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Fatty acid composition of plasma lipids in Nigerian children with protein-energy malnutrition*

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Abstract. The fatty acid (FA) composition of the main plasma lipids was analysed in eight well-nourished, generally healthy Nigerian children aged 14.1 ± 7.2 months and in 17 malnourished children (8 marasmus, 9 kwashiorkor) aged 14.6 ± 3.8 months within the first 2 days of admission at the Dept. of Child Health, University of Benin. In comparison to the control group, the malnourished children showed a marked decrease of polyunsaturated FA with low linoleic acid, mainly in sterolesters (STE), and severely reduced linoleic acid metabolites, including arachidonic acid, in all lipid fractions. ω-3-FA were not altered except for a reduction of docosapentaenoic and docosahexaenoic acids in phospholipids. Clearly increased values were found for saturated FA in STE and for the non-essential monoenoic FA in all lipid classes. This pattern indicates the presence of essential fatty acid deficiency in the malnourished children. There was no significant difference between marasmus and kwashiorkor. Eight malnourished children were followed up in the early phase of recovery during hospital treatment 14.0 ± 3.1 days after obtaining the first sample. Linoleic acid had increased again in STE, but its metabolites were as low or even lower than before. An impaired activity of delta-6-desaturase, the rate limiting enzyme of linoleic acid metabolism, in suggested by elevated substrate-product-ratios of this enzyme in untreated children with protein energy malnutrition and in the early phase of recovery, which may be due to low insulin levels, protein and zinc deficiency. The trien-tetraen-ratio (20:3ω9/20:4ω6) thus is not a reliable indicator of essential FA status in protein-energy malnutrition.

Key words: Essential fatty acids – Delta-6-desaturase – Nigeria – Protein energy malnutrition – Children

Introduction

In protein-energy malnutrition (PEM), today one of the most common health hazards in young children, lipid metabolism is disturbed. There is a marked reduction of adipose tissue, and hepatomegaly due to fatty liver, in that triglycerides may account for up to 50% weight, is a common feature of the disease [21, 25, 64]. Most investigators found decreased serum triglycerides (TG), cholesterolesters (STE) and phospholipids (PL) [22, 43, 50, 51, 63]. Very low density lipoproteins disappear and low density lipoproteins are diminished [14, 64].

As early as 1959 Schendel and Hansen [56] reported a decreased proportion of unsaturated fatty acids (FA) in treated kwashiorkor patients, as measured by alkali isomerisation. It has been proposed that deficiency of essential fatty acids (EFA) may contribute to a number of clinical problems associated with PEM, e.g. scaly dermatitis, loss of hair, susceptibility to infections, fatty liver, impaired wound healing, psychomotor changes and growth retardation, which are also observed in experimental EFA deficiency with an adequate supply of protein and calories [2, 23, 27, 29, 32, 52]. However, today there are still only scanty data on the supply and metabolism of EFA in PEM children. In plasma total lipids linoleic acid and its functionally important metabolites have been found to be decreased, accompanied by an increase of the saturated and the non-essential monoenoic FA, in Nigerian children with kwashiorkor [47, 59] and in Peruvian and Honduran children with different types of malnutrition [10, 69]. In PEM the relative distribution of the distinct plasma lipid classes, which differ in EFA content, is markedly altered [43, 59, 64], which may influence the FA composition of plasma total lipids. Therefore analysis of the different lipid classes of serum or plasma is preferred for evaluation of EFA status in PEM, but this has been published by two groups only: Holman et al. [35] performed very detailed analysis in Argentine children with malnutrition, obviously varied forms, and found a moderate deficiency of EFA. A similar result was obtained by Macdonald et al. [43] in South African kwashiorkor patients, in whom also a follow-up study during treatment was performed. Due to limitations of the analytical methods in the early 1960s these authors were able to give data only for the principal FA.

In this paper the FA composition of the major plasma lipid fractions in malnourished Nigerian children at the time of hospital admission and during the early phase of recovery is presented.

