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Short review

Dietary omega-3 fatty acids for women

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Abstract

This review details the specific needs of women for omega-3 fatty acids, including alpha linoleic acid (ALA) and the very long chain fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Omega-3 fatty acid (dietary or in capsules) ensures that a woman's adipose tissue contains a reserve of these fatty acids for the developing fetus and the breast-fed newborn infant. This ensures the optimal cerebral and cognitive development of the infant. The presence of large quantities of EPA and DHA in the diet slightly lengthens pregnancy, and improves its quality. Human milk contains both ALA and DHA, unlike that of other mammals. Conditions such as diabetes can alter the fatty acid profile of mother's milk, while certain diets, like those of vegetarians, vegans, or even macrobiotic diets, can have the same effect, if they do not include seafood.

ALA, DHA and EPA, are important for preventing ischemic cardiovascular disease in women of all ages. Omega-3 fatty acids can help to prevent the development of certain cancers, particularly those of the breast and colon, and possibly of the uterus and the skin, and are likely to reduce the risk of *postpartum* depression, manic-depressive psychosis, dementias (Alzheimer's disease and others), hypertension, toxemia, diabetes and, to a certain extend, age-related macular degeneration. Omega-3 fatty acids could play a positive role in the prevention of menstrual syndrome and postmenopausal hot flushes.

The normal western diet contains little ALA (less than 50% of the RDA). The only adequate sources are rapeseed oil (canola), walnuts and so-called ''omega-3'' eggs (similar to wild-type or Cretan eggs). The amounts of EPA and DHA in the diet vary greatly from person to person. The only good sources are fish and seafood, together with ''omega-3'' eggs.

Keywords: Omega-3 fatty acids; Polyunsaturated fatty acids; Woman; Pregnancy; Lactation; Cancer; Infant; ALA; DHA

1. Introduction

The two fatty acids, the fundamental member of the omega-6 family, linoleic (LA, 18:2(n-6)) and alpha-linolenic acid (ALA, 18:3(n-3)) are physiologically essential and complementary, but they compete as substrates for desaturases. Not only is the intake of ALA far too low, but also its conversion to longer chain fatty acids is reduced because it has to compete with the larger quantities of LA for the same enzymes. Indeed, polyunsaturated fatty acids are dramatically involved in human health and pathologies [1], the ratio omega-6/omega-3 being important [2]. Interestingly, dietary omega-3 fatty acids content is largely below the recommended quantities.

Holman [3] was the first to describe a young girl with neurological signs due to a lack of ALA who was successfully treated with oral ALA; this was later confirmed by treating another girl [4] aged 7 with linseed and cod liver oils. It has been known for several years that a lack of dietary omega-3 fatty acids is offset in tissues by an increase in their contents of omega-6 fatty acids, particularly 22: 5 omega-6.

2. Methods

Systematic review of all pertinent original publication, not all of which are included in MedLine.

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3. The length of pregnancy

3.1. Eating fish

Women living in the Faroe Islands consume more fish oil than those living in Denmark, and their babies (weighing 141 g more) are born after a pregnancy that is 5.7 days longer [5]. Eating a diet of eggs that provides 133 mg DHA during the third trimester lengthens pregnancy by 6 days [6]; this increases the amount of omega-3 fatty acids in the plasma phospholipids of both the mother and the baby without resulting in an uncomfortably longer pregnancy. A diet containing fatty fish also reduces hypertension in pregnant Eskimo women [7], and may well prevent preeclampsia [8], perhaps because it competes with the ARA derivatives that are involved in this disorder. Some studies indicate that vegetarians are more prone to premature births, and that Caesarean sections are more likely. The average pregnancy is 5.6 days shorter [9], while the birth weights are slightly lower.

3.2. Fish oils

A dietary supplement of fish oil that has a high DHA content but little EPA is good for increasing the DHA in tissue, but may be bad for omega-6 fatty acids [10]. However, a daily intake of 500–1000 mg of a DHA/EPA mixture (enriched milk or capsules) increases the omega-3 fatty acid status of the fetus [11]. A pregnant mother taking an oral supplement of 200 mg DHA per day has increased plasma DHA, which is good for fetus development [12]. The concentrations of DHA and ARA in the maternal blood and cord blood are correlated; the concentrations of omega-3 fatty acids in the fetal blood are greater than in the maternal blood. Little is presently known of the role of the placenta, whether it has specific transfer systems or whether it can produce DHA from ALA.

4. Providing for the fetus

There are several lines of experimental evidence showing that omega-3 fatty acids are most important as structural elements in the developing nervous systems of the fetus and newborn, and that this is linked to the mother' food. The initial experimental studies were on the differentiation and function of brain cells in primary culture [13] and on membranes of brain cells and organelles [14]. ALA is the first dietary component that experiments in a range of disciplines, including chemistry, physical chemistry, biochemistry, enzymology, toxicology, physiology, electrophysiology, vision and behaviour have shown to influence brain structure and function [15]. This led to the demonstration that adding omega-3 fatty acids to baby formula, to make it more like mother's milk, influences the visual, cerebral and intellectual capacities of newborn babies, as assessed by the neural and intellectual development quotients and neuromotor activity. The pregnant woman and her fetus each has specific requirements. The fetus uses most of the portion of dietary omega-3 fatty acids supplied to it for its developing brain. The brain also has the highest lipid concentration of all tissues, except adipose tissue.

