



Smart Fats for Kids

EDITED BY KATHERINE TOYE BSC (HONS), DIP ION & KATY PETTER BSC (HONS)

During recent years a large number of studies have shown the importance of intake of polyunsaturated fatty acids for the health of children. This is true especially for long-chain, highly unsaturated fatty acids, LC-PUFA. In this article Ann-Sofie Saldeen, MD, The National University Hospital (Rigshospitalet), Copenhagen, Denmark and Professor Tom Saldeen, MD, PhD, University of Uppsala, Sweden present a review concerning the importance of these fatty acids for the health of children and the development of the brain.

While human adults often suffer from a deficiency of omega-3 fatty acids but seldom get an excess of omega-6 fatty acids, both omega-3 and omega-6 fatty acids are necessary and important components in the diet of children, especially small children.

EPA and DHA are two important omega-3 fatty acids necessary for the development of the child. When these fatty acids are supplied in large amounts, the blood level of arachidonic acid (AA), an important omega-6 fatty acid, can decrease, an effect which may have a negative influence on the growth of the child. For this reason precursors of AA, e.g. linoleic acid, should be supplied to the child together with the omega-3 fatty acids. In children above the age of 12 and in adults such an addition of omega-6 fatty acids is not necessary, and can even be detrimental.

The importance of the fatty acids for the development of the brain.

There are old sayings that "eating fish will make you intelligent" and that "fish is brain food". Recent studies have shown that this may well be true and that the reason lies in the omega-3 fatty acids DHA and EPA. There is an interesting theory that consumption of fish may be a major reason why, with our large brain, we have become superior to animals, and the fish fatty acids may have been of crucial importance for the development of human intelligence. Since the time of the ape our brain has become three times larger. According to this theory the ape in eastern Africa should have had an advantage, since they started to live on fish, which should have contributed to the growth of the brain. The fatty acid pattern in the fish from that area is closer to that in the human brain than any other source of nutrition.

Our intake of fish containing omega-3 fatty acids has decreased drastically during the last century and there is therefore reason to believe that an increased intake of omega-3 fatty acids would be of great importance for the function of the brain.

Many investigations, including a meta-analysis (Anderson et al 1999), have shown that children fed breast milk have a better problem-solving capacity and a higher IQ than children given ordinary milk substitutes (Morrow-Tlucak et al 1988, Lucas et al 1999). One reason for this is thought to be that

infant formulas have lacked omega-3 fatty acids, particularly DHA, which is an important fatty acid for brain structure.

It has recently been shown that addition of LC-PUFA to infant formula from birth to four months of age increases the problem-solving capacity in children at the age of ten months (Willats et al 1998). The test used was a 3-step problem-solving test, the results of which have been shown to be correlated to the IQ measured later during childhood.

Supplementation with DHA and AA in children during the first four months resulted in improved mental development at the age of 18 months (Birch et al 2000). The improvement was correlated to the plasma level of DHA, but not that of AA. Some other studies, however, did not show a similar positive effect (Lucas et al 1999, Makrides et al 2000).

The stability of the fatty acids may be of importance

One explanation for the lack of improvement in certain studies may be that under certain circumstances supplementation with highly unsaturated fatty acids may increase the risk of cell injury, since peroxidation may occur at the site of the double bonds. It is therefore important that the fatty acid preparation used is stable, which means that it should contain an appropriate amount of antioxidants.

It is also possible that the studies have used unsuitable preparations of AA and DHA without the necessary EPA. Breast milk contains a high concentration of linoleic acid, which may be important for the effect. The triglycerides in breast milk usually contain only one LC-PUFA, while those used in certain therapeutic trials contained three LC-PUFAs which make them very susceptible to oxidation. Further, the concentration of omega-3 fatty acids in the blood at birth may be of importance. In children with low blood levels of these fatty acids, e.g. preterm babies, the fatty acids seem to have a better effect.

The fatty acid composition of a cell membrane partly determines the physico-chemical properties of the membrane and can thus influence the activity of various proteins in the membrane, e.g. in receptors, enzymes and ion channels. Certain LC-PUFAs such as AA and EPA act, like their metabolites, the eicosanoids, as signal substances and influence gene expression, while fatty acids such as DHA and AA are responsible for the structure of the membrane. These two fatty acids constitute 20 % of the dry weight of the brain. DHA is also considered to be

involved in the metabolism of dopamine and serotonin (Innis 2000). DHA is found in high concentrations in the synapses and selectively accumulates in the brain of the fetus and the young infant.