Patients and methods

Three groups of Nigerian children attending the Dept. of Child Health, University of Benin, participated in the study:

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Abbreviations: EFA = essential fatty acids; FA = fatty acids; PEM = protein energy malnutrition; PL = phospholipids; STE = sterolesters; TG = triglycerides; PUFA = polyunsaturated fatty acids

A: Eight well-nourished children with trivial complaints not affecting the gastrointestinal tract or general health served as a control group. Their age was 14.1 ± 7.2 months (range 5–24 months, median 15 months) and their body weight was 9.8 ± 2.2 kg. B: Seventeen children with protein-energy malnutrition (PEM) within the first 2 days of hospital-admission. Eight children with marasmus and 9 with kwashiorkor were selected according to clinical criteria and estimation of serum protein [45]. The age of these children was 14.6 ± 3.8 months (range 5–23 months, median 13 months) and their weight was 6.7 ± 1.4 kg. C: Eight children out of group B (four marasmus, four kwashiorkor) in the recovery phase 14.0 ± 3.1 days after the first sample. They had received the usual hospital treatment with a high-calorie and high-protein diet with Pap (maize) and milk, eggs, beans, vegetables, fish, meat, vegetable and palm oil. Their weight had increased to 7.7 ± 1.6 kg.

With informed consent of the patients' parents, blood samples were collected when venipuncture had to be performed for other diagnostic reasons. The time interval after the last feeding was at least 4 h in infants, in the older children blood samples were taken after an overnight fast. Centrifugation was performed within 1 h, and 1 ml EDTA-plasma was injected forcefully through a teflon-coated rubber septum into a dark brown glass vial pre-filled with 5 ml chloroform/methanol 1:1 and 1 ml of an internal standard (heptadecanoylphosphatidylcholine) in chloroform. The solvents contained 0.1 g/l butylated hydroxytoluene and most of the air in the vials was replaced by nitrogen to prevent oxidation of unsaturated bonds. After injection of the sample, the vials were thoroughly shaken and then stored in the dark at −20°C until they were sent to Düsseldorf by air at room temperature. The FA composition of plasma treated in this way is stable [39]. Lipid extraction, separation of lipid classes and preparation of FA methylesters were performed as described earlier [40]. FA were analysed on a Packard-Becker-417 gaschromatograph fitted with a 25 m WG 11 hard glass capillary column (WGA, Düsseldorf) temperature programmed from 130° to 230°C at 7°/min with helium carrier gas, 0.7 bar, split ratio 1:10. Peaks were identified by comparison of retention times with standard substances and, if necessary, by mass-spectrometry (Dr. U. Matthiesen, Institut für Physiologische Chemie II, Universität Düsseldorf). Amounts of FA quantified with a Shimadzu CR1B digital integrator and expressed as percentage by weight of all FA with a chain length of C14 to C22.

In some of the FA of low concentration the difference of mean −2SD results in negative values, suggesting a possible divergence from normal distribution, a problem which was present in all other investigations on FA in PEM [10, 35, 43,

Table 1. Fatty acid composition of plasma sterolesters in 8 well-nourished Nigerian children, 17 children with PEM and 8 children during recovery from PEM