4.1. ALA

The importance of dietary ALA for the development and function of the retina and brain has been clear since 1997. There is a direct relationship between the dietary intake of ALA and its concentration, and that of its derivative DHA, in the tissues of both mother and fetus.

4.2. DHA

The concentration of DHA in the plasma phospholipids and erythrocytes of the mother begins to increase very early in pregnancy, regardless of the diet. This increase is the result of an early change in the maternal metabolism to supply the needs of the rapidly proliferating cells, particularly those of the brain of the fetus [16]. A dietary supplement of DHA increases the maternal DHA and limits the decrease during the last trimester in which there is a preferential transfer from the mother to the fetus [17]. The overall DHA status decreases during pregnancy [18], and this could be severe in a multiple pregnancy [19].

5. Adipose tissue and lactation

The fatty acids in milk are derived directly from the diet or indirectly from a body pool [20], particularly adipose tissue, depending on the nature of the dietary fatty acids [21]. The amounts of DHA and ARA in the brain and the liver exceed the dietary intake and thus require the use of this reserve [22]. There is also a correlation between certain fatty acids in adipose tissue and those in the milk of lactating women [23]. Ingesting fish oil increases the DHA and EPA contents of adipose tissue [24].

6. Composition of human milk

Several studies have shown the importance of breast-feeding, and some have emphasized the provision of polyunsaturated fatty acids, especially omega-3 fatty acids. The cerebral and overall DHA status of breast-fed babies is better than that of infants fed formula lacking DHA [25]. Human milk contains considerable concentrations of both DHA and ALA and these concentrations are not greatly influenced by the metabolism of the mammary glands. Instead, they depend on the blood plasma concentrations, which in turn are linked to the dietary intake. This is well illustrated by the link between the consumption of fatty fish and fish oil capsules and the DHA in the milk [26,27]. Eating eggs enriched in omega-3 fatty acids also increases the amounts of ALA and DHA in mother's milk [28]. A diet containing linseed oil, which has a high ALA content, increases the ALA and EPA in the milk and erythrocytes of lactating women, but not DHA [29]; this is in contrast with situation in experimental

animals, suggesting that the limiting step of desaturase activity varies from one species to another.

6.1. Disorders

Some disorders, such as diabetes, alter the composition of mother's milk; ALA accounts for only 0.87% of total fatty acids in the milk of diabetics, much lower than the normal figure of 2.3%, while DHA accounts for only 0.11%, compared to 0.3% in the milk of normal women [30].

6.2. Special diets

Although the diets of vegans and vegetarians contain reasonable amounts of ALA, it is unlikely that enough is converted to DHA to satisfy the needs of pregnancy and lactation, particularly as these diets contain large amounts of competing omega-6 fatty acids. The milk of vegetarians, defined as those whose diet includes eggs and milk, contains more ALA (that is found in plants), while the quantities of DHA are either normal [31] or low, with 2.6 times less DHA and 2.7 times more ALA [32]. The amount of DHA is usually reduced [33]. The tissues of their offspring have above normal concentrations of LA and ARA, but subnormal DHA [34]. While the ALA (and LA) concentrations in the milk of women on a macrobiotic diet are generally higher, they should try to consume at least one serving of fatty fish per week [35]. Thus dietary fish or any seafood, or supplements, are advisable, and prudent for pregnant *and* lactating women: the mental performance of children born to mothers who take cod liver oil during these periods is above normal when measured at the age of 4 years [36].

7. The special requirements of neurosensory organs

7.1. Vision

DHA is important for the retina (the highest DHA contents of all body tissues), the brain, photoreceptors, neurotransmission, rhodopsin activity, the development of rods and cones neuronal connections and the maturation of cerebral structures [37,38]. As a result omega-3 fatty acids may well be important for preventing age-related macular degeneration, and perhaps certain retinopathies [39]. There is no doubt that supplements of omega-3 fatty acids, generally taken as fish oil, improve infant visual acuity [40].

7.2. Hearing

A lack of omega-3 fatty acids damages hearing, particularly the cerebral response; it also leads to premature aging of the auditory nervous system [41]. The DHA content of the milk of a lactating rat modulates the auditory system of her pups [42]. The evoked auditory potentials of human babies fed formula supplemented with long chain polyunsaturated fatty acids or mother's milk for the first 16 weeks of life develop particularly rapidly [43]. Consequently, omega-3 fatty acids are important dietary components for preserving hearing throughout life.

8. Diabetes

Children given cod liver oil during the first year of life seem less likely to develop type I diabetes, perhaps because of the anti-inflammatory action of very long chain omega-3 fatty acids [44]. In addition, omega-3 fatty acids may be beneficial for diabetic women during pregnancy, helping to prevent their children developing long-term metabolic abnormalities linked to macrosomia [45]. These are some debates as to how effective omega-3 fatty acids are at preventing the development of type 2 diabetes insulin resistance and obesity [46]. There could be a link between obesity, BMI (body mass index), and the tissue concentrations of ARA in children rather than with omega-3 fatty acids [47]. Experiments have shown that omega-3 fatty acids influence body weight and glucose metabolism [48].

