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Docosahexaenoic Acid Status of Term Infants Fed Breast Milk or Infant Formula Containing Soy Oil or Corn Oil

DEBRA L. PONDER, SHEILA M. INNIS, JOHN D. BENSON, AND JOEL S. SIEGMAN

Medical Department, Pediatrics, Ross Laboratories, Columbus, Ohio 43215-1724; and Department of Pediatrics, University of British Columbia, Vancouver, Canada

ABSTRACT. The objective of this study was to compare circulating lipid docosahexaenoic acid [22:6(n-3), DHA] levels in term infants fed a powdered (CORN oil) or liquid (SOY oil) infant formula or human milk (HM). Infants whose mothers chose not to breast feed were randomly assigned to the CORN or SOY formula group. The formula fat differed in linolenic acid [18:3(n-3)] content: it was 0.8% for the CORN and 4.8% for the SOY. Linoleic acid [18:2(n-6)] was 31.5 and 34.2% fatty acids in the CORN and SOY formula, respectively. The formulas or HM were fed from birth through 8 wk of age, and growth and the plasma and red blood cell (RBC) phospholipid fatty acid composition was determined at 3 d, 4 wk, and 8 wk of age. Growth did not differ among groups. The plasma phospholipid and RBC phosphatidylethanolamine DHA was similar in the CORN and SOY formula groups at all ages. Plasma and RBC phosphatidylethanolamine levels of DHA were significantly lower in infants fed the CORN or SOY formula than in infants fed HM during wk 4 and 8. Plasma and RBC 22:5(n-6) was not increased in the formula groups at any age. The formula content of linolenic acid had no effect on the RBC or plasma DHA levels of the infants. The biologic or functional significance of the lower plasma and RBC DHA in infants fed formula rather than HM is unknown. The need for a dietary source of DHA and specificity of plasma or RBC phospholipid DHA as a measure of desaturation and elongation of linolenic acid in developing organs remains uncertain. (*Pediatr Res* 32: 683–688, 1992)

Abbreviations

DHA, docosahexaenoic acid or 22:6(n-3)
AA, arachidonic acid or 20:4(n-6)
RBC, red blood cell
HM, human milk
PE, phosphatidylethanolamine
PC, phosphatidylcholine
SOY, 40% coconut oil and 60% soy oil (liquid formula)
CORN, 50% corn oil and 50% coconut oil (powdered formula)
ERG, electroretinogram

The essentiality of linolenic acid 18:3(n-3) in human nutrition is now well accepted (1–7). The dietary requirements for infants, children, and adults are unknown, but suggested amounts have ranged from 0.2 to 1.0% of total dietary energy (1–3). Linolenic acid is the precursor of DHA, which is an important structural component of retinal, neural, and other cell membranes (8–10). The particularly high concentration of DHA in the excitable membranes of the CNS, such as the retina and synaptic terminals, has led to the belief that DHA is important for normal functioning of these membranes. Diets providing less than 0.08% kcal 18:3(n-3) have been shown to alter learning behavior and visual function in the rat (4, 7, 11–14) and visual function in nonhuman primates (5, 6). The control diets provided 0.3% or more 18:3(n-3) from vegetable oils as kcal, but they provided no preformed DHA and supported deposition of high levels of DHA in the growing CNS (6, 7, 11–14). The changes in learning behavior and visual function in the animals fed the diets deficient in 18:3(n-3) were accompanied by reduced DHA and increased 22:5(n-6) (docosapentaenoic acid) in the CNS lipids.

Lower levels of DHA have been reported in the RBC lipids of term and preterm infants fed formulas when compared with infants fed human milk (15–20). This has led to concern over the ability of the neonate to desaturate and elongate 18:3(n-3) to DHA. However, other information suggests that the percentage of DHA in RBC lipid reflects the intake of preformed DHA from the diet of adults (21, 22) and animals (23) as well as from HM or formula in infants (20, 24–26). Recent studies have also shown that the RBC levels of DHA in infants fed formula were within the range of breast-fed infants, when infants fed by women following both vegan and omnivorous diets were considered (26).