Sterolesters		A: well-nourished ($n = 8$)	B: PEM ($n = 17$)	P B vs A	C: PEM-recovery ($n = 8$)	P C vs B	P C vs A
Myristic acid	14:0	1.31 ± 0.57	2.65 ± 1.57	<0.05	3.36 ± 1.50		<0.005
Palmitic acid	16:0	13.79 ± 1.86	17.87 ± 5.64	<0.10	16.69 ± 2.85		
Stearic acid	18:0	1.68 ± 0.34	4.35 ± 2.77	<0.02	3.46 ± 2.18		<0.05
Sum saturated FA		16.78 ± 1.87	24.87 ± 8.90	<0.02	23.51 ± 5.00		<0.005
Palmitoleic acid	16:1ω7	1.88 ± 0.72	3.67 ± 1.04	<0.01	2.86 ± 1.42		
Oleic acid	18:1ω9	23.04 ± 1.98	30.59 ± 5.50	<0.01	24.55 ± 5.29	<0.02	
Eicosatrienoic acid	20:3ω9	ND	0.49 ± 0.31		0.50 ± 0.21		
Linoleic acid	18:2ω6	47.41 ± 4.94	33.13 ± 10.11	<0.01	40.98 ± 9.13	<0.10	
γ-Linolenic acid	18:3ω6	1.78 ± 1.25	0.92 ± 0.75		0.44 ± 0.17		<0.02
Eicosadienoic acid	20:2ω6	ND	ND		ND		
Dihomo-γ-linolenic acid	20:3ω6	1.13 ± 0.48	1.35 ± 1.25		0.81 ± 0.82		
Arachidonic acid	20:4ω6	6.17 ± 1.27	3.70 ± 1.59	<0.01	3.78 ± 1.67		<0.01
Sum n-6-FA		56.19 ± 4.25	38.33 ± 11.20	<0.10	45.92 ± 10.05	<0.10	<0.02
α-Linolenic acid	18:3ω3	0.39 ± 0.14	0.53 ± 0.25		0.41 ± 0.14		
Eicosatrienoic acid	20:3ω3	0.74 ± 0.73	0.55 ± 0.38		1.01 ± 0.62		
Eicosapentaenoic acid	20:5ω3	1.30 ± 0.69	1.37 ± 0.83		1.52 ± 1.27		
Docosapentaenoic acid	22:5ω3	ND	ND		ND		
Docosahexaenoic acid	22:6ω3	1.05 ± 0.37	1.67 ± 1.21		1.70 ± 1.50		
Sum n-3-FA		2.74 ± 1.08	3.02 ± 1.74		2.98 ± 0.76		
Sum PUFA		58.59 ± 3.98	40.87 ± 12.33	<0.001	48.04 ± 11.03		<0.05
P/S-ratio		3.56 ± 0.55	1.90 ± 1.04	<0.001	2.18 ± 0.78		<0.005
Ratio	20:3ω9/20:4ω6	ND	0.19 ± 0.08		0.21 ± 0.08		
Ratio	18:2ω6/20:4ω6	7.95 ± 1.72	10.48 ± 3.58	<0.10	12.64 ± 5.74		<0.05
Ratio	18:2ω6/18:3ω6	24.44 ± 14.33	53.20 ± 32.85	<0.10	120.57 ± 78.77	<0.10	<0.05
Ratio	18:3ω6/20:3ω6	1.74 ± 1.18	1.16 ± 0.70		0.93 ± 0.91		
Ratio	20:3ω6/20:4ω6	0.28 ± 0.22	0.42 ± 0.39		0.27 ± 0.19		

Mean ± SD, weight %. ND = not detectable

Table 2. Fatty acid composition of plasma triglycerides in 8 well-nourished Nigerian children, 17 children with PEM and 8 children during recovery from PEM