9. Breast and colorectal cancers

9.1. Breast cancer

Nutritional factors are one of the preventable causes of 20–60% of breast cancers, depending on the geographic region [49]. Ecological studies have found a negative correlation between the risk of developing breast cancer and fish consumption [50,51]; this has been confirmed by measurements of fish consumption [52]. A Chinese prospective study found that eating fish reduces the risk, but other studies are not in agreement. Most studies have found no effect of EPA, but a link between DHA and reduced risk. One case–control study found that the risk was 70% lower when there was a high concentration of DHA in the mammary gland adipose tissue [53]. Another cohort study showed that the highest concentrations of DHA in erythrocytes were linked to a 52% reduction in the risk of developing breast cancer [54]. Excess omega-6 fatty acids seems to increase the risk of breast cancer metastasis, while omega-3 fatty acids have the opposite action. Thus the omega-3/omega-6 fatty acid ratio is of prime importance [49]. A case–control study of non-menopausal women found that the risk of developing breast cancer was 50% lower in those women with the lowest omega-6/omega-3 ratio than in the group with the highest ratio [55]. ALA may also have a positive effect. One case–control study in three [56] and one of two cohorts [57] found that the risk of breast cancer was 30% lower in women taking ALA. And this can be as high as 60% in women with high concentrations of omega-3 fatty acids in their mammary adipose tissue [58]. However, there should always be a good intake of antioxidants to restrict the peroxidation of fatty acids [58], as these peroxide derivatives are genotoxic and cytotoxic. A cohort study on postmenopausal women showed a lower incidence of breast cancer in those with a high intake of vitamin C and beta-carotene. But this was true only for women with a high intake of polyunsaturated fatty acid [59].

9.2. Colorectal cancer

Not taking into account genetic predisposition to this cancer, it is estimated that 90% of the risk is due to environmental factors, principally foodstuffs [49]. Epidemiology has implicated dietary fat in mortality associated with colorectal neoplasia [60]. Several studies have shown that those people who eat most fish are at the lowest risk of colon cancer [61]; this has been confirmed in several case–control studies [62,63]. People who ate 80 g or more fish per day had a 40% less chance of developing colorectal cancer than did those who ate less than 10 g per day [64]. The action of DHA in preventing colon cancer is at least partly due to the prevention of inflammation and neoplasia. Whatever the cause of the cancer, and high intakes of saturated fats increase the risk, the omega-6/omega-3 fatty acid ratio is an important parameter; a ratio of 1–2 seems to help to prevent this cancer [49]. The effective intake of EPA + DHA is estimated to be about 2.5 g per day, or 1.4–4.2 g of EPA and 1.2–3.6 g per day of DHA [65,66].

9.3. Other cancers

Australian studies have shown a negative correlation between the intake of polyunsaturated fatty acids and the skin cancer, melanoma. Omega-3 fatty acids may well be important for controlling other types of cancer [65], such as that of the uterus. Women whose diet includes two portions of fish per week have a 40% lower risk of contracting this cancer than those eating only 0.2 portions per week [67]. But these studies are too fragmentary and contradictory to be definitive.

10. Inflammatory diseases

Omega-3 fatty acids if adequately preserved from oxidation [68,69], are involved in atherosclerosis, chronic hepatitis, inflammatory bowel diseases, psoriasis, and rheumatoid arthritis [70], unfortunately, specific action has not been studied in women so far.

11. Psychiatric disorders

The influence of omega-3 fatty acids on psychiatric disorder was reviewed recently [71]. There is a negative correlation between the risk of depression and the DHA concentration in adipose tissue [72]. An epidemiological study covering 23 countries showed that the risk of *postpartum* depression was inversely proportional to fish consumption and the DHA in the mother's milk [73], thus pregnant women are invariably likely to benefit from a prophylactic treatment based on DHA and EPA [74]. At least seven epidemiological studies have found a relationship between the depression and the consumption of fatty fish, a major dietary source of omega-3 fatty acids.

Eating fish could also reduce the risk of attempted suicide [75]. Comparisons of data from several countries show that consuming over 65 g of seafood per day reduces the frequency of bipolar disorder (manic-depressive patients), but seems to have no effect on schizophrenia [76]. Five studies have shown that eating fish reduces the risk of dementia, particularly Alzheimer's disease. Increasing the daily intake of DHA from 30 mg to 100 mg (over one portion per week) lowers the risk by 60%; the ALA in fish is also involved, but not the EPA [77]. The risk is reduced by about 40% in France [78].

12. Cardiovascular disease

12.1. ALA

The Cretan diet showed the importance of ALA for protecting against cardiovascular disease. The "Lyon" study on patients of both sexes found only five non-mortal infarcts and three deaths in those patients taking ALA supplements, while there were 17 infarcts and 16 deaths in controls [79].

12.2. Fish consumption

Epidemiological studies in many countries have examined the influence of dietary fish on all sorts of populations, including women, although the proportions of men and women are frequently not given. The importance of including fish in the diet for cardiovascular protection has been well documented over many years and is beyond dispute. This is true for people of all ages and both sexes, but particularly for women [80]. The "Nurses health study" showed that eating fish five times a week reduced the risk of death from cardiovascular disease by 50%; even those eating fish only 1–3 times a month had a 20% better chance of survival [81]. The fish intake was more effective for diabetic women; the high consumption reduced the risk by 60% and the low consumption by 30%. The effect was also seen in young women, even in those who were overweight [82]. Those women taking part in this study who consumed most omega-3 fatty acids had the lowest concentrations of markers of inflammation and endothelial cell activation [83]. A prospective study [84] has shown that women are also protected after the menopause, including older women [85]. A meta-analysis showed that omega-3 fatty acids are the most effective plasma–lipid lowering agents at preventing death from cardiovascular disease [86]. A diet that includes as little as 30 g per day of fish can protect a man or woman against the development of cardiovascular disease [87]. Any increase of as little as 20 g fish per day will reduce the risk of a person who eats little fish dying from cardiovascular disease by 7% [88]. A study on patients of average age 45 years, 70% of whom were women, was used to define an "omega-3 index" as an indicator of cardiovascular risk as the EPA + DHA concentration in erythrocytes [89].

