4. Essential fatty acids

Physiology and metabolism

Dietary fat is a major source of energy and also provides fat soluble vitamins and essential fatty acids. The properties of dietary fat are primarily determined by the composition of its fatty acids, which may be saturated (no double bonds), monounsaturated (one double bond) or polyunsaturated (2 or more double bonds).

Certain polyunsaturated fatty acids (PUFA) of the n-6 and n-3 series (with the terminal double bond 6 or 3 carbon atoms from the methyl end) cannot be synthesized by man and must be supplied with the diet to avoid deficiency. The major PUFA in vegetable oils, linoleic acid (18:2n-6*), until recently was thought to be the only true essential fatty acid. Linoleic acid can be converted into other n-6 fatty acids, such as dihomo-γ-linolenic acid (20:3n-6) and arachidonic acid (20:4n-6), by consecutive desaturation and chain elongation. These longer chain n-6 fatty acids have an even stronger essential fatty acid activity and specific physiological functions [1,2].

N-6 fatty acids are not interconvertible with n-3 fatty acids, such as α-linolenic (18:3n-3) found in some vegetable oils, and eicosapentaenoic (20:5n-3) and docosahexaenoic acids (22:6n-3) found in marine fish. N-3 fatty acids must be independently supplied in the diet.

Linoleic acid (18:2n-6) and α-linolenic acid (18:3n-3) compete for binding to the same enzyme system, for which α-linolenic acid has a higher affinity. Excessive dietary intakes of α-linolenic acid in relation to linoleic acid may reduce tissue levels of linoleic acid metabolites.

PUFA are indispensable lipid components of cellular and subcellular membranes in all tissues. The extent to which they are incorporated into membranes consequent upon their availability modulates a variety of membrane functions, including membrane fluidity, permeability for metabolite exchange, activity of membrane-bound

---

* In the short formula describing fatty acids, the first figure represents the number of carbon atoms, the second figure after a colon represents the number of double bonds, and finally the position of the terminal double bond is indicated (n-x).

enzymes and receptors, electrical and humoral signal transduction, and hence properties of cells and organs [1,2].

Some highly unsaturated fatty acids (20:3n-6, 20:4n-6, 20:5n-3) are also required as precursors for the synthesis of eicosanoids. These biologically active compounds, which include prostaglandins, thromboxanes, prostacyclins and leukotrienes, are regulators of the cardiovascular system, blood coagulation, renal function, inflammation and immune response, and a large variety of other tissue functions.

The quality and quantity of dietary fat intake is related to several risk factors for the occurrence of coronary heart disease. This report however is restricted to the requirements for essential fatty acids and is not concerned with recommendations for the reduction of risk of coronary heart disease.

Levels of deficiency and excess

Clinical signs of linoleic acid (18:2n-6) deficiency, such as growth failure and skin changes, may develop in healthy newborn infants fed a diet with less than 1 % of energy as linoleic acid for 2-3 months [2,3]. In human adults, clinical linoleic acid deficiency has been described only in individuals with chronic disease states or after long-term intravenous feeding. Minimal requirements of linoleic acid for preventing clinical signs of deficiency in healthy adults are not well defined. The occurrence of human α-linolenic acid (18:3n-3) deficiency has been reported [4,5] but the evidence has been questioned [6,7]. Deficiency of n-6 and n-3 very long-chain PUFA (metabolites of linoleic and α-linolenic acids) may occur during the perinatal period [8] but has not been documented in human adults. However, it must be assumed that human adults do require a certain amount of n-3 fatty acids to replace physiological losses (e. g. oxidation and eicosanoid formation, losses with cellular debris).

A large number of infants have been fed formulas with very high amounts of linoleic acid (60 % of total fat) without the occurrence of any apparent short term adverse effects [9]. Nonetheless side effects of very high consumptions of PUFA are conceivable, including formation of potentially toxic lipid peroxides and alterations of immune functions. Diets with a very high ratio of PUFA to saturated fatty acids (P/S-ratio) cause an undesirable decrease of high-density lipoprotein (HDL) cholesterol, while similar absolute PUFA intakes with higher fat intakes and lower P/S-ratios are not associated with this side effect [10,11,12]. High intakes of very long-chain n-3 fatty acids may increase rates of bleeding and apoplectic insults. Therefore, it appears prudent to avoid extremely high dietary intakes of PUFA.