Triglycerides		A: well-nourished ($n = 8$)	B: PEM ($n = 17$)	P B vs A	C: PEM-recovery ($n = 8$)	P C vs B	P C vs A
Myristic acid	14:0	3.32 ± 1.62	3.28 ± 1.81		4.04 ± 2.21		
Palmitic acid	16:0	25.68 ± 2.66	25.64 ± 4.35		25.59 ± 2.32		
Stearic acid	18:0	5.32 ± 1.27	5.14 ± 0.76		5.36 ± 1.47		
Sum saturated FA		34.42 ± 4.54	34.16 ± 5.03		35.11 ± 3.15		
Palmitoleic acid	16:1ω7	2.01 ± 0.78	3.29 ± 0.91	<0.01	2.41 ± 1.38	<0.01	
Oleic acid	18:1ω9	36.43 ± 3.39	41.82 ± 6.81	<0.10	40.27 ± 5.82		
Eicosatrienoic acid	20:3ω9	0.19 ± 0.12	0.30 ± 0.47		0.10 ± 0.03		
Linoleic acid	18:2ω6	19.69 ± 4.42	16.22 ± 5.54		16.53 ± 4.23		
γ-Linolenic acid	18:3ω6	0.94 ± 1.02	0.17 ± 0.14	<0.02	0.51 ± 0.49	<0.05	
Eicosadienoic acid	20:2ω6	0.18 ± 0.13	0.26 ± 0.23		0.10 ± 0.05		
Dihomo-γ-linolenic acid	20:3ω6	0.71 ± 0.44	0.51 ± 0.33		0.23 ± 0.11	<0.05	<0.001
Arachidonic acid	20:4ω6	1.52 ± 0.49	0.93 ± 0.35	<0.01	0.72 ± 0.15		<0.001
Sum n-6-FA		22.85 ± 5.08	17.98 ± 5.46	<0.10	18.07 ± 4.30		<0.10
α-Linolenic acid	18:3ω3	0.71 ± 0.29	0.60 ± 0.38		0.84 ± 0.72		
Eicosatrienoic acid	20:3ω3	ND	ND		ND		
Eicosapentaenoic acid	20:5ω3	0.73 ± 0.75	0.49 ± 0.44		0.57 ± 0.57		
Docosapentaenoic acid	22:5ω3	0.33 ± 0.14	0.33 ± 0.25		0.26 ± 0.08		
Docosahexaenoic acid	22:6ω3	2.19 ± 1.42	2.17 ± 1.90		1.10 ± 0.87		
Sum n-3-FA		3.92 ± 2.05	3.30 ± 2.42		2.71 ± 2.24		
Sum PUFA		25.95 ± 5.42	21.54 ± 7.14		20.30 ± 5.27		<0.10
P/S-ratio		0.78 ± 0.22	0.64 ± 0.22		0.58 ± 0.18		<0.10
Ratio	20:3ω9/20:4ω6	0.19 ± 0.15	0.58 ± 0.96		0.13 ± 0.06		
Ratio	18:2ω6/20:4ω6	13.88 ± 4.67	19.64 ± 9.31		24.59 ± 10.16		<0.02
Ratio	18:2ω6/18:3ω6	58.67 ± 59.08	142.79 ± 97.65	<0.10	78.82 ± 55.29		
Ratio	18:3ω6/20:3ω6	1.24 ± 1.16	0.52 ± 0.43	<0.10	3.22 ± 3.99	<0.05	
Ratio	20:3ω6/20:4ω6	0.40 ± 0.13	0.66 ± 0.66		0.36 ± 0.13		

Mean ± SD, weight %. ND = not detectable

47, 59, 69]. However, we did not find any indication of a bimodal, logarithmic normal or any other type of systematic distribution, and in many other FA the distribution appeared to be normal. Therefore the results were evaluated by a two-tailed Student's t-test, that tolerates slightly skewed distributions relatively well.

Results

The plasma lipids in the well-nourished Nigerian children were well equipped with polyunsaturated FA (Tables 1–3; see also [39]). In contrast, the PEM children presented dramatically decreased essential FA levels with low linoleic acid mainly in STE and, even more pronounced, low linoleic acid metabolite levels including arachidonic acid in all lipid classes. The relative decrease of linoleic acid metabolites in comparison to linoleic acid, as expressed by the high 18:2ω6/20:4ω6 ratio, indicates impairment of enzymatic desaturation. Increased values were found for the saturated FA in STE and the non-essential monoenoic FA in all fractions. There was only a slight but insignificant rise of n-9-eicosatrienoic acid. The n-3-FA were not altered except for a reduction of docosapentaenoic and docosahexaenoic acids in PL. The total amount of polyunsaturated FA (sum PUFA) as well as the ratio of polyunsaturated to saturated FA (P/S-ratio) were severely reduced in STE and PL.

There was no significant difference between children with marasmus and those with kwashiorkor (Table 4).

In the recovering children linoleic acid had increased again in STE, though it did not reach the value of the control group, but there was no clear change in PL or TG. At the same time oleic acid, which is found to be increased in essential FA deficiency, decreased again in PL and STE. However, in all lipid classes levels of the metabolically important linoleic acid metabolites were as low as before and the 18:2ω6/20:4ω6 ratio was even higher, though the difference was not significant, which is probably due to the high coefficient of variation of this parameter. The long-chain ω-3-FA had increased again in PL, but the overall P/S ratio remained low in all fractions.

