Eur J Nutr (2010) 49:189–195
DOI 10.1007/s00394-009-0067-1

ORIGINAL CONTRIBUTION

Dietary intake and plasma concentrations of PUFA and LC-PUFA in breastfed and formula fed infants under real-life conditions

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Received: 24 July 2009 / Accepted: 6 October 2009 / Published online: 23 October 2009

Abstract
Background The breastfed infant is usually used as standard for formula feeding, also regarding long-chain polyunsaturated fatty acids (LC-PUFA). Here, plasma fatty acid concentrations in formula fed infants and the effects of LC-PUFA supplementation were investigated under real-life conditions.
Method Term healthy infants being fully milk fed until the age of 4 months were categorized as breast milk "BM" ($n = 73$) if consuming >95% of energy from breast milk or formula (F) if consuming >95% of energy from formula subdivided into formula without (F−) ($n = 15$) and with LC-PUFA supplementation (F+) ($n = 15$). Formula as marketed was chosen by the parents. Dietary fatty acids (FA) intake was calculated from continuous dietary records from 2 months of age onwards. Total plasma FA were analyzed at the age of 4 months with docosahexaenoic acid (DHA) as primary outcome.
Results Dietary ratios of the polyunsaturated fatty acids (PUFA; linoleic acid/alpha-linolenic acid) were smaller in both F groups than in the BM group. Plasma DHA as % of total FA was similar in BM and F(+) but higher in BM in absolute amounts (mg/L). Plasma DHA as % of total FA in F(−) was higher than what might be supposed on the basis of dietary intake.
Conclusion Infants consuming present-day LC-PUFA-supplemented formula achieved plasma LC-PUFA concentrations similar to breastfed infants. In infants consuming non-LC-PUFA-supplemented formula, the favorable PUFA pattern of the formula may have supported n-3 LC-PUFA biosynthesis.

Keywords LC-PUFA · PUFA · Biomarkers · Breast milk · Formula

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Introduction

A well-balanced status of n-3 and n-6 long-chain (≥20 carbon units) polyunsaturated fatty acids (LC-PUFA) and in particular of docosahexaenoic acid (DHA, n-3) is important for the development of brain and retina of infants [14, 17, 29].

The model of the breastfed infant is usually used as standard for design and evaluation of formula feeding, also regarding LC-PUFA. Human milk contains LC-PUFA in contrast to only tiny amounts in cow's milk. However, LC-PUFA content of human milk is influenced among others by the diet of the mother, in particular for DHA [12].

Preterm [21] and term [31] infants are able to synthesize LC-PUFA from their precursors, the essential polyunsaturated fatty acids (PUFA) [linoleic acid (LA, n-6) and alpha-linolenic acid (ALA, n-3)]. Relatively small dietary ratios of LA/ALA around 5/1 to 10/1 favor the endogenous synthesis of n-3 LC-PUFA [9, 10, 18, 32]. In

addition, infants may profit from their prenatal LC-PUFA stores [17].

The concentration of PUFA in term formula has been regulated by EU law since many years whereas supplementation with LC-PUFA is still facultative [5]. At present, about half of term infant formula on the German market are supplemented with LC-PUFA and numbers are increasing. However, FA intake and FA biomarkers of infants under these conditions have not yet been investigated.

Recently, we could show in a double-blinded, randomized, controlled trial, the Dortmund Intervention Trial for Optimization of Infant Nutrition (DINO), that a food-based modification of the dietary PUFA pattern via rapeseed oil in complementary feeding was effective to support n-3 LC-PUFA synthesis in infants during the second 6 months of life [24]. As a secondary analysis of the DINO study, we examined the dietary FA intake and plasma FA concentrations before the start of complementary feeding at the age of 4 months while parents were free to choose the milk for their infant.

In detail, the objective of this secondary data analysis was to investigate (1) how dietary and plasma PUFA and LC-PUFA of infants consuming common non-supplemented formula compare to breastfed infants and (2) how far present-day practice of LC-PUFA supplementation of formula improves the infants' plasma LC-PUFA concentrations.