12.3. Fish oils

Hundreds of publications describing studies on animals and humans (mainly on men) have shown how effective omega-3 fatty acids from fish oil are at preventing ischemic cardiovascular disease and cerebral infarcts. One major effect is to reduce mortality by 20%, deaths due to cardiovascular accident by 30% and sudden deaths by 50% [90]. Omega-3 fatty

acids act mainly by reducing the concentration of plasma triglycerides. This is particularly important for women, especially those on oral contraceptives. A combination of proposals [91] can be summarized as follows: at least 450 mg per day EPA + DHA for prevention by those not suffering from cardiovascular disease and 1 g per day for those having detected cardiovascular disease, with higher doses for people who have had a cardiovascular accident.

12.4. Metabolism of omega-3 fatty acids in women: desaturases

The DHA in all organs, including the nervous system and the heart, comes directly from the diet or is produced by transformation of dietary ALA in the liver; through the actions of desaturases. There is some doubt about whether an optimum dietary intake of ALA can adequately cover the needs of the human body for DHA. This probably becomes critical if the ALA intake is insufficient, in combination with amounts of the competing LA. A study using stable isotopes showed that newborn babies can convert ALA to DHA, but only in small quantities [92]. And these capacities vary with age and physiological conditions; conversion is more active in young women than in men or older people and is changed in lactating women. As a result, it has also been proposed that DHA is an essential nutrient [93].

13. The reality of a lack of dietary omega-3 fatty acids

13.1. ALA

The diets of women, both pregnant and women of childbearing age, provide less than 50% of the RDA [94–96]. The findings for women in Canada [97] and for pregnant women in Hungary [98], in Sweden [99] and in the United States [77,100] are similar. A lack of dietary ALA probably leads to reduced DHA synthesis.

13.2. DHA

In Canada 90% of the women had less than the recommended intake [101]; the situation was similar in Australia, and in Hungary [98]. It has been estimated that French women obtain an average of twice the RDA from their diet [95]; but these intakes vary widely: the lowest intake found in the French cohort was 6.5 mg per day, while the highest was 1770 mg per day, which is about the same as that of Eskimos [102]. The present generation of Eskimos consumes less than their parents, who were the subject of surveys for disorders such as cardiovascular disease. In contrast, the subjects of the French Brittany study (people encouraged to eat no animal lipids) consumed about half the RDA [97]. The intake of women varies widely between individuals and regions and countries. Those with the lowest intake should be identified and encouraged to eat fish and seafood [103]. Wild fatty fish contain good amounts of DHA and ALA, as do fish farmed under suitable conditions [103].

14. Conclusions

Omega-3 fatty acids may be beneficial in situations other than those described above. They are frequently said to help to prevent menstrual syndromes, particularly dysmenorrhea. They are believed to do this by reducing the production of eicosanoid pro-inflammatory molecules derived from omega-6 fatty acids by competing with their common metabolic enzymes. This is also why other problems, such as menopausal hot flushes, are less frequent in Japanese women who eat large amounts of fish. Bone formation and mineralization also seems to benefit from a high omega-3/omega-6 fatty acid ratio, which could reduce the risk of osteoporosis. All these proposals are not as well as documented as the other topics covered here.

The dietary lack of ALA is readily overcome. The only rich foods are rapeseed (canola) and walnut oils (soybean oil has an imbalance of omega-3 and omega-6 fatty acids) and so-called "omega-3" eggs (Columbus® or Benefic®). Vegetables that contain over 50% rapeseed oil are most useful, as are some rare vegetable foods rich in ALA [103].

Only seafood provides adequate EPA and DHA. Even fish with the lowest DHA content has 20 times more than red meat, i.e. pork from pigs fed linseed. There is practically no toxicological risk from eating too much omega-3 fatty acid, as this would require an intake far above that provided by a normal diet, 50–100 times more than the present occidental intake. But there is always a risk of undesirable effects, such as bleeding due to impaired coagulation and platelet aggregation if they are combined with certain drugs. Women therefore have specific requirements for omega-3 fatty acids that should be recognized and fulfilled, either by the diet or with capsules.