Discussion

This study shows in Nigerian children with PEM, a deficiency of EFA, particular of linoleic acid metabolites, which persists

Table 3. Fatty acid composition of plasma phospholipids in 8 well-nourished Nigerian children, 17 children with PEM and 8 children during recovery from PEM

Phospholipids		A: well-nourished ($n = 8$)	B: PEM ($n = 17$)	P B vs A	C: PEM recovery ($n = 8$)	P C vs B	P C vs A
Myristic acid	14:0	0.38 ± 0.10	0.53 ± 0.20	<0.10	0.43 ± 0.11		
Palmitic acid	16:0	28.78 ± 2.00	32.71 ± 4.13	<0.05	30.12 ± 2.15	<0.10	
Stearic acid	18:0	17.50 ± 1.93	13.46 ± 2.17	<0.01	15.16 ± 2.46	<0.10	
Sum saturated FA		43.89 ± 5.49	46.92 ± 3.21		45.80 ± 2.53		
Palmitoleic acid	16:1ω7	0.51 ± 0.42	0.91 ± 0.42	<0.10	0.70 ± 0.56		
Oleic acid	18:1ω9	12.74 ± 1.83	19.73 ± 3.86	<0.01	16.04 ± 4.76	<0.05	
Eicosatrienoic acid	20:3ω9	0.18 ± 0.12	0.23 ± 0.12		0.23 ± 0.14		
Linoleic acid	18:2ω6	21.40 ± 3.69	20.60 ± 3.93		21.25 ± 2.57		
γ-Linolenic acid	18:3ω6	0.30 ± 0.05	0.15 ± 0.12		0.09 ± 0.10		<0.01
Eicosadienoic acid	20:2ω6	0.45 ± 0.08	0.30 ± 0.13	<0.05	0.20 ± 0.09	<0.10	<0.01
Dihomo-γ-linolenic acid	20:3ω6	3.38 ± 0.49	1.85 ± 1.04	<0.01	2.11 ± 1.00		<0.02
Arachidonic acid	20:4ω6	8.44 ± 2.42	5.67 ± 1.85	<0.01	5.54 ± 2.26		<0.05
Sum n-6-FA		33.74 ± 4.73	28.26 ± 4.15	<0.02	29.15 ± 3.04		<0.05
α-Linolenic acid	18:3ω3	0.17 ± 0.12	0.24 ± 0.11		0.20 ± 0.10		
Eicosatrienoic acid	20:3ω3	ND	ND		ND		
Eicosapentaenoic acid	20:5ω3	1.06 ± 0.55	1.26 ± 1.09		1.34 ± 1.16		
Docosapentaenoic acid	22:5ω3	0.99 ± 0.33	0.54 ± 0.23	<0.01	0.91 ± 0.35	<0.02	
Docosahexaenoic acid	22:6ω3	5.59 ± 1.11	3.52 ± 1.78	<0.05	4.99 ± 2.07	<0.05	
Sum n-3-FA		6.48 ± 3.06	5.03 ± 2.17		7.03 ± 2.72	<0.10	
Sum PUFA		40.25 ± 5.28	33.33 ± 4.53	<0.01	36.03 ± 4.44		
P/S-ratio		0.93 ± 0.14	0.71 ± 0.12	<0.01	0.79 ± 0.10		<0.05
Ratio	20:3ω9/20:4ω6	0.02 ± 0.01	0.04 ± 0.01		0.03 ± 0.01		
Ratio	18:2ω6/20:4ω6	2.74 ± 0.94	4.10 ± 1.80	<0.10	4.49 ± 2.04		<0.10
Ratio	18:2ω6/18:3ω6	63.37 ± 5.35	206.63 ± 168.21		323.87 ± 296.20		
Ratio	18:3ω6/20:3ω6	0.09 ± 0.03	0.09 ± 0.06		0.05 ± 0.03		
Ratio	20:3ω6/20:4ω6	0.42 ± 0.10	0.33 ± 0.15		0.67 ± 0.44		

Mean ± SD, weight %. ND = not detectable

Table 4. Comparison of values for oleic, linoleic and arachidonic acid in plasma lipids of nine children with kwashiorkor and eight children with marasmus