Methods

Study design

Participants for DINO were enrolled in delivery hospitals in Dortmund, Germany, from September 2005 to July 2006. Inclusion criteria were: a term newborn infant (gestational age > 37 weeks, birth weight $> 2{,}500$ g); German speaking mother; the intention of the mother to breastfeed the child and to use the study-specific complementary food from the age of 4 months at the earliest. After stopping breastfeeding, the choice of type or brand of formula was left free to the participants. A sample of 132 participants was enrolled for the RCT. Out of the starting sample of 132 participants, 123 were available at the age of 4 months. Reasons for dropping out were: parents not compliant with the study protocol ($n = 3$); no follow-up contact possible ($n = 2$); parents afraid about blood collection ($n = 2$); reason not obvious ($n = 2$). Another 20 were excluded from this analysis because the proportions of breast milk or formula during months 3 and 4 did not fit in the definition for the study groups (see below).

Dietary intake

From the age of 2 months onwards, parents kept a daily record of any food consumed by the child. They also collected packages of formula providing information about nutrient content. Parents were strictly advised to follow the package instructions for formula preparation. They read off and recorded the formula amount from the bottle before the meal as well as the amount of the leftovers [26].

To enable the assessment of dietary intake also for the breastfed infant and avoid the high burden of test weighing, we used a statistical approach to estimate breast milk quantity that proved to be valid throughout the first year of life on a group level in infants fully breastfed for at least 4 months [22, 23]. The individual intake of breast milk (assuming 69 kcal/100 g) [30] was estimated based on the assumption that normally growing infants regulate their energy intake by their total energy expenditure (TEE). Data on TEE were taken from recent references [4]. For partially breastfed infants, the difference between the calculated energy intake from formula and the estimated TEE was assumed as energy intake from breast milk [23, 30].

Data on FA content of formula were taken from the packages and missing data were provided by the manufacturers. FA data for mature breast milk were taken as mean values from the German Standard Food Composition Tables [30] except for AA and DHA. Here, fortunately recent analyses of milk samples from German women participating in the non-supplemented group of an LC-PUFA intervention study were available [6] and these were similar to another German LC-PUFA intervention study stating that the breast milk DHA content in the non-supplemented group reflected the breast milk composition in societies such as Germany [2].

Fatty acid biomarkers

At the age of 4 months, a medical examination including blood sampling was performed at the Pediatric Clinic Dortmund. Two milliliters of non-fasting venous blood were collected in plastic EDTA tubes and immediately transported to the in-house lab. By centrifugation, the plasma was separated and stored at -80 °C. Plasma samples were analyzed by the Institute of Arteriosclerosis Research, Muenster (Germany). Total FA of plasma were converted into their fatty acid methyl esters (FAME) and then analyzed by gas–liquid chromatography. The peak area ratio of each FAME was calculated to the internal standard with the data-processing software Kontron-MT2 [16, 19]. In total, ten FA were analyzed. Here, we report on the PUFA linoleic acid (LA; C18:2n-6), gamma-linolenic acid (GLA; C18:3n-6), alpha-linolenic acid (ALA; C18:3n-3) and the LC-PUFA arachidonic acid (AA; C20:4n-6),

eicosapentaenoic acid (EPA; C20:5n-3) and docosahexaenoic acid (DHA; C22:6n-3).

Statistics

Infants were categorized into three groups, based on the predominant type of milk cumulatively consumed during months 3 and 4: 'breast milk' (BM) means more than 95% of total energy intake from breast milk ($n = 73$); 'formula' (F) means less than 5% of total energy intake from breast milk and at least 95% from formula. The F group was subdivided into a group in which parents had chosen formula without LC-PUFA supplementation (F(−), $n = 15$), and a group in which parents had chosen formula supplemented with LC-PUFA (F(+), $n = 15$). Data were analyzed with SAS® (SAS Institute Inc., Cary, USA, version 8.2).

Dietary intake data (per kg and day) and plasma FA (as % of total FA) for the three study groups are presented as mean and SD. Statistics of absolute values (mg/L) for plasma LC-PUFA are depicted as box plots.

Differences between the BM group and each formula group were tested separately.

For differences in basic characteristics, either the Chi-square test or Wilcoxon test was used (Table 1). For dietary intake (Table 3) and plasma FA (Table 4; Fig. 1), ANOVA was used controlling for sex and birth weight as potential confounders.