Corn and soy oils are frequently used as the source of linoleic acid [18:2(n-6)] in infant formulas and contain about 0.8–1.0% and 8–10% 18:3(n-3), respectively. Neither of these vegetable oils provide preformed DHA. Traditionally, many powdered infant formulas have contained corn rather than soy oil because of the susceptibility of the large amounts of 18:3(n-3) in soy oil to oxidative degradation (27). When blended with a source of saturated fatty acids, the 18:3(n-3) content of formulas containing corn oil as the only other oil is usually 0.7–1.3% fatty acids, compared with 3.9–5.1% 18:3(n-3) in formulas containing 40–50% fat as soy oil. Because corn and soy oils contain similar proportions of 18:2(n-6), the 18:2(n-6)/18:3(n-3) ratio of powdered and liquid formulas containing corn and soy oil differs, and is usually about 30:1 and 7:1, respectively. The effect of the formula content of 18:3(n-3), or 18:2(n-6)/18:3(n-3) ratio, on the plasma and RBC levels of DHA in infants has not been well established. This study, therefore, compared the plasma and RBC n-6 and n-3 fatty acid composition of term infants fed a liquid formula with 40% coconut oil and 60% soy oil (vol/vol) (SOY) with a similar powdered formula containing 50% corn oil and 50% coconut oil (vol/vol) (CORN) with that of infants fed HM from birth for 8 wk.

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Correspondence: Sheila M. Innis, Ph.D., The Research Centre, Department of Paediatrics, University of British Columbia, 950 W. 28th Ave., Vancouver, BC, V5Z 4H4 Canada.
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MATERIALS AND METHODS

Three groups of healthy term infants were the subjects in this 8-wk feeding study. The infants were enrolled and studied at the Children's Hospital of Philadelphia and the Pennsylvania Hospital, both in Philadelphia. The analyses of plasma and RBC fatty acids were done in Vancouver, British Columbia. The study protocol and parental consent form were approved by the Institutional Review Board of the Pennsylvania Hospital, and written parental consent was obtained for each subject. Infants of mothers who elected not to breast-feed were randomly assigned to either the SOY (Similac with Iron 20 ready-to-feed) or CORN (Similac with Iron 20 powder, Ross Laboratories, Columbus, OH) formula group. Breast-fed infants were enrolled concurrently. The formulas both contained 36.5 g fat/L, and they differed only in the fat blend. The CORN contained (% of fat blend) 50% corn oil and 50% coconut oil, and the SOY contained 60% soy oil and 40% coconut oil. The fatty acid composition of the formula fat (Table 1) differed primarily in the percentage of of 18:3(n-3) and 18:2(n-6)/18:3(n-3) ratio. The 18:3(n-3) content of the CORN and SOY formula was 0.8 and 4.5 g/100 g of total fatty acids (0.4 and 2.3% total energy), respectively. The 18:2(n-6)/18:3(n-3) ratio in the SOY formula was about 7:1 and in the CORN formula was 39:1.

Eligible infants were full-term, 37 to 42 wk of gestation at birth, with a weight, length, and head circumference between the 5th and 95th percentile of the National Center for Health Statistics reference data (28). No vitamin or mineral supplementation was given to the infants fed formula; breast-fed infants received routine vitamin D supplementation.

Infants were enrolled at birth, assigned to the feeding group, and followed for an additional 8 wk, during which they were fed exclusively the designated formula or breast milk. Formula intake was recorded on dietary records for the 3 d immediately preceding blood sampling at 4 and 8 wk. Formula intake from birth to 3 d of age was obtained from the hospital charts. Anthropometric measurements of crown-heel length, head circumference, and body weight were recorded, and a blood sample (2 mL) was collected by venipuncture with disodium EDTA (1.5 mg/mL) as the anticoagulant at 3 d, 4 wk, and 8 wk of age. Plasma was separated by centrifugation, and the RBC pellet was washed and plasma was recentrifuged twice with ice-cold normal saline. The plasma and RBC pellets were then frozen and shipped on dry ice to Vancouver, where they were kept in frozen storage (−70 to −80°C) until analysis. The plasma phospholipid and RBC PC and PE were prepared and analyzed for fatty acid composition as described in detail elsewhere (29). Samples of the breast milk were not available for fatty acid analyses in this study but have been extensively described for other North American women (30). The fatty acid composition of the formula was determined using published methods (31).