An increased intake of PUFA raises the need for vitamin E to prevent unwanted oxidation. Fortunately foods rich in PUFA tend to contain sufficient vitamin E, but this is not always the case, and may not necessarily be so in preparations of supplements. With high dietary intakes of PUFA it is essential to ensure that the intake of vitamin E is adequate.

Methods of establishing physiological requirements

Adults

Minimal requirements for linoleic acid in human adults are not well established. There are no long-term studies on the amount of linoleic acid required to maintain a stable body pool. In laboratory rats a low dietary intake of linoleic acid leads to an increase of a specific trienoic acid (20:3n-9) and the triene-tetraene ratio (ratio 20:3n-9/20:4n-6). It has been proposed that an increased triene-tetraene ratio may also indicate linoleic acid deficiency in human adults, but there are not enough data to support this assumption or to establish a reliable threshold level of this ratio above which clinical signs of deficiency would appear. Therefore, linoleic acid requirements of healthy adults can only be estimated roughly from the results of feeding studies in infants. As a lower threshold of habitual intake below which deficiency is probable or metabolic integrity is unlikely to be maintained, 0.5 % of dietary energy is suggested. Average physiological requirements are estimated to be 1 % of dietary energy. With a certain margin of safety, a Population Reference Intake of 2 % of dietary energy is proposed.

In addition to n-6 fatty acids, n-3 PUFA (α-linolenic acid and its metabolites) should be supplied to replace physiological losses of endogenous stores. It may be concluded from data on current dietary habits in Europe that an intake of 0.2 % of energy as n-3 PUFA results in no apparent clinical signs and appears to meet average physiological requirements. With a certain margin of safety, a Population Reference Intake of 0.5 % of dietary energy is proposed.

It appears prudent to set upper limits for the dietary intake of PUFA because of potential untoward side effects of excessive consumption, such as lipid peroxidation, immunosuppression and bleeding.

Administration of fish oil providing 1.5 % n-3 PUFA (mainly eicosapentaenoic acid)/d over several months was associated with bleeding problems in adolescents and young adults [13]. Suppression of antiinfective functions of leukocytes occurred in human subjects consuming diets containing 6.3 % of energy as α-linolenic acid [14] or receiving fish oil supplements providing approximately 1.5 % of energy as

eicosapentaenoic plus docosahexaenoic acids [15,16]. Dietary n-3 PUFA usually consist mostly of α-linolenic acid, and only a smaller portion is contributed by its metabolites.

It is recommended that habitual intakes of total n-3 PUFA should not exceed 5 % of energy and intakes of total PUFA (n-6 + n-3) should not exceed 15 % of energy.

Other groups

There is no evidence that essential fatty acid requirements during pregnancy and lactation are different, if they are expressed as percentages of energy intake.

It has been suggested [9] that the dietary essential fatty acid intakes for formula-fed infants should be 4.5 % of energy for n-6 PUFA and approximately 0.5 % of energy for n-3 PUFA and these are now put forward as PRIs for infants 6-11m. Population Reference Intakes for children aged 1-3 years should be 3 % of energy for n-6 PUFA and 0.5 % of energy for n-3 PUFA. Population Reference Intakes for children from 4 years, expressed as percentages of energy intake, should be the same as those for adults.

Summary

Expressed as a percentage of dietary energy

Adults		
	n-6 polyunsaturated fatty acids	**n-3 polyunsaturated fatty acids**
Average Requirement	1	0.2
Population Reference Intake	2	0.5
Lowest Threshold Intake	0.5	0.1
Pregnancy	As for all adults	
Lactation	As for all adults	
Children	**PRI**	
Age	n-6 PUFA	n-3 PUFA
6 - 11 m	4.5	0.5
1 - 3 y	3	0.5
4 - 6 y	2	0.5
7 - 10 y	2	0.5
11 - 14 y	2	0.5
15 - 17 y	2	0.5

These values can be expressed for average energy expenditures in g PUFA/d.