Primary outcome was DHA as % of total plasma FA because of its importance for the development of brain and retina [15]. Secondary outcome variables were the plasma PUFA and other LC-PUFA as well as specific ratios with relevance for metabolism: n-6 LC-PUFA/n-3 LC-PUFA, LA/ALA. In addition, absolute amounts (mg/L) were evaluated for LC-PUFA since plasma is the main provider of LC-PUFA to the brain [8, 13].

A test result of $p < 0.05$ was considered as statistically significant. With regard to the plasma FA as outcome variables, only the p value related to the primary outcome DHA was considered as confirmatory, whereas all other p values were interpreted in a more descriptive exploratory sense, since no adjustment for multiplicity was planned.

Ethical considerations

The DINO study was approved by the Ethics Committee of the University of Muenster, Germany. Written informed consent of parents was obligatory for study participation.

Results

Sample

Consistent differences in basic characteristics between the BM group and both F groups were only found for a higher educational level of mothers of the BM group which was to be expected (Table 1), while there was no difference in educational level between F(−) and F(+) (data not shown). Frequency of fish consumption during pregnancy was neither different between the BM group and each of the F groups nor between the F groups (data not shown).

Regarding the FA composition of milks, ALA content estimated for breast milk was lower than in the two types of formula (Table 2). In LC-PUFA-supplemented formula, levels of AA were lower and levels of DHA were similar to estimated contents in breast milk. The data for DHA and AA in breast milk showed smaller variations than the data for DHA and AA in supplemented formula because the breast milk data were reported as interquartile ranges

Table 1 Characteristics of the study groups

	BM ($n = 73$)	F(−) ($n = 15$)	F(+) ($n = 15$)	p	
				BM vs. F(−)	BM vs. F(+)
Infant					
Sex, m/w, n[a]	38/35	3/12	7/8	0.0234	0.7038
Gestational age (weeks)[b,c]	39.6 (1.2)	39.1 (1.6)	39.5 (1.3)	0.3348	0.6071
Birth weight (kg)[b,c]	3.48 (0.41)	3.31 (0.37)	3.18 (0.42)	0.0949	0.0305
Weight at 4 months (kg)[b,c]	6.95 (0.8)	6.9 (0.6)	6.9 (0.5)	0.6936	0.6531
Mother					
Age (years)[b,c]	33.2 (4.2)	29.2 (5.4)	33.7 (3.1)	0.0032	0.7595
First child (%)[a]	60	67	67	0.3675	0.8476
University entrance diploma (%)[a]	80	47	40	0.0156	0.0183

[a] Chi-square

[b] Mean (SD)

[c] Wilcoxon

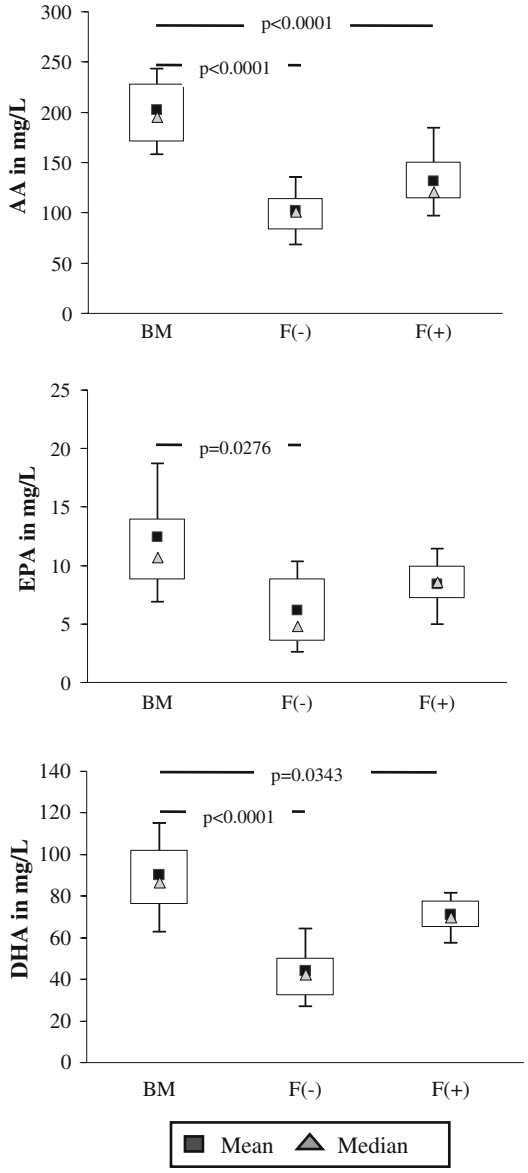

Fig. 1 Concentrations (mg/L) of AA, EPA and DHA in plasma at the age of 4 months by type of milk feeding

whereas data for supplemented formula were available for the individual brands (Table 2).

