary alpha-linolenate/linoleate balance on brain lipid composition and learning ability of rats. Journal of Lipid Research, 28(2): 144-151.

Zeijdner, E.E., Houwellingen, A.C., Kester, A.D.M. & Hornstra, G. 1997. Essential fatty acid status in plasma phospholipids of mother and neonate after multiple pregnancy. Prostaglandins, Leuk, EFAs, 56: 395-401.

Potential benefits of fish for maternal, foetal and neonatal nutrition: a review of the literature

The health of many poor populations is affected by deficiencies in essential n-3 fatty acids and amino acids, as well as minerals and vitamins. A focus of research is the potential impact of including essential fatty acids (EFAs) derived from fish in the diets of women of childbearing age. An adequate amount of dietary fat is essential for health, and is particularly important prior to and during pregnancy and lactation. The consumption of EFAs is important for normal growth and development in infants. The most vulnerable period of neural development is during embryonic and foetal growth. A concept of dietary enhancement or fortification of the diets of women of childbearing age (and their families) before and during pregnancy, rather than after the child is born, is more likely to lead to sustainable good health than any other policy. However, the evidence to justify such an intervention is conflicting. The authors of this article provide an extensive review of the current scientific literature and identify the need for further applied research, especially in Africa

The staple food of people in many African countries is maize. While deficiencies in essential amino acids, vitamins, minerals and calories in maize-based diets have been widely studied, their unbalanced and deficient EFA content has not attracted the same interest. Food consumption studies are needed in order to understand the potential of supplementing maize-based diet with EFAs from fish and of consuming n-3-rich foods, such as green leafy vegetables, legumes, fish and other seafood. An intervention study might aim to supplement the maize diet with n-3 fatty acids and other nutrients known to be lacking in these diets, such as vitamins (A, B [thiamine, niacin, riboflavin, folate] and C) and minerals (calcium, zinc, iron, iodine and, to some extent, magnesium). In addition to correcting deficiencies resulting from an unbalanced diet, other objectives of supplementation may be to restore the nutrients that are lost during cereal processing to obtain flour or to use new technologies in order to protect the nutrients during processing. A range of safety issues to eliminate the risk of adverse effects on health have to be analysed. Finally, product-specific attributes, such as the reactivity of each supplemented compound and its possible impact on stability, as well as market availability and costs, have to be analysed.

Avantages potentiels du poisson pour la nutrition maternelle, fœtale et néonatale: examen de la littérature à ce sujet

La santé de nombreuses populations démunies est affectée par des carences en acides gras n-3 essentiels et en acides aminés, ainsi qu'en minéraux et en vitamines. Des travaux de recherche visent à évaluer l'impact potentiel de l'inclusion d'acides gras essentiels (AGE) dérivés du poisson dans le régime alimentaire des femmes en âge de procréer. Une quantité suffisante de graisses alimentaires est indispensable à la santé, notamment avant et pendant la grossesse et l'allaitement au sein. La consommation d'AGE est indispensable à une croissance normale et au développement des nourrissons. La phase la plus vulnérable du développement neuronal est celle de la croissance de l'embryon et du fœtus. Le concept d'un renforcement du régime alimentaire des femmes en âge de procréer (et des membres de leur famille) avant et pendant la grossesse, plutôt qu'après la naissance de l'enfant, est sans doute préférable à toute autre politique pour garantir la santé à long terme des populations concernées. Toutefois, les preuves invoquées pour justifier une telle intervention sont parfois contradictoires. Les auteurs passent en revue la littérature scientifique actuellement disponible et identifient les besoins en ce qui concerne la poursuite de la recherche appliquée en Afrique.