Supply of omega-3 during pregnancy

The mother's intake of omega-3 during pregnancy probably influences the development of the child after birth. Supplementation with fish oil containing omega-3 fatty acids during pregnancy may therefore be important. Unfortunately fatty fish often contains environmental poisons, and fish oil supplementation may therefore be necessary. Such a fish oil must be purified and should not of course contain pollution products; it must be well tested and preferably stable and natural, and should not be chemically modified.

Fish oil supplementation during pregnancy has been shown to lower the risk of premature birth, increase the length of the pregnancy and result in infants with a higher birthweight (Olsen et al 1992). Omega-3 fatty acids increase the tissue levels of prostacyclin, which relax the uterine muscles, resulting in with delay of onset of labour.

Low blood levels of LC-PUFA may not always be due to low dietary intake of these fatty acids, but might also be due to disturbed metabolism, e.g. inability to transform alpha-linolenic acid into EPA and DHA, and/or increased degradation of LC-PUFA in the phospholipids in the cell membrane.

Many mothers who develop post partum depression have a low intake of fish and lower levels of DHA in the breast milk than mothers who do not develop depression (Hibbeln 2001). The mother's DHA level can decrease to half during pregnancy and the value is not restored until six months after the birth of the child.

The importance of fatty acids for ADHD and dyslexia

Attention-deficit/hyperactivity disorder (ADHD) is characterised by frequent jumps from one activity to another, unfinished activities, and hyperactivity such as constant restlessness and jumping and running. More boys than girls suffer from ADHD. Boys are also more sensitive than girls to shortage of LC-PUFA. Between 10 and 20% of all children are considered to suffer from at least mild forms of ADHD and/or dyslexia.

Children with ADHD often have low blood levels of DHA, EPA and AA (Mitchell et al 1987; Stevens et al 1995,1996; Stordy 2000). The aetiology of ADHD and the closely related condition dyslexia is probably multifactorial, but deficiency of LC-PUFA may play a role at least in some cases. Treatment with fatty acids is attractive, since it does not have side effects, in contrast to the pharmacological treatment currently used.

Children with ADHD and dyslexia often show symptoms of deficiency of LC-PUFA, with increased thirst, dry skin, dry hair and brittle nails. It has been shown that treatment with a combination of DHA, EPA and AA with predominance of DHA and EPA decreases the symptoms of ADHD and normalises the fatty acid pattern in these children. On the contrary, DHA alone has no effect (Voigt 1998), indicating that EPA is necessary.

People with dyslexia show phospholipase A2 hyperactivity, which removes LC-PUFA from the cell membrane. This phospholipase A2 hyperactivity is inhibited by EPA. In children aged between 8 and 12 years with dyslexia

who were given fish oil and a small amount of evening primrose oil, certain symptoms such as the problems reading, learning, memory and concentration improved (Richardson et al 1999).

Fatty acids and asthma

Asthma is very uncommon among the Eskimos, whose intake of omega-3 fatty acids in the diet is very high. Fish consumption can protect against development of asthma (Peat et al 1992, Hodge et al 1997). Children with asthma or atopic dermatitis have been shown to have low blood levels of omega-3 fatty acids (Yu and Björkstén 1998). Low blood levels of EPA were associated with high levels of IgE antibodies.

A very interesting study on the effect of fish oils on asthma in children was recently published (Nagakura et al 2000). In order to minimize the influence of the often varying environments with different allergen concentrations and diets, this study was performed in children who were treated in hospital for fairly long periods of time. The children were given fish oil containing EPA and DHA, 20 mg and 10 mg/kg body weight and day, respectively.

The asthma was markedly improved after 6 months in the children given fish oil supplementation but no change occurred in the control group given olive oil. A mechanism underlying the effect of the fish oil may be that it inhibits IgE-induced release of prostaglandins from the mast cells, e.g. by inhibition of cyclo-oxygenase-2 (Obatta et al 1999). It should also be mentioned that deficiency of LC-PUFAs such as EPA and DHA has been shown to contribute to an increased disposition to infections (Horrobin 1990, Alexander 1998, Miles and Calder 1998).

Various types of fatty acid preparations

Cod liver oil has been given to children for more than one century. It contains vitamins A and D, which has been the main reason for its use. Cod liver oil, however, also contains omega-3 fatty acids, both EPA and DHA, and can be used to supply these important fatty acids. Recently the interest in cod liver oil has decreased markedly in many countries for several reasons. Since the source of this oil is the liver of the cod, and many environmental poisons accumulate in the liver and are difficult to remove, there is a fear of giving cod liver oil to children.

Furthermore, recent studies have shown that a high intake of vitamin A can be harmful (Melhus et al 1998) and can be one cause of osteoporosis and hip fractures. Norwegians and Swedes, who previously had the highest intake of cod liver oil, also have the highest frequency of osteoporosis and hip fractures worldwide, and a connection between intake of cod liver oil in children and later occurrence of osteoporosis has been proposed. In addition, cod liver oil is sensitive to oxidation and many children have difficulties in tolerating the taste and smell of rancidity in this type of oil.