Total recorded milk consumption was higher and fat intake was lower in the two F groups than estimated for the BM group (Table 3). The dietary LA/ALA ratio was much lower in the two F groups than in the BM group.

Fatty acid biomarkers

The time span between the last meal and blood sampling was not different among the groups (data not shown). In total, dietary PUFA and LC-PUFA pattern in the study groups was well reflected in plasma (Table 4). Although the non-supplemented F(−) group had a negligible intake

Table 2 PUFA and LC-PUFA content of mature breast milk from literature and of formula chosen by study participants from manufacturers, recalculated as % of total fat and per 100 mL milk

	BM	F(−)[a]	F(+)[a]
Total energy (kcal)	68[b]	72 (4)	68 (2)
Total fat (g)	4.0[b]	3.5 (0.3)	3.5 (0.1)
% of total fat			
LA	13.5[b]	14.8 (4.1)	14.7 (2.2)
ALA	0.55[b]	2.61 (1.33)	3.05 (2.02)
AA	0.43 (0.40–0.51)[c]	n.d.	0.23 (0.18)
DHA	0.21 (0.19–0.23)[c]	n.d.	0.19 (0.17)
mg/100 mL			
LA	413[b]	543 (184)	552 (127)
ALA	22[b]	97 (52)	113 (72)
AA	17[c]	n.d.	9.4 (8.2)
DHA	8.4[c]	n.d.	7.6 (6.7)

n.d. not determined

[a] Mean (SD) based on data provided by manufacturers

[b] Ref. [30], mean values

[c] Ref. [6], mean values (interquartile ranges)

of LC-PUFA, it achieved considerable LC-PUFA plasma levels even though significantly lower than the BM group. The F(+) group achieved a plasma DHA level similar to the BM group. Absolute plasma values (mg/L) of LC-PUFA were always higher in the BM group than in the F(+) group and lowest in the F(−) group (Fig. 1).

Discussion

The main findings of this investigation of dietary and plasma PUFA and LC-PUFA in fully milk fed infants under real-life conditions were the following: (1) infants consuming non-LC-PUFA-supplemented formula may have profited for their n-3 LC-PUFA plasma levels from a favorable dietary PUFA pattern; (2) infants consuming LC-PUFA-supplemented formula achieved similar values to breastfed infants for relative plasma levels of n-3 LC-PUFA, but not for absolute ones.

Dietary data

Strength of this examination is the detailed dietary data from diet records and from estimations of breast milk consumption as exact as possible under real-life conditions. Brand-specific FA data for formula were provided by manufacturers and despite large variations of LC-PUFA intake in the F(+) group and small samples of both formula groups, the resulting plasma FA profiles are plausible in total.

For breast milk, recent LC-PUFA analyses from Germany were available [6] which are of particular interest for

Table 3 Basic dietary characteristics and intake of PUFA and LC-PUFA during months 3 and 4 of postnatal life in the study groups

	BM[a] ($n = 73$)	F(−)[b] ($n = 15$)	F(+)[b] ($n = 15$)	p	
				BM vs. F(−)	BM vs. F(+)
Milk (g/kg day)	127 (2)	151 (21)	147 (20)	<0.0001	<0.0001
Energy (kcal/kg day)	87 (1)	99 (14)	94 (14)	<0.0001	0.0002
Fat (g/kg day)	5 (0.1)	4.9 (0.7)	4.9 (0.7)	0.0090	0.0036
LA (g/kg day)	0.5 (0.0)	0.7 (0.2)	0.7 (0.2)	<0.0001	<0.0001
ALA (mg/kg day)	28 (1)	117 (43)	151 (103)	<0.0001	<0.0001
AA (mg/kg day)	22.1 (0.3)	0.2 (0.3)[c]	13.7 (6.3)	<0.0001	<0.0001
DHA (mg/kg day)	10.7 (0.1)	0.1 (0.2)[c]	12.60 (7.1)	<0.0001	0.0653
LA/ALA	18.7 (0.3)	8.4 (6.5)	6.1 (1.9)	<0.0001	<0.0001