References

[1] Tapiero H, Ba GN, Couvreur P, Tew KD. Polyunsaturated fatty acids (PUFA) and eicosanoids in human health and pathologies. Biomed Pharmacother 2002;56:215.
[2] Simopoulos AP. The importance of the ratio of omega-6/omega-3 essential fatty acids. Biomed Pharmacother 2002;56:365.
[3] Holman RT. Control of polyunsaturated acids in tissue lipids. J Am Coll Nutr 1986;5:183.
[4] Bjerve KS, Thoresen L, Borsting S. Linseed and cod liver oil induce rapid growth in a 7-year-old girl with N-3-fatty acid deficiency. J Parenter Enteral Nutr 1988;12:521.
[5] Olsen SF, Hansen HS, Sommer S, Jensen B, Sorensen TI, Secher NJ, et al. Gestational age in relation to marine n-3 fatty acids in maternal erythrocytes: a study of women in the Faroe Islands and Denmark. Am J Obstet Gynecol 1991;64:1203.
[6] Smuts CM, Huang M, Mundy D, Plasse T, Major S, Carlson SE. A randomized trial of docosahexaenoic acid supplementation during the third trimester of pregnancy. Obstet Gynecol 2003;101:469.
[7] Gerrard J, Popeski D, Ebbeling L, Brown P, Hornstra G. Dietary omega 3 fatty acids and gestational hypertension in the Inuit. Arctic Med Res 1991;(Suppl):763.
[8] D'Almeida A, Carter JP, Anatol A, Prost C. Effects of a combination of evening primrose oil (gamma linolenic acid) and fish oil (eicosapentaenoic + docahexaenoic acid) versus magnesium, and versus placebo in preventing pre-eclampsia. Women Health 1992;19:117.