The interest in other sources of these fatty acids has therefore increased, and the focus has been placed on oils from body fat and muscles of oily fish such as sardines, salmon and mackerel. These sources not only contain a higher concentration of omega-3 fatty acids than the cod liver, they also contain fewer poisons and lack vitamin A.

In Sweden, about 15 years ago, a natural and stable fish oil was introduced containing a mixture of natural antioxidants in addition to EPA and DHA. During purification of fish oil the antioxidants are lost. In this particular fish oil the

antioxidant activity has been restored. This means that the oil does not oxidize outside or within the body, a fact that has been shown to be of great importance for its odour, taste and effect.

In England it was first thought that fish oil for children should contain DHA only and no EPA, and a preparation especially intended for children with dyslexia was introduced. Later on in England the opposite was postulated that it is EPA and not DHA that is of importance, and another preparation introduced.

Fatty acid preparation especially for children

Based upon the most recent research findings, a preparation especially intended for children was introduced in Sweden and Norway. It contains both EPA and DHA and in addition omega-6 and omega-9, and vitamin D and E. The stability of the fish oil has been shown to be of great importance, for example, for the uptake of DHA in the brain and for the brain activity of nitric oxide synthase (Saldeen et al 1996), an enzyme of great importance for learning ability and memory.

The omega-6 fatty acids in a children's preparation should be supplied as linoleic acid, which is found in high concentrations in breast milk. It has been shown that AA can be produced in the body from linoleic acid in small children, who on the other hand seem to lack the ability to convert alpha-linolenic acid to EPA or DHA (Salem et al 1996). Omega-9 fatty acids are considered to be of importance for the effect of the healthy Mediterranean diet. The omega-9 fatty acids also help to protect the cells from the toxic oxygen free radicals. Both vitamin D and omega-3 fatty acids are needed for normal bone development in the growing child.

Ann-Sofie Saldeen, MD
Department of Neonatology,
The National University Hospital (Rigshospitalet), Copenhagen

Tom Saldeen, MD, PhD
Professor
Department of Surgical Sciences
University of Uppsala