Mean (SD); ANOVA, controlled for birth weight and sex

[a] Based on milk amounts derived from estimated individual energy requirement and mean energy content of breast milk [30] and from FA [6] from the literature

[b] Based on measured milk amounts and brand-specific FA data (see Table 2)

[c] From small amounts of breast milk allowed (<5% of energy intake)

Table 4 Plasma FA (% of total FA) at age 4 months in the study groups

	BM ($n = 73$)	F(−) ($n = 15$)	F(+) ($n = 15$)	p	
				BM vs. F(−)	BM vs. F(+)
Primary outcome					
DHA	2.8 (0.8)	1.4 (0.3)	2.6 (0.5)	<0.0001	0.2104
Secondary outcome					
LA	25.5 (2.8)	29.3 (1.9)	30.1 (2.0)	<0.0001	<0.0001
GLA	0.6 (0.1)	0.7 (0.1)	0.7 (0.1)	<0.0001	0.0001
ALA	0.6 (0.2)	1.4 (0.4)	1.3 (0.4)	<0.0001	<0.0001
AA	6.3 (1.3)	3.6 (0.8)	4.7 (0.9)	<0.0001	<0.0001
EPA	0.4 (0.2)	0.2 (0.1)	0.3 (0.1)	<0.0001	0.1403
Ratios					
LA/ALA	46.1 (16.1)	24.1 (11.3)	25.6 (8.2)	<0.0001	<0.0001
n-6/n-3 LC-PUFA	2.1 (0.4)	2.2 (0.3)	1.7 (0.3)	0.2778	0.0042

Mean (SD); ANOVA, controlled for birth weight and sex

DHA that is prone to influence from maternal dietary intake [12, 14]. Since our study sample was participating in an intervention study as the samples were providing the analytical data of breast milk FA, the literature data may fit to our sample as well. The proportion of DHA (0.21 or 0.26% of total fat) in the German breast milk samples reflects the FA composition in low-fish-eating populations [2] and tends to be lower than internationally (0.32 or 0.45–0.88%) [3, 11].

Since the educational level was similar in our F groups, we do not expect an influence of the socio-demographic status on the choice of formula.

Plasma biomarkers

A limitation of our study is the use of total plasma FA as biomarker. Plasma reflects the FA composition of the diet for a period of only a few hours up to 1 day before [1]. However, in case of exclusive milk feeding and the strict definitions for our feeding groups, the dietary FA pattern was almost stable in the last 2 months before the plasma analysis. Plasma phospholipids where PUFA and LC-PUFA are more concentrated [7] or erythrocyte cell membranes might have provided even more pronounced differences between feeding types than total plasma.

Metabolism

A dietary LA/ALA ratio of 5/1 in formula increased the endogenous synthesis of n-3 LC-PUFA in infants compared to a ratio of 10/1 [18]. In both our formula groups, the dietary LA/ALA ratio (8.4/1 and 6.1/1, respectively; Table 3) ranged between these figures and was much smaller than assumed for breast milk (18.7), because the

ALA content in formula is much higher than in breast milk. The reflection of the small ratios in plasma should have supported n-3 FA pathways. There might also be an influence of LC-PUFA stores from the late period of pregnancy [17] but those stores are probably quite similar in our three groups due to their similar fish consumption during pregnancy.

LC-PUFA synthesis has been demonstrated in term infants [18, 20]. This fact taken together with findings in young animals (mice) [25] leads to the speculation that an ample ALA intake in our F(−) group was preferably metabolized to DHA in case of lacking preformed DHA.

Effective endogenous synthesis in case of high requirements in non-supplemented infants may be one of the reasons why recent reviews did not find sustaining developmental benefits of LC-PUFA supplementation for term and preterm infants [27, 28].

Usually, relative amounts of plasma FA are reported for comparing study groups in the literature. In case of DHA, absolute amounts are of additional interest because plasma is the main provider of DHA to the brain. Interestingly, in our study, relative amounts of DHA did not differ between the BM and F groups but were higher in the BM group in absolute amounts.