	Kwashiorkor ($n = 9$)	Marasmus ($n = 8$)
Sterolesters		
18:1ω9	31.15 ± 5.17	30.20 ± 5.65
18:2ω6	32.88 ± 8.97	33.41 ± 10.66
20:4ω6	3.26 ± 1.37	4.20 ± 1.89
Triglycerides		
18:1ω9	43.20 ± 6.89	39.97 ± 5.60
18:2ω6	14.65 ± 4.17	18.33 ± 5.95
20:4ω6	0.92 ± 0.37	0.93 ± 0.30
Phospholipids		
18:1ω9	20.85 ± 3.31	18.41 ± 3.53
18:2ω6	20.56 ± 3.29	20.64 ± 4.38
20:4ω6	4.94 ± 1.42	6.59 ± 1.80

There were no significant differences

in the early phase of recovery. To investigate possible differences between kwashiorkor and marasmus we concentrated on patients with these two syndromes only, that represent the two ends of a continous spectrum of pathological conditions resulting from malnutrition. In contrast to Wolff et al. [69], who reported lower values of linoleic acid in marasmus and of arachidonic acid in kwashiorkor, we did not find a clear difference although arachidonic acid tended to lower proportions – kwashiorkor in STE and PL (cf. Table 4). Our data are similar to the findings in South African kwashiorkor patients, in whom the linoleic acid desaturation was impaired before treatment and during rehabilitation [43]. In contrast, mean FA values in South American malnourished children did not indicate disturbed linoleic acid metabolism, but Holman et al. [35] state that half of their children had low values of arachidonic acid with normal or high linoleic acid levels. The different results may be explained by an on average more serious degree of PEM in the African children.

Elevation of ω-9-eicosatrienoic acid (20:3ω9) and of the 20:3ω9/20:4ω6 ratio are generally accepted indicators of EFA deficiency. In our PEM group 20:3ω9 showed only a slight and insignificant rise, and the mean 20:3ω9/20:4ω6-values

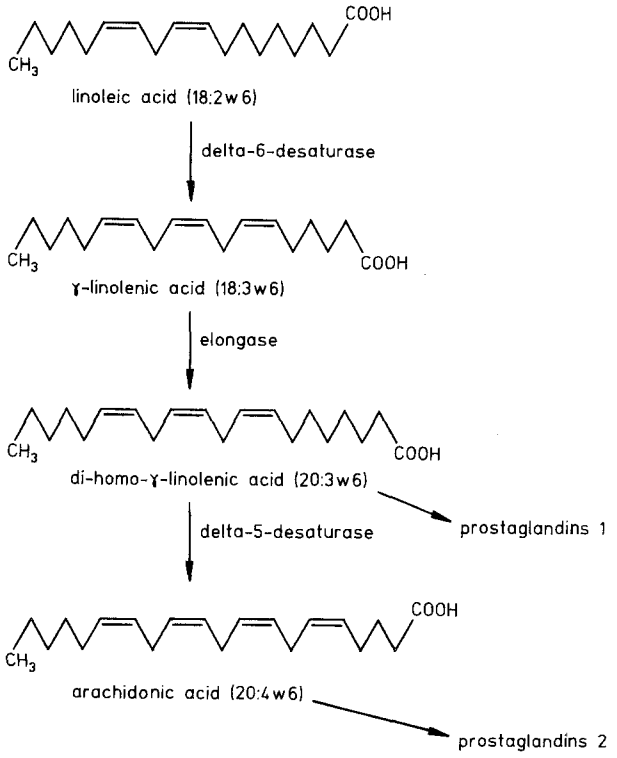

Fig. 1. Biosynthesis of arachidonic acid from linoleic acid. Delta-6-desaturase, the rate limiting key enzyme, appears to be impaired in protein-energy malnutrition

exceeded the normal range defined by Holman [34] as 0.03 ± 0.04 in STE and 0.22 ± 0.26 in TG, but not in PL (normal 0.10 ± 0.07; cf. Tables 1–3). However, in PEM, EFA deficiency is not necessarily accompanied by a marked rise of 20:3ω9. In healthy individuals linoleic acid competitively inhibits δ-6-desaturation of oleic acid and thereby formation of 20:3ω9, which is synthesised only in linoleic acid deficiency with intact activities of δ-5- and δ-6-desaturases [36, 38]. The PEM children were deficient not only in linoleic acid, but mainly in its metabolites with a higher biological value. Furthermore the activity of the desaturating enzyme system appears to have been impaired (cf. below), thus impeding 20:3ω9-synthesis.