Table 1. *Select fatty acid composition of formulas and human milk**

	Fatty acid	Ready-to-feed (SOY)	Powder (CORN)	North American HM (range)†
Saturates	6:0	0.2	0.3	
	8:0	2.4	3.4	0.2–0.3
	10:0	2.1	2.9	0.97–1.6
	12:0	16.8	22.0	4.2–6.2
	14:0	7.0	8.8	5.7–7.6
	16:0	10.1	10.3	21–23
	18:0	4.6	2.4	7.7–9.0
	20:0	0.5	0.4	0.3–0.6
Monoenes	18:1	17.3	17.1	33–38
n-6	18:2	34.2	31.4	15–16
	18:3			Trace
	20:3			0.2–0.5
	20:3			0.3–0.6
	20:4			0.4–0.7
	22:4			0.07–0.2
	22:5			0.03–0.1
n-3	18:3	4.8	0.8	0.8–1.9
	20:5			Trace
	22:5			0.1
	22:6			0.1–0.3
n-6/n-3		7:1	39:1	7:1–18:1

* Data represent g/100 g.

† Data from references 18 and 30.

Two-way repeated-measures analyses of variance were used to test for diet group by age interactions in the anthropometric variates and the plasma and RBC fatty acids. The anthropometric variates were also analyzed by one-way analysis of variance for diet group differences at each individual time point. Kruskal-Wallis procedures were used to test for potential effects of diet at each age, and Friedman's procedures were used to test for effects of age within each diet group on the plasma and RBC fatty acids. When diet group and/or age differences were identified, Tukey's multiple comparison procedures were used in pairwise comparisons to test for statistically significant differences. p values for all tests considered significant are provided in the tables and were based on two-tailed tests.

RESULTS

Forty-three infants successfully completed the study and were included in the data analyses: 18 in the HM, 11 in the SOY, and 14 in the CORN group. Birth weight, Apgar score, and gestational age were not significantly different among the three groups of infants. The weight, length, and head circumference measurements were not significantly different among the groups at any time in the study (Table 2). The intake of the CORN and SOY formulas was similar, with the mean intake over the 8-wk study, ranging between 101 and 125 kcal/kg/d in both formula groups (data not shown).

The fatty acid composition of the infants' phospholipids, and RBC PE and PC after 3 d, 4 wk, and 8 wk feeding is given in Tables 3, 4, and 5, respectively. Time-dependent changes that occurred in all diet groups included a significant increase in 18:3(n-6) and decrease in AA and DHA in the plasma phospholipid, and a significant increase in the percentage of 18:2(n-6) and decrease in the percentage of DHA in the RBC PC and PE. A significant decrease in the percentage of 20:3(n-6) in the RBC PC and an increase in the percentage of 22:5(n-3) in the RBC PE was also found.

The difference in 18:3(n-6) intake among the formula-fed and breast-fed infants was not accompanied by any significant difference in the infants' plasma phospholipid or RBC PE or PC 18:3(n-3) (Tables 3–5). The percentages of DHA in the circulating lipids of infants fed the CORN and SOY formulas were also similar despite the 6-fold difference in 18:3(n-3) intake. Both groups of formula-fed infants had significantly lower levels of DHA in plasma phospholipids at 4 and 8 wk, and in RBC PC and PE at 8 wk, than the breast-fed infants. No consistent significant differences in the percentage of other C20 or 22 (n-3) fatty acids were found among the groups of infants in the lipids analyzed or between the 4- and 8-wk samples. The plasma phospholipid percentage of 20:5(n-3) was significantly lower at 4 wk, but higher at 8 wk, in infants fed the CORN compared with those fed the SOY formula. The percentage of 20:5(n-3), however, was not significantly different in the RBC PC or PE between the two groups of formula-fed infants at any time. Levels of 20:5(n-3), 22:4(n-3), and 22:5(n-3) in plasma and RBC phospholipids were similar in breast-fed infants and infants fed the SOY formula at 4 and 8 wk, except for a significantly lower percentage of 20:5(n-3) in the RBC PC of the SOY than breast-fed infants