Product development

Our data show that the present-day practice of LC-PUFA supplementation of formula is well designed to achieve relative n-3 LC-PUFA plasma levels (% FA) similar to the standard of breastfeeding. To achieve this also for absolute plasma levels as special DHA providers for brain [13, 17], two strategies for modifying formula design are possible: to raise LC-PUFA intake by increasing total fat content of formula within the legal range (4.4–6 g/100 kcal) [5] while keeping the existing LC-PUFA concentrations, or to keep total fat content and increase LC-PUFA concentration.

The non-supplemented infants seem to have profited from the favorable PUFA composition for their endogenous synthesis of n-3 LC-PUFA. Further lowering the LA/ALA ratio that was on average 8/1 and 6/1 in the formula used here and is 5/1 in the EC law might approximate n-3 LC-PUFA status in formula fed infants even closer to the standard of breastfeeding.

Conclusion

Our finding that small dietary LA/ALA ratios probably favor n-3 LC-PUFA synthesis in young infants are supported by results from intervention studies, and recently also from a food-based intervention via rapeseed oil in complementary feeding in this study sample. Interestingly, our findings reflect real-life conditions and an age where requirement for DHA is still high, but where milk as DHA source will be soon replaced more and more by complementary food low in DHA. The higher fat content of breast milk compared to the present day supplemented formula probably led to the higher absolute DHA plasma levels in breastfed infants.

Acknowledgments The study was supported by the Central Marketing Organization of German Agricultural Economics (CMA), Union for the Promotion of Oil and Protein Plants (UFOP), Brökelmann+Co, Oil mill GmbH+Co and Seed and Seed stock Group of North Germany AG Georg Lembke. We thank the two pediatricians from the Pediatric Clinic, Dortmund (Germany) for medical examinations and blood sampling. We thank Dr. P-E. Reimitz for statistical advice. The cooperation of the maternity clinics in the Dortmund region during recruitment of mothers and newborns is gratefully acknowledged.

References

1. Arab L (2003) Biomarkers of fat and fatty acid intake. J Nutr 133(Suppl 3):925S–932S
2. Bergmann RL, Haschke-Becher E, Klassen-Wigger P, Bergmann KE, Richter R, Dudenhausen JW, Grathwohl D, Haschke F (2008) Supplementation with 200 mg/day docosahexaenoic acid from mid-pregnancy through lactation improves the docosahexaenoic acid status of mothers with a habitually low fish intake and of their infants. Ann Nutr Metab 52:157–166
3. Brenna JT, Varamini B, Jensen RG, Diersen-Schade DA, Boettcher JA, Arterburn LM (2007) Docosahexaenoic and arachidonic acid concentrations in human breast milk worldwide. Am J Clin Nutr 85:1457–1464
4. Butte NF (2005) Energy requirements of infants. Public Health Nutr 8:953–967
5. Commission D (2006) Commission Directive 2006/141/EC of 22 December 2006 on infant formulae and follow-on formulae and amending Directive 1999/21/EC. In, p L 401/402
6. Fidler N, Sauerwald T, Pohl A, Demmelmair H, Koletzko B (2000) Docosahexaenoic acid transfer into human milk after dietary supplementation: a randomized clinical trial. J Lipid Res 41:1376–1383
7. Guerra A, Demmelmair H, Toschke AM, Koletzko B (2007) Three-year tracking of fatty acid composition of plasma phospholipids in healthy children. Ann Nutr Metab 51:433–438
8. Innis SM (2007) Dietary (n-3) fatty acids and brain development. J Nutr 137:855–859
9. Innis SM (2003) Perinatal biochemistry and physiology of long-chain polyunsaturated fatty acids. J Pediatr 143:S1–S8
10. Jensen CL, Chen H, Fraley JK, Anderson RE, Heird WC (1996) Biochemical effects of dietary linoleic/alpha-linolenic acid ratio in term infants. Lipids 31:107–113
11. Jensen RG (1999) Lipids in human milk. Lipids 34:1243–1271
12. Jensen RG, Bitman J, Carlson SE, Hamosh M, Newburg DS (1995) Milk lipids. In: Jensen RG (ed) Handbook of milk composition. Academic Press, San Diego, pp 495–576
13. Kim HY (2007) Novel metabolism of docosahexaenoic acid in neural cells. J Biol Chem 282(26):18661–18665
14. Koletzko B, Cetin I, Brenna JT (2007) Dietary fat intakes for pregnant and lactating women. Br J Nutr 98:873–877
15. Koletzko B, Lien E, Agostoni C, Bohles H, Campoy C, Cetin I, Decsi T, Dudenhausen JW, Dupont C, Forsyth S, Hoesli I,