L'aliment de base de nombreux pays d'Afrique est le maïs. Si les carences en acides aminés essentiels, en vitamines, en minéraux et en calories des régimes alimentaires à base de maïs ont été largement étudiées, les carences et déséquilibres en AGE n'ont pas suscité le même intérêt. Des études sur la consommation alimentaire sont nécessaires pour comprendre les possibilités offertes par l'ingestion d'un supplément d'AGE de poisson dans le cadre d'un régime à base de maïs et la consommation d'aliments riches en n-3, tels que

les légumes à feuilles vertes, les légumineuses, le poisson et d'autres produits de la mer. Une étude en vue d'une intervention éventuelle pourrait viser à compléter le régime à base de maïs par des acides gras n-3 et d'autres nutriments dont ces régimes manquent, tels que des vitamines (A, B [thiamine, niacine, riboflavine, folate] et C) et des minéraux (calcium, zinc, fer et iode et, dans une certaine mesure, magnésium). Outre la correction des carences résultant d'un régime alimentaire déséquilibré, la supplémentation pourrait aussi viser à restituer les nutriments perdus au cours de la transformation des céréales en farine; une autre solution consisterait à utiliser de nouvelles technologies pour protéger les nutriments au cours de la transformation. Il convient d'analyser un large éventail de questions liées à la sécurité afin d'éliminer le risque d'effets négatifs sur la santé. Enfin, les attributs spécifiques des produits, tels que la réactivité de chaque substance ajoutée et son impact éventuel sur la stabilité du supplément, ainsi que la disponibilité et les coûts sur le marché, doivent être analysés.

Posibles ventajas del pescado para la nutrición materna, fetal y neonatal: examen bibliográfico

Las carencias de aminoácidos y ácidos grasos esenciales n-3, así como de minerales y vitaminas, afectan a la salud de muchas personas pobres. Esta investigación se centra en los posibles efectos de la inclusión de ácidos grasos esenciales derivados del pescado en la alimentación de mujeres en edad de procrear. Una cantidad suficiente de grasa alimentaria resulta fundamental para la salud. Es especialmente importante antes del embarazo y la lactancia y en el curso de ellos. El consumo de ácidos grasos esenciales es importante para el crecimiento y desarrollo normales de los lactantes. El período más vulnerable del desarrollo neuronal es el del crecimiento embriónico y fetal. La mejora o fortalecimiento de la alimentación de las mujeres en edad de procrear (y de sus familias) antes del embarazo y en el curso de éste, y no después de que haya nacido el niño, ya que tiene más probabilidades que cualquier otra medida de traducirse en un estado de salud satisfactorio y duradero. Sin embargo, los datos indicados para justificar una intervención de esta índole son contradictorios. Los autores hacen un amplio examen de la bibliografía científica actual y señalan la necesidad de seguir realizando investigaciones aplicadas en África.

El alimento básico de la población de muchos países africanos es el maíz. Mientras que las carencias de aminoácidos esenciales, vitaminas, minerales y calorías en regímenes alimenticios basados en el maíz han sido objeto de amplios estudios, el contenido no equilibrado e insuficiente de ácidos grasos esenciales no ha recibido la misma atención. Hacen falta estudios sobre el consumo de alimentos para comprender las posibilidades de complementar un régimen alimenticio basado en el maíz con ácidos grasos esenciales derivados del pescado y el consumo de alimentos ricos en n-3, como hortalizas de hoja verde, leguminosas, pescado y otros alimentos marinos. Podría realizarse un estudio sobre intervenciones encaminadas a complementar la alimentación basada en el maíz con ácidos grasos n-3 y otros nutrientes cuya carencia es conocida en esos regímenes alimenticios, por ejemplo vitaminas A, B (tiamina, niacina, riboflavina, folato) y C y minerales (calcio, zinc, hierro y yodo y, en cierta medida, magnesio). Además de corregir las carencias derivadas de un régimen alimenticio no equilibrado, otros objetivos de la alimentación suplementaria podrían ser el restablecimiento de los nutrientes que se pierden durante la elaboración de los cereales para obtener harina o la utilización de nuevas tecnologías con el fin de proteger los nutrientes durante la elaboración. Es necesario analizar una serie de cuestiones relacionadas con la inocuidad para eliminar el riesgo de efectos perjudiciales sobre la salud. Por último, han de estudiarse los atributos específicos de los productos, como la reactividad de cada compuesto y sus posibles efectos sobre la estabilidad del suplemento, así como la disponibilidad en el mercado y los costos.