A number of different factors may have contributed to the EFA deficiency of the malnourished children. Traditional weaning foods in Nigeria contain only 0.13 to 0.74 Cal% of linoleic acid [47], an amount that does not meet the requirements of the growing child [19]. In addition there is an impaired intestinal absorption of dietary lipids in the protein-energy malnourished child [26, 31, 61, 66, 68]. Triglyceride digestion is hindered by premature bile salt deconjugation and thus impaired micellular solubisation of lipids [53, 57] and by diminished production of pancreas lipase [3, 57, 62, 67]. Furthermore the jejunal absorptive surface area is decreased [44, 60]. The inadaequate supply cannot be compensated for, because the chronically malnourished child has only minor reserves of EFA, as it has consumed most of its body lipid stores.

These limited amounts of linoleic acid are not metabolised properly. The increased ratio 18:2ω6/20:4ω6 in PEM and in PEM recovery indicates an impaired biosynthesis of arachidonic acid from linoleic acid. The reactions of this pathway are catabolised by three enzymes (Fig. 1), of which δ-6-desaturase is the regulatory key enzyme with a low relative rate of conversion [6, 33]. The substrate-product ratio of this enzyme (18:2ω6/18:3ω6), though subject to a wide variation, shows increased values in PEM and PEM recovery, while there was no consistent elevation of the ratios for the elongase and the δ-5-desaturase (18:3ω6/20:3ω6 and 20:3ω6/20:4ω6 respectively; cf. /Tables 1–3). Thus we conclude that the activity of δ-6-desaturase was reduced in the malnourished children and in the early phase of recovery. In animal experiments this enzyme is inhibited by protein deficiency and by fasting [7, 17]. Also low insulin levels, which are found in untreated kwashiorkor and marasmus as well as for weeks and months after recovery [5, 37, 49] impair δ-6-desaturase [7]. A further important determinant is the deficiency of zinc common in PEM [12, 18, 24, 30, 41, 55, 58], that modulates enzymatic desaturation of linoleic acid [4, 11, 15, 28].

In addition to decreased intake and synthesis, increased oxidative decomposition of PUFA may contribute to the deficiency of EFA. Antioxidative means of protection are impaired in PEM: Both vitamin E and selenium, a cofactor of glutathionperoxidase, are low and remain so during refeeding [9, 22, 42, 54].

Possible consequences of EFA deficiency in PEM are not fully understood. EFA are precursors of prostaglandins, thromboxanes and leucotrienes and their deficiency may interfere with a number of regulatory processes. As essential components of PL, PUFA are part of all cell membranes, and their shortage may be one of the causes of the decreased cell membrane production observed in PEM [60]. In particular, the disturbance of red cell membrane lipids in PEM associated with a reduced red cell survival and the presence of target cells, which mimics the situation of patients with EFA deficiency due to cholestasis, could be correlated with this shortage [8, 13, 22]. The formation and function of lipoprotein structures may be altered and lead to fatty liver in PEM [13, 21, 63]. One of the most common clinical symptoms in PEM, the dry scaly dermatitis with a tendency to superinfection and increased water permeability, resembles the same lesion occurring in other forms of EFA-deficiency [20, 33, 48, 55]. Furthermore, lack of EFA may aggravate PEM and impede recovery by its impairment of nitrogen retention and utilisation of dietary calories [1, 46].

A number of questions remain to be answered. Though it appears sensible to include an adequate amount of linoleic acid in the form of vegetable fat, which is well tolerated and absorbed [16, 65], in the diet of PEM children, this dietary measure does not influence the disturbed linoleic-acid-metabolism.

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