Table 2. *Anthropometric measurements**

	Day 3			Week 4			Week 8		
	HM (n = 18)	SOY (n = 11)	CORN (n = 14)	HM (n = 18)	SOY (n = 11)	CORN (n = 14)	HM (n = 18)	SOY (n = 11)	CORN (n = 14)
Weight (g)	3407 ± 103	3119 ± 132	3239 ± 69	4398 ± 92	4127 ± 148	4296 ± 114	5184 ± 124	5101 ± 148	5145 ± 142
Length (cm)	51.3 ± 0.3	50.0 ± 0.6	50.0 ± 0.5	55.3 ± 0.5	53.5 ± 0.8	53.1 ± 0.3	57.8 ± 0.5	56.5 ± 0.6	56.8 ± 0.5
Head circumference (cm)	34.9 ± 0.3	33.4 ± 0.3	34.3 ± 0.3	37.6 ± 0.3	36.6 ± 0.3	37.0 ± 0.4	39.1 ± 0.3	38.5 ± 0.2	38.9 ± 0.4

* Mean ± SEM.

Table 3. *Plasma phospholipid fatty acid composition*

	Day 3*			Week 4*			Week 8*			Statistics (p value)		
Fatty acid	HM	SOY	CORN	HM	SOY	CORN	HM	SOY	CORN	Diet	Age	Diet × Age
n-6 series												
18:2	11.0 ± 1.0^{b}	17.4 ± 2.1^{a}	15.7 ± 1.3^{a}	20.3 ± 0.9^{b}	28.3 ± 1.3^{a}	26.5 ± 1.3^{a}	21.9 ± 1.1^{b}	28.1 ± 0.7^{a}	27.3 ± 0.9^{a}	<0.01	<0.001	NS
18:3	0.2 ± 0.1	0.1 ± 0.0	0.1 ± 0.0	0.1 ± 0.0^{a,b}	0.1 ± 0.0^{b}	0.2 ± 0.1^{a}	0.1 ± 0.0^{a,b}	0.1 ± 0.0^{b}	0.2 ± 0.0^{a}	<0.05	NS	NS
20:2	0.2 ± 0.0	0.2 ± 0.0	0.2 ± 0.0	0.2 ± 0.0	0.1 ± 0.0	0.2 ± 0.1	0.2 ± 0.0	0.1 ± 0.0	0.2 ± 0.0	NS	NS	NS
20:3	2.8 ± 0.2^{a}	2.2 ± 0.3^{b}	1.9 ± 0.1^{b}	3.0 ± 0.2^{a}	2.3 ± 0.1^{b}	2.2 ± 0.1^{b}	2.7 ± 0.2^{a}	1.9 ± 0.1^{b}	2.1 ± 0.2^{b}	<0.01	NS	NS
20:4	17.5 ± 0.5	14.4 ± 1.4	15.3 ± 1.1	12.5 ± 0.5^{a}	8.7 ± 0.4^{b}	9.6 ± 0.7^{b}	11.9 ± 0.6^{a}	7.3 ± 0.4^{b}	8.8 ± 0.4^{b}	<0.001	<0.001	NS
22:4	1.0 ± 0.1	0.9 ± 0.1	0.9 ± 0.1	0.8 ± 0.1	0.8 ± 0.1	0.9 ± 0.1	0.7 ± 0.1	0.8 ± 0.1	0.8 ± 0.1	NS	NS	NS
22:5	1.0 ± 0.1	0.8 ± 0.3	0.8 ± 0.2	1.0 ± 0.1	0.8 ± 0.1	0.7 ± 0.1	1.0 ± 0.1^{a}	0.7 ± 0.1^{a,b}	0.6 ± 0.1^{b}	<0.05	NS	NS
n-3 series												
18:3	0.6 ± 0.1	0.7 ± 0.1	0.6 ± 0.1	0.6 ± 0.0	0.6 ± 0.0	0.6 ± 0.1	0.6 ± 0.1	0.7 ± 0.1	0.7 ± 0.1	NS	NS	NS
18:4	0.1 ± 0.0	0.1 ± 0.0	0.1 ± 0.0	0.1 ± 0.0	0.1 ± 0.0	0.1 ± 0.0	0.1 ± 0.0^{b}	0.1 ± 0.0^{a}	0.1 ± 0.0^{a,b}	<0.05	NS	NS
20:5	0.6 ± 0.1	0.5 ± 0.1	0.5 ± 0.1	0.6 ± 0.1^{a,b}	0.8 ± 0.1^{a}	0.3 ± 0.1^{b}	0.6 ± 0.1^{a}	0.7 ± 0.1^{a}	0.2 ± 0.1^{b}	<0.01	NS	<0.05
22:4	1.1 ± 0.1	1.5 ± 0.2	1.5 ± 0.2	0.8 ± 0.1^{b}	0.9 ± 0.2^{b}	1.2 ± 0.1^{a}	1.0 ± 0.1	0.9 ± 0.2	1.1 ± 0.1	<0.05	NS	<0.10
22:5	0.5 ± 0.0	0.4 ± 0.1	0.5 ± 0.1	0.8 ± 0.1^{a}	0.8 ± 0.1^{a}	0.5 ± 0.1^{b}	0.9 ± 0.1^{a}	0.8 ± 0.1^{a}	0.4 ± 0.1^{b}	<0.01	<0.001	<0.001
22:6	5.3 ± 0.2^{a}	3.7 ± 0.4^{b}	4.4 ± 0.4^{a,b}	3.9 ± 0.2^{a}	2.8 ± 0.1^{b}	2.4 ± 0.3^{b}	4.0 ± 0.3^{a}	2.3 ± 0.2^{b}	2.2 ± 0.3^{b}	<0.01	<0.01	NS