[9] Reddy S, Sanders TA, Obeid O. The influence of maternal vegetarian diet on essential fatty acid status of the newborn. Eur J Clin Nutr 1994;48:358.
[10] Lapillonne A, Brossard N, Claris O, Reygrobellet B, Salle BL. Erythrocyte fatty acid composition in term infants fed human milk or a formula enriched with a low eicosapentanoic acid fish oil for 4 months. Eur J Pediatr 2000;159:49.
[11] Velzing-Aarts FV, van der Klis FR, van der Dijs FP, van Beusekom CM, Landman H, Capello JJ, et al. Effect of three low-dose fish oil supplements, administered during pregnancy, on neonatal long-chain polyunsaturated fatty acid status at birth. Prostaglandins Leukot Essent Fatty Acids 2001;65:51.
[12] Sanjurjo P, Ruiz-Sanz JI, Jimeno P, Aldamiz-Echevarria L, Aquino L, Matorras R, et al. Supplementation with docosahexaenoic acid in the last trimester of pregnancy: maternal–fetal biochemical findings. J Perinat Med 2004;32:132.
[13] Bourre JM, Faivre A, Dumont O, Nouvelot A, Loudes C, Puymirat J, et al. Effect of polyunsaturated fatty acids on fetal mouse brain cells in culture in a chemically defined medium. J Neurochem 1983;41: 1234.
[14] Bourre JM, Pascal G, Masson M, Dumont O, Durand G, Picioti M. Alterations in the fatty acid composition of rat brain cells (neurons, astrocytes and oligodendrocytes) and of subcellular fractions (myelin and synaptosomes) induced by a diet devoided of (n-3) fatty acids. J Neurochem 1984;43:342.
[15] Bourre JM, François M, Youyou A, Dumont O, Piciotti M, Pascal G, et al. 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 task in rat. J Nutr 1880;1989:119.
[16] Otto SJ, van Houwelingen AC, Badart-Smook A, Hornstra G. Changes in the maternal essential fatty acid profile during early pregnancy and the relation of the profile to diet. Am J Clin Nutr 2001; 73:302.
[17] Montgomery C, Speake BK, Cameron A, Sattar N, Weaver LT. Maternal docosahexaenoic acid supplementation and fetal accretion. Br J Nutr 2003;90:135.
[18] Al MD, van Houwelingen AC, Kester AD, Hasaart TH, de Jong AE, Hornstra G. Maternal essential fatty acid patterns during normal pregnancy and their relationship to the neonatal essential fatty acid status. Br J Nutr 1995;74:55.
[19] Zeijdner EE, van Houwelingen AC, Kester AD, Hornstra G. Essential fatty acid status in plasma phospholipids of mother and neonate after multiple pregnancy. Prostaglandins Leukot Essent Fatty Acids 1997; 56:395.
[20] Martin JC, Bougnoux P, Fignon A, Theret V, Antoine JM, Lamisse F, et al. Dependence of human milk essential fatty acids on adipose stores during lactation. Am J Clin Nutr 1993;58:653.
[21] Baylin A, Kabagambe EK, Siles X, Campos H. Adipose tissue biomarkers of fatty acid intake. Am J Clin Nutr 2002;76:750.
[22] Hamosh M, Henderson TR, Kemper MA, Orr NM, Gil A, Hamosh P. Long-chain polyunsaturated fatty acids (LC-PUFA) during early development: contribution of milk LC-PUFA to accretion rates varies among organs. Adv Exp Med Biol 2001;501:397.
[23] Martin JC, Niyongabo T, Moreau L, Antoine JM, Lanson M, Berger C, et al. Essential fatty acid composition of human colostrum triglycerides: its relationship with adipose tissue composition. Am J Clin Nutr 1991;54:829.
[24] Leaf DA, Connor WE, Barstad L, Sexton G. Incorporation of dietary n-3 fatty acids into the fatty acids of human adipose tissue and plasma lipid classes. Am J Clin Nutr 1995;62:68.
[25] Cunnane SC, Francescutti V, Brenna JT, Crawford MA. Breast-fed infants achieve a higher rate of brain and whole body docosahexaenoate accumulation than formula-fed infants not consuming dietary docosahexaenoate. Lipids 2000;35:105.
[26] Lauritzen L, Jorgensen MH, Hansen HS, Michaelsen KF. Fluctuations in human milk long-chain PUFA levels in relation to dietary fish intake. Lipids 2002;37:237.
[27] Henderson RA, Jensen RG, Lammi-Keefe CJ, Ferris AM, Dardick KR. Effect of fish oil on the fatty acid composition of human milk and maternal and infant erythrocytes. Lipids 1992;27:863.
[28] Cherian G, Sim JS. Changes in the breast milk fatty acids and plasma lipids of nursing mothers following consumption of n-3 polyunsaturated fatty acid enriched eggs. Nutrition 1996;12:8.
[29] Francois CA, Connor SL, Bolewicz LC, Connor WE. Supplementing lactating women with flaxseed oil does not increase docosahexaenoic acid in their milk. Am J Clin Nutr 2003;77:226.
[30] Hamosh M, Bitman J. Human milk in disease: lipid composition. Lipids 1992;27:848.
[31] Specker BL, Wey HE, Miller D. Differences in fatty acid composition of human milk in vegetarian and nonvegetarian women: long-term effect of diet. J Pediatr Gastroenterol Nutr 1987;6:764.
[32] Sanders TA, Reddy S. The influence of a vegetarian diet on the fatty acid composition of human milk and the essential fatty acid status of the infant. J Pediatr 1992;120:S71.
[33] Strucinska M. Vegetarian diets of breastfeeding women in the light of dietary recommendations. Rocz Panstw Zakl Hig 2002;53:65.
[34] Sanders TA, Ellis FR, Dickerson JW. Studies of vegans: the fatty acid composition of plasma choline phosphoglycerides, erythrocytes, adipose tissue, and breast milk, and some indicators of susceptibility to ischemic heart disease in vegans and omnivore controls. Am J Clin Nutr 1978;31:805.
[35] Dagnelie PC, van Staveren WA. Macrobiotic nutrition and child health: results of a population-based, mixed-longitudinal cohort study in The Netherlands. Am J Clin Nutr 1994;59:1187S.
[36] Helland IB, Smith L, Saarem K, Saugstad OD, Drevon CA. Maternal supplementation with very-long-chain n-3 fatty acids during pregnancy and lactation augments children's IQ at 4 years of age. Pediatrics 2003;111:e39.
[37] Neuringer M. Infant vision and retinal function in studies of dietary long-chain polyunsaturated fatty acids: methods, results, and implications. Am J Clin Nutr 2000;71:256S.
[38] Agostoni C, Giovannini M. Cognitive and visual development: influence of differences in breast and formula fed infants. Nutr Health 2001;15:183.
[39] Desmettre T, Lecerf JM, Souied EH. Nutrition and age-related macular degeneration. J Fr Ophtalmol 2004;27:3S38.
[40] Carlson SE, Werkman SH, Rhodes PG, Tolley EA. Visual-acuity development in healthy preterm infants: effect of marine-oil supplementation. Am J Clin Nutr 1993;58:35.
[41] Bourre JM, Durand G, Erre JP, Aran JM. Changes in auditory brainstem responses in alpha-linolenic acid deficiency as a function of age in rat. Audiology 1999;38:13.
[42] Haubner LY, Stockard JE, Saste MD, Benford VJ, Phelps CP, Chen LT, et al. Maternal dietary docosahexanoic acid content affects the rat pup auditory system. Brain Res Bull 2002;58:1.
[43] Unay B, Sarici SU, Ulas UH, Akin R, Alpay F, Gokcay E. Nutritional effects on auditory brainstem maturation in healthy term infants. Arch Dis Child Fetal Neonatal 2004;89:F177.
[44] Stene LC, Joner G. Use of cod liver oil during the first year of life is associated with lower risk of childhood-onset type 1 diabetes: a large, population-based, case–control study. Am J Clin Nutr 2003;78:1128.
[45] Merzouk H, Khan NA. Implication of lipids in macrosomia of diabetic pregnancy: can n-3 polyunsaturated fatty acids exert beneficial effects? Clin Sci (Lond) 2003;105:519.
[46] Delarue J, LeFoll C, Corporeau C, Lucas D. N-3 long chain polyunsaturated fatty acids: a nutritional tool to prevent insulin resistance associated to type 2 diabetes and obesity? Reprod Nutr Dev 2004; 44:289.
[47] Savva SC, Chadjigeorgiou C, Hatzis C, Kyriakakis M, Tsimbinos G, Tornaritis M, et al. Association of adipose tissue arachidonic acid content with BMI and overweight status in children from Cyprus and Crete. Br J Nutr 2004;91:643.
[48] Jayasooriya AP, Weisinger RS, Weisinger HS, Mathai M, Puskas L, Kitajka K, et al. Dietary omega-3 fatty acid supply influences