Adults	*Males*		*Females*	
	n-6 PUFA	n-3 PUFA	n-6 PUFA	n-3 PUFA
Average requirement	3	0.6	2.5	0.5
Population Reference Intake	6	1.5	4.5	1
Pregnancy (from 10th week)			5	1
Lactation			5.5	1

Population Reference Intakes for younger age groups **(g PUFA/d)**

Age group		n-6 PUFA	n-3 PUFA
	6 - 11 m	4	0.5
	1 - 3 y	4	0.7
	4 - 6 y	4	1
	7 - 10 y	4	1
Males	11-14 y	5	1
	15-17 y	6	1.5
Females	11-14 y	4	1
	15-17 y	5	1

Level above which concern should be expressed about possible development of metabolic abnormalities:

n-3 PUFA	5% of dietary energy
n-3 PUFA + n-6 PUFA	15% of dietary energy

References

1. Yamanaka WK, Clemans GW, Hutchinson ML. (1981). Essential fatty acid deficiency in humans. *Prog Lipid Res*, **19:** 187-215.

2. Koletzko B. (1986). Essentielle Fettsäuren: Bedeutung für Medizin und Ernährung. *Akt Endokrin Stoffw*, **7:** 18-27.

3. Hansen AE, Wiese HF, Boelsche AN, Haggard ME, Adam DJD, Davis H. (1963). Role of linoleic acid in infant nutrition. Clinical and chemical study of 428 infants fed on milk mixtures varying in kind and amount of fat. *Pediatrics*, **31:** 171-192.

4. Holman RT, Johnson SB, Hatch TF. (1982). A case of human linolenic acid deficiency involving neurological abnormalities. *Am J Clin Nutr*, **35:** 617-523.

5. Bjerve KS, Fischer S, Alme K. (1987). Alpha-linolenic acid deficiency in man: effect of ethyl linolenate on plasma and erythrocyte fatty acid composition and biosynthesis of prostanoids. *Am J Clin Nutr*, **46:** 570-576.

6. Koletzko B, Cunnane S. (1988). Human alpha-linolenic acid deficiency. *Am J Clin Nutr*, **47:** 1084-1085.

7. Anderson GJ, Connor WE. (1989). On the demonstration of ω-3 essential-fatty-acid deficiency in humans. *Am J Clin Nutr*, **49:** 585-587.

8. European Society for Paediatric Gastroenterology and Nutrition, Committee on Nutrition (1991). Committee report – Comment on the content and composition of lipids in infant formulas. *Acta Paediatr Scand*, **80:** 887-96.

9. Widdowson EM. (1989). Upper limits of intakes of total fat and polyunsaturated fatty acids in infant formulas. *J Nutr*, **119:** 1814-1817.

10. Bonanome A, Grundy SM. (1988). Effect of dietary stearic acid on plasma cholesterol and lipoprotein levels. *N Engl J Med*, **318:** 1244-1248.

11. Brinton EA, Eisenberg S, Breslow L. (1990). A low-fat diet decreases high-density lipoprotein (HDL) cholesterol levels by decreasing HDL apolipoprotein transport rates. *J Clin Invest*, **85:** 144-51.

12. Mensink RP, Katan MB. (1989). Effect of a diet enriched with monounsaturated or polyunsaturated fatty acids on levels of low-density and high-density lipoprotein cholesterol in healthy women and men. *N Engl J Med,* **321:** 436-441.

13. Clarke JTR, Cullen-Dean G, Regelink E, Chan L, Rose V. (1990). Increased incidence of epistaxis in adolescents with familial hypercholesterolemia treated with fish oil. *J Pediatr,* **116:** 139-141.

14. Kelley DS, Branch LB, Love JE, Taylor PC, Rivera YM, Iacono JM. (1991). Dietary α-linolenic acid and immunocompetence in humans. *Am J Clin Nutr,* **53:** 40-46.

15. Lee TH, Hoover RL, Williams JD, Sperling RI, Ravalese J, Spur BW *et al.* (1989). Effect of dietary enrichment with eicosapentaenoic and docosahexaenoic acids on *in vitro* neutrophil and monocyte leukotriene generation and neutrophil function. *N Engl J Med,* **312:** 1217-1224.

16. Endres S, Ghorbani R, Kelley VE, Georgilis K, Lonnemann G, van der Meer JWM *et al.* (1989). The effect of dietary supplementation with n-3 polyunsaturated fatty acids on the synthesis of interleukin-1 and tumor necrosis factor by mononuclear cells. *N Engl J Med,* **320:** 265-271.