* Values are expressed as g/100 g (means ± SEM). Values with like superscripts are not significantly different and refer only to diet effects at the time point indicated. Age effects are discussed in the text.

Table 4. *RBC PC fatty acid composition*

	Day 3*			Week 4*			Week 8*			Statistics (p value)		
Fatty acid	HM	SOY	CORN	HM	SOY	CORN	HM	SOY	CORN	Diet	Age	Diet × Age
n-6 series												
18:2	8.7 ± 0.6	12.6 ± 2.5	10.1 ± 1.0	15.6 ± 0.8^{b}	21.3 ± 0.8^{a}	20.9 ± 1.1^{a}	16.1 ± 0.6^{b}	20.7 ± 0.8^{a}	21.0 ± 1.0^{a}	<0.001	<0.05	NS
18:3	0.1 ± 0.0	0.1 ± 0.0	0.1 ± 0.0	0.1 ± 0.0	0.2 ± 0.0	0.2 ± 0.1	0.2 ± 0.1	0.1 ± 0.0	0.1 ± 0.0	NS	<0.05	<0.10
20:2	0.2 ± 0.0	0.2 ± 0.1	0.2 ± 0.0	0.1 ± 0.0	0.2 ± 0.1	0.2 ± 0.0	0.2 ± 0.0	0.2 ± 0.0	0.2 ± 0.1	NS	NS	NS
20:3	2.2 ± 0.1^{a,b}	2.0 ± 0.3^{b}	2.7 ± 0.2^{a}	1.7 ± 0.1	1.8 ± 0.1	1.7 ± 0.2	1.7 ± 0.1	1.6 ± 0.2	1.3 ± 0.1	<0.05	<0.01	<0.01
20:4	10.9 ± 0.6	9.5 ± 1.3	12.9 ± 0.6	7.7 ± 0.5^{a}	6.2 ± 0.8^{b}	6.5 ± 0.6^{a,b}	7.5 ± 0.7	7.4 ± 0.9	7.1 ± 0.7	<0.05	<0.001	<0.10
22:4	0.8 ± 0.1	1.0 ± 0.1	1.1 ± 0.1	1.1 ± 0.1	0.9 ± 0.2	1.2 ± 0.3	0.9 ± 0.1	1.3 ± 0.3	0.7 ± 0.1	NS	NS	<0.10
22:5	0.3 ± 0.1	0.5 ± 0.1	0.5 ± 0.1	0.3 ± 0.1	0.7 ± 0.2	0.4 ± 0.1	0.3 ± 0.1	0.5 ± 0.2	0.6 ± 0.2	NS	NS	NS
n-3 series												
18:3	0.7 ± 0.1	0.7 ± 0.1	0.6 ± 0.1	0.8 ± 0.0	1.1 ± 0.1	0.6 ± 0.1	1.0 ± 0.1	1.0 ± 0.2	0.6 ± 0.1	NS	NS	NS
18:4	0.1 ± 0.0	0.1 ± 0.0	0.1 ± 0.0	0.1 ± 0.0	0.1 ± 0.1	0.1 ± 0.0	0.1 ± 0.0	0.1 ± 0.0	0.1 ± 0.0	NS	NS	NS
20:5	0.4 ± 0.1	0.4 ± 0.1	0.6 ± 0.1	0.4 ± 0.1	0.5 ± 0.1	0.7 ± 0.2	0.7 ± 0.1^{a}	0.4 ± 0.1^{b}	0.3 ± 0.0^{b}	<0.01	NS	<0.01
22:4	0.6 ± 0.1	0.6 ± 0.1	0.6 ± 0.1	0.7 ± 0.1	0.7 ± 0.2	0.7 ± 0.2	0.7 ± 0.1	1.0 ± 0.3	0.4 ± 0.1	NS	NS	NS
22:5	0.6 ± 0.2	0.4 ± 0.1	0.4 ± 0.1	0.6 ± 0.1^{a}	0.5 ± 0.1^{a,b}	0.4 ± 0.1^{b}	0.5 ± 0.1^{a,b}	0.6 ± 0.1^{a}	0.3 ± 0.1^{b}	<0.05	NS	NS