mechanisms controlling body weight and glucose metabolism. Asia Pac J Clin Nutr 2004;13:S51.
[49] Chajes V, Bougnoux P. Omega-6/omega-3 polyunsaturated fatty acid ratio and cancer. World Rev Nutr Diet 2003;92:133.
[50] Kaizer L, Boyd NF, Kriukov V, Tritchler D. Fish consumption and breast cancer risk: an ecological study. Nutr Cancer 1989;12:61.
[51] Guo WD, Chow WH, Zheng W, Li JY, Blot WJ. Diet, serum markers and breast cancer mortality in China. Jpn J Cancer Res 1994;85:572.
[52] Braga C, La Vecchia C, Negri E, Franceschi S, Parpinel M. Intake of selected foods and nutrients and breast cancer risk: an age- and menopause-specific analysis. Nutr Cancer 1997;28:258.
[53] Maillard V, Bougnoux P, Ferrari P, Jourdan ML, Pinault M, Lavillonniere F, et al. N-3 and N-6 fatty acids in breast adipose tissue and relative risk of breast cancer in a case–control study in Tours, France. Int J Cancer 2002;98:78.
[54] Pala V, Krogh V, Muti P, Chajes V, Riboli E, Micheli A, et al. Erythrocyte membrane fatty acids and subsequent breast cancer: a prospective Italian study. J Natl Cancer Inst 2001;93:1088.
[55] Goodstine SL, Zheng T, Holford TR, Ward BA, Carter D, Owens PH, et al. Dietary (n-3)/(n-6) fatty acid ratio: possible relationship to premenopausal but not postmenopausal breast cancer risk in U.S. women. J Nutr 2003;133:1409.
[56] Franceschi S, Favero A, Decarli A, Negri E, La Vecchia C, Ferraroni M, et al. Intake of macronutrients and risk of breast cancer. Lancet 1996;347:1351.
[57] Voorrips LE, Brants HA, Kardinaal AF, Hiddink GJ, van den Brandt PA, Goldbohm RA. Intake of conjugated linoleic acid, fat, and other fatty acids in relation to postmenopausal breast cancer: the Netherlands Cohort Study on Diet and Cancer. Am J Clin Nutr 2002; 76:873.
[58] Bougnoux P. n-3 polyunsaturated fatty acids and cancer. Curr Opin Clin Nutr Metab Care 1999;2:121.
[59] Verhoeven DT, Assen N, Goldbohm RA, Dorant E, Sturmans F, Hermus RJ, et al. Vitamins C and E, retinol, beta-carotene and dietary fibre in relation to breast cancer risk: a prospective cohort study. Br J Cancer 1997;75:149.
[60] McEntee MF, Whelan J. Dietary polyunsaturated fatty acids and colorectal neoplasia. Biomed Pharmacother 2002;56:380.
[61] Caygill CP, Hill MJ. Fish, n-3 fatty acids and human colorectal and breast cancer mortality. Eur J Cancer Prev 1995;4:329.
[62] Willett WC, Stampfer MJ, Colditz GA, Rosner BA, Speizer FE. Relation of meat, fat, and fiber intake to the risk of colon cancer in a prospective study among women. N Engl J Med 1990;323:1664.
[63] Kato I, Akhmedkhanov A, Koenig K, Toniolo PG, Shore RE, Riboli E. Prospective study of diet and female colorectal cancer: the New York University Women's Health Study. Nutr Cancer 1997;28:276.
[64] Norat T, Bingham S, Ferrari P, Jenab M, Mazuir M, Overvad K, et al. Meat, fish, and colorectal cancer risk: the European Prospective Investigation into cancer and nutrition. J Natl Cancer Inst 2005;97:906.
[65] European food safety authority (EFSA). Opinion on the CONTAM panel related to the safety assessment of wild and farmed fish. The EFSA Journal 2005;1–118.
[66] De Deckere E. Possible beneficial effect of fish and fish n-3 polyunsaturated fatty acids in breast and colorectal cancer. Eur J Cancer Prev 1999;8:213.
[67] Terry P, Wolk A, Vaino H, Weiderpass E. Fatty fish consumption lowers the risk of endometrial cancer: a natonwide case–control study in Sweden. Cancer Epidemiol Biomarkers Prev 2002;11:143.
[68] McCord JM, Edeas MA. SOD, oxidative stress and human pathologies: a brief history and a future vision. Biomed Pharmacother 2005;59:139.
[69] Emerit J, Edeas M, Bricaire F. Neurodegenerative diseases and oxidative stress. Biomed Pharmacother 2004;58:39.
[70] Gil A. Polyunsaturated fatty acids and inflammatory diseases. Biomed Pharmacother 2002;56:388.
[71] Bourre JM. Dietary omega-3 fatty acids and psychiatry: mood, behaviour, stress, depression, dementia and aging. J Nutr Health Aging 2005;9:31.
[72] Mamalakis G, Tornaritis M, Kafatos A. Depression and adipose essential polyunsaturated fatty acids. Prostaglandins Leukot Essent Fatty Acids 2002;67:311.
[73] Hibbeln JR. Seafood consumption, the DHA content of mothers' milk and prevalence rates of postpartum depression: a cross-national, ecological analysis. J Affect Disord 2002;69:15.
[74] De Vriese SR, Christophe AB, Maes M. Lowered serum n-3 polyunsaturated fatty acid (PUFA) levels predict the occurrence of postpartum depression: further evidence that lowered n-PUFAs are related to major depression. Life Sci 2003;73:3181.
[75] Huan M, Hamazaki K, Sun Y, Itomura M, Liu H, Kang W, et al. Suicide attempt and n-3 fatty acid levels in red blood cells: a case control study in China. Biol Psychiatry 2004;56:490.
[76] Noaghiul S, Hibbeln JR. Cross-national comparisons of seafood consumption and rates of bipolar disorders. Am J Psychiatry 2003; 160:2222.
[77] Morris MC, Evans DA, Bienias JL, Tangney CC, Bennett DA, Wilson RS, et al. Consumption of fish and n-3 fatty acids and risk of incident Alzheimer disease. Arch Neurol 2003;60:940.
[78] Barberger-Gateau P, Letenneur L, Deschamps V, Peres K, Dartigues JF, Renaud S. Fish, meat, and risk of dementia: cohort study. BMJ 2002;325:932.
[79] de Lorgeril M, Renaud S, Mamelle N, Salen P, Martin JL, Monjaud I, et al. Mediterranean alpha-linolenic acid-rich diet in secondary prevention of coronary heart disease. Lancet 1994;343:1454.
[80] Iso H, Rexrode KM, Stampfer MJ, Manson JE, Colditz GA, Speizer FE, et al. Intake of fish and omega-3 fatty acids and risk of stroke in women. JAMA 2001;285:304.
[81] Hu FB, Bronner L, Willett WC, Stampfer MJ, Rexrode KM, Albert CM, et al. Fish and omega-3 fatty acid intake and risk of coronary heart disease in women. JAMA 2002;287:1815.
[82] Oh K, Hu FB, Manson JE, Stampfer MJ, Willett WC. Dietary fat intake and risk of coronary heart disease in women: 20 years of follow-up of the nurses health study. Am J Epidemiol 2005;161:672.
[83] Lopez-Garcia E, Schulze MB, Manson JE, Meigs JB, Albert CM, Rifai N, et al. Consumption of (n-3) fatty acids is related to plasma biomarkers of inflammation and endothelial activation in women. J Nutr 2004;134:1806.
[84] Erkkila AT, Lichtenstein AH, Mozaffarian D, Herrington DM. Fish intake is associated with a reduced progression of coronary artery atherosclerosis in postmenopausal women with coronary artery disease. Am J Clin Nutr 2004;80:626.
[85] Mozaffarian D, Longstreth WT, Lemaitre RN, Manolio TA, Kuller LH, Burke GL, et al. Fish consumption and stroke risk in elderly individuals: the cardiovascular health study. Arch Intern Med 2005;165:200.
[86] Studer M, Briel M, Leimenstoll B, Glass TR, Bucher HC. Effect of different antilipidemic agents and diets on mortality: a systematic review. Arch Intern Med 2005;165:725.
[87] Kromhout D, Bosschieter EB, de Lezenne CC. The inverse relation between fish consumption and 20-year mortality from coronary heart disease. N Engl J Med 1985;312:1205.
[88] He K, Song Y, Daviglus ML, Liu K, Van Horn L, Dyer AR, et al. Accumulated evidence on fish consumption and coronary heart disease mortality: a meta-analysis of cohort studies. Circulation 2004;109:2705.
[89] Harris WS, Von Schacky C. The Omega-3 Index: a new risk factor for death from coronary heart disease? Prev Med 2004;39:212.
[90] GISSI. Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial. Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto miocardico. Lancet 1999;354:447.
[91] Harris WS. Are omega-3 fatty acids the most important nutritional modulators of coronary heart disease risk? Curr Atheroscler Rep 2004;6:447.
[92] Burdge GC, Calder PC. Conversion of alpha-linolenic acid to longer-chain polyunsaturated fatty acids in human adult. Reprod Nutr Dev 2005;45:581.
[93] Muskiet FA, Fokkema MR, Schaafsma A, Boersma ER, Crawford MA. Is docosahexaenoic acid (DHA) essential? Lessons from DHA status