References

- Alexander JW. Immunonutrition: the role of omega-3 fatty acids. *Nutr* 14: 627-633, 1998
- Anderson JW, Johnstone BM, Remley DT. Breast-feeding and cognitive development: A meta-analysis. *Am J Clin Nutr* 70: 525-535, 1999
- Birch EE, Hoffman DR, Uauy R, Birch DG, Prestidge C. Visual acuity and the essentiality of docosahexaenoic acid and arachidonic acid in the diet of term infants. *Pediatric Research* 44: 201-209, 1998
- Broadhurst LL, Cunnane SC, Crawford M. Rift Valley lake fish and shellfish provided brain-specific nutrition for early Homo. *British Journal of Nutrition* 79:3-21, 1998
- Forsyth JS, Carlson SE. Long-chain polyunsaturated fatty acids in infant nutrition: effects on infant development. *Current Opinion in Clinical Nutrition and Metabolic Care* 4: 123-126, 2001
- Hibbeln JR. Seafood consumption, the DHA content of mothers' milk and prevalence rates of postpartum depression: a cross-national, ecological analysis. *J Affect Disord* 69: 15-29, 2002
- Hibbeln JR. Fish consumption and major depression. *Lancet* 351: 1213, 1998
- Heird WC. The role of polyunsaturated fatty acids in term and preterm infants and breast-feeding mothers. *Pediatric Clinics of North America* 48: 173-188, 2001
- Hodge L, Salome CM, Hughes JM, et al. Effects of dietary intake of omega-3 and omega-6 fatty acids on severity of asthma in children. *Eur Respir J* 11: 361-365, 1997
- Horrobin D. Essential fatty acids, immunity and viral infections. *J Nutr Med* 1: 145-151, 1990
- Innis S M. The role of dietary n-6 and n-3 fatty acids in the developing brain. *Developmental Neuroscience* 22: 474-480, 2000
- Kidd P M. Attention deficit/hyperactivity disorder (ADHD) in children: rationale for its integrative management. *Alternative Medicine Review* 5: 402-428, 2000
- Lucas A, Stafford M, Morley R, et al. Efficacy and safety of long-chain polyunsaturated fatty acid supplementation of infant-formula milk: a randomized trial. *Lancet* 354: 1948-1954, 1999
- Makrides M, Neumann MA, Simmer K, et al. A critical appraisal of the role of dietary long-chain polyunsaturated fatty acids on neural indices of term infants: A randomized, controlled trial. *Pediatrics* 105: 32-38, 2000
- Melhus H, Michaelsson K, Kindmark A, et al. Excessive dietary intake of vitamin A is associated with reduced bone mineral density and increased risk for hip fracture. *Ann Intern Med* 129: 770-778, 1998
- Miles EA and Calder PC. Modulation of immune function by dietary fatty acids. *Proc. Nutr Soc* 57: 277-292, 1998
- Mitchell EA, Aman MG, Turbott SH, et al. Clinical characteristics and serum essential fatty acid levels in hyperactive children. *Clin Pediatr* 26: 406-411, 1987
- Morrow-Tlucak M, Haude RH, Ernhart CB. Breastfeeding and cognitive development. *Soc Sci Med* 26: 635-639, 1988
- Nagakura T, Matsuda S, Shichijyo, Sugimoto H, Hata K. Dietary supplementation with fish oil rich in omega-3 polyunsaturated fatty acids in children with bronchial asthma. *Eur Respir J* 16: 861-865, 2000
- Obata T, Nagakura T, Masaki T, et al. Eicosapentaenoic acid inhibits prostaglandin D2 by inhibition of cyclooxygenase-2 in cultured human mast cells. *Clin Exp Allergy* 29: 1129-1133, 1999
- Olsen SF, Sørensen JD, Secher NJ, et al. Randomised controlled trial of effect of fish-oil supplementation on pregnancy duration. *Lancet* 339: 1003-1007, 1992.
- Peat JK, Salome SM, Woolcock AJ. Factors associated with bronchial hyper-responsiveness in Australian adults and children. *Eur Respir J* 5: 921-929, 1992
- Richardson AJ, Easton T, McDaid AM, et al. Essential fatty acids in dyslexia: theory, evidence, and clinical trials. In Peet M, Glen I, Horrobin DF, eds. *Phospholipid spectrum disorder in psychiatry*. Carnforth: Marius Press, 1999: 225-241
- Richardson AJ, Puri BK. The potential role of fatty acids in attention-deficit/hyperactivity disorder. *Prostaglandins, Leukotrienes and Essential Fatty Acids* 63:79-87, 2000
- Richardson AJ, McDaid AM, Calvin CM, Higgins CJ, Puri BK. Reduced behavioural and learning problems in children with specific learning difficulties after supplementation with highly unsaturated fatty acids. *European Journal of Neuroscience* 12: Suppl 11:296, 2000
- Saldeen A-S, Yang B, Chen L, Engström K, Mehta JL, Saldeen T. Importance of long chain fatty acids and antioxidants in fish oils for their effect on vascular tissue and brain. *Journal of Investigative Medicine* 45: 209, 1997
- Saldeen T. *Fish oil and health*. SwedeHealth Press, Uppsala, Sweden, 1997

Salem N, Wegher B, Mena P, et al. Arachidonic and docosahexaenoic acids are biosynthesized from their 18-carbon precursors in human infants. *Proc Natl Acad Sci USA* 93: 49-54, 1996

Stevens LJ, Zentall SS, Deck JL, et al. Essential fatty acid metabolism in boys with attention-deficit hyperactivity disorder. *Am J Clin Nutr* 62: 761-768, 1995

Stevens LJ, Zentall SS, Abate ML et al. Omega-3 fatty acids in boys with behavior, learning and health problems. *Physiol Behav* 59: 915-920, 1996

Stoll AL, Severus We, Freeman MP, Reuter S, Zboyan HA, Diamoind E, Cress KK; Marangell LB. Omega-3 fatty acids in bipolar disorder: a preliminary double-blind, placebo-controlled trial. *Archives of General Psychiatry* 56: 407-412, 1999

Stordy BJ. Dark adaption, motor skills, docosahexaenoic acid, and dyslexia. *Am J Clin Nutr* 71 (suppl 1): 323S-326S, 2000

Voigt R. Attention deficit hyperactivity disorder: observational and interventional studies. NIH workshop on omega-3 essential fatty acids and psychiatric disorders. National Institutes of Health: Bethesda, 1998, Sept 2-3

Willatts P, Forsyth JS, DiModugno MK, Varma S, Colvin M. Effect of long-chain polyunsaturated fatty acids in infant formula on problem solving at 10 months of age. *Lancet* 352: 688-691, 1998

Willatts P, Forsyth JS. The role of long-chain polyunsaturated fatty acids in infant cognitive development. *Prostaglandins, Leukotrienes and Essential Fatty Acids* 63: 95-100, 2000

Yu G, Björkstén B. Polyunsaturated fatty acids in school children in relation to allergy and serum IgE levels. *Pediatr Allergy Immunol* 9: 133-138, 1998