Holzgreve W, Lapillonne A, Putet G, Secher NJ, Symonds M, Szajewska H, Willatts P, Uauy R (2008) The roles of long-chain polyunsaturated fatty acids in pregnancy, lactation and infancy: review of current knowledge and consensus recommendations. J Perinat Med 36:5–14
16. Kratz M, Cullen P, Kannenberg F, Kassner A, Fobker M, Abuja PM, Assmann G, Wahrburg U (2002) Effects of dietary fatty acids on the composition and oxidizability of low-density lipoprotein. Eur J Clin Nutr 56:72–81
17. Lauritzen L, Hansen HS, Jorgensen MH, Michaelsen KF (2001) The essentiality of long chain n-3 fatty acids in relation to development and function of the brain and retina. Prog Lipid Res 40:1–94
18. Makrides M, Neumann MA, Jeffrey B, Lien EL, Gibson RA (2000) A randomized trial of different ratios of linoleic to alpha-linolenic acid in the diet of term infants: effects on visual function and growth. Am J Clin Nutr 71:120–129
19. Michalsen A, Lehmann N, Pithan C, Knoblauch NT, Moebus S, Kannenberg F, Binder L, Budde T, Dobos GJ (2006) Mediterranean diet has no effect on markers of inflammation and metabolic risk factors in patients with coronary artery disease. Eur J Clin Nutr 60:478–485
20. Salem N Jr, Wegher B, Mena P, Uauy R (1996) Arachidonic and docosahexaenoic acids are biosynthesized from their 18-carbon precursors in human infants. Proc Natl Acad Sci USA 93:49–54
21. Sauerwald TU, Hachey DL, Jensen CL, Chen H, Anderson RE, Heird WC (1997) Intermediates in endogenous synthesis of C22:6 omega 3 and C20:4 omega 6 by term and preterm infants. Pediatr Res 41:183–187
22. Scanlon K, Alexander M, Serdula M, Davis M, Bowman B (2002) Assessment of infant feeding: the validity of measuring milk intake. Nutr Rev 60:235–251
23. Schoen S, Sichert-Hellert W, Kersting M (2009) Validation of energy requirement equations for estimation of breast milk consumption in infants. Public Health Nutr (in press)
24. Schwartz J, Dube K, Sichert-Hellert W, Kannenberg F, Kunz C, Kalhoff H, Kersting M (2009) Modification of dietary PUFA via complementary food enhances n-3 LC-PUFA synthesis in healthy infants—a double blinded randomized controlled trial. Arch Dis Child [Epub ahead of print]
25. Scott BL, Bazan NG (1989) Membrane docosahexaenoate is supplied to the developing brain and retina by the liver. Proc Natl Acad Sci USA 86:2903–2907
26. Sichert-Hellert W, Kersting M, Chada C, Schäfer R, Kroke A (2007) German food composition database for dietary evaluations in children and adolescents. J Food Compos Anal 20:63–70
27. Simmer K, Patole SK, Rao SC (2008) Longchain polyunsaturated fatty acid supplementation in infants born at term. Cochrane Database Syst Rev:CD000376
28. Simmer K, Schulzke SM, Patole S (2008) Longchain polyunsaturated fatty acid supplementation in preterm infants. Cochrane Database Syst Rev:CD000375
29. Simopoulos AP (2003) Importance of the ratio of omega-6/omega-3 essential fatty acids: evolutionary aspects. In: Simopoulos AP, Cleland LG (eds) Omega-6/omega-3 essential fatty acid ratio: the scientific evidence. World Rev Nutr Diet, Karger, Basel, pp 1–22
30. Souci SW, Fachmann W, Kraut H (2000) Die Zusammensetzung der Lebensmittel Nährwert-Tabellen. Medpharm Scientific Publishers, Stuttgart
31. Uauy R, Mena P, Wegher B, Nieto S, Salem N Jr (2000) Long chain polyunsaturated fatty acid formation in neonates: effect of gestational age and intrauterine growth. Pediatr Res 47:127–135
32. Uauy R, Rojas C, Llanos A, Mena P (2005) Dietary essential fatty acids in early postnatal life: long-term outcomes. Nestlé Nutrition Workshop Series Pediatric Program 55:101–136