regulation, our ancient diet, epidemiology and randomized controlled trials. J Nutr 2004;134:183.
[94] Legrand P, Bourre JM, Descomps B, Durand G, Renaud S. Lipides. Apports nutritionnels conseillés pour la population française. In: Martin A, editor. Tec et Doc. Lavoisier; 2000. p. 63.
[95] Astorg P, Arnault N, Czernichow S, Noisette N, Galan P, Hercberg S. Dietary intakes and food sources of n-6 and n-3 PUFA in French adult men and women. Lipids 2004;39:527.
[96] Weill P, Schmitt B, Chesneau G, Daniel N, Safraou F, Legrand P. Effects of introducing linseed in livestock diet on blood fatty acid composition of consumers of animal products. Ann Nutr Metab 2002;46:182.
[97] Innis SM, Elias SL. Intakes of essential n-6 and n-3 polyunsaturated fatty acids among pregnant Canadian women. Am J Clin Nutr 2003;77:473.
[98] Antal M, Regoly-Merei A, Varsanyi H, Biro L, Sagi K, Molnar DV, et al. Nutritional survey of pregnant women in Hungary. Int J Vitam Nutr Res 1997;67:115.
[99] Xiang M, Alfven G, Blennow M, Trygg M, Zetterstrom R. Long-chain polyunsaturated fatty acids in human milk and brain growth during early infancy. Acta Paediatr 2000;89:142.
[100] Allison D, Egan K, Barraj L, Coughman C, Infante M, Heimbach J. Estimated intakes of trans fatty and other fatty acids in the US population. J Am Diet Assoc 1999;99:166.
[101] Denomme J, Stark KD, Holub BJ. Directly quantitated dietary (n-3) fatty acid intakes of pregnant Canadian women are lower than current dietary recommendations. J Nutr 2005;135:206.
[102] Dewailly E, Blanchet C, Lemieux S, Sauvé L, Gingras Ayotte PS, Holub BJ. n-3 fatty acids and cardio-vascular disease risk factors among the inuit of Nunavik. Am J Clin Nutr 2001;74:464.
[103] Bourre JM. Where to find omega-3 fatty acids and how feeding animals with diet enriched in omega-3 fatty acids to increase nutritional value of derived products for human: what is actually useful? J Nutr Health Aging 2005;9:232.