22:6	2.8 ± 0.2	1.9 ± 0.3	2.8 ± 0.1	2.1 ± 0.2	1.6 ± 0.2	1.5 ± 0.2	2.2 ± 0.2^{a}	1.3 ± 0.2^{b}	1.0 ± 0.2^{b}	<0.001	<0.05	<0.05

* Values are expressed as g/100 g (means ± SEM). Values with like superscripts are not significantly different and refer only to diet effects at the time point indicated. Age effects are discussed in the text.

at 8 wk. The plasma and RBC lipid (n-3) fatty acids were similar in the infants fed the CORN formula and those who were breast-fed, with the exception of significantly lower levels of 22:5(n-3) in the plasma phospholipid and RBC PE at 4 and 8 wk and in the RBC PC at 4 wk in infants fed the CORN formula.

Both groups of formula-fed infants had significantly higher levels of 18:2(n-6) in their plasma phospholipids than infants fed HM. This was evident as early as 3 d of age, and the difference continued and increased with the duration of formula feeding to 8 wk (Table 3). Plasma phospholipid levels of AA did not differ between infants fed the SOY and CORN formulas at any time, but were significantly lower than in the breast-fed infants at 4 and 8 wk. As in the plasma phospholipids, the RBC PC and PE percentages of 18:2(n-6) were similar in the SOY and CORN groups, and higher than in the breast-fed group at 4 and 8 wk. No significant differences, however, were found in the percentage of 20:4(n-6) in the RBC PE or PC among the diet groups at 8 wk. After 4 wk of feeding, the RBC PC but not PE percentage of AA was significantly lower in the SOY than in the breast-fed group. No differences in the plasma or RBC percentages of 22:5(n-6) were found among the diet groups at any time, with the single exception of a significantly lower percentage of 22:5(n-

Table 5. *RBC PE fatty acid composition*

Fatty acid	Day 3*			Week 4*			Week 8*			Statistics (p value)		
	HM	SOY	CORN	HM	SOY	CORN	HM	SOY	CORN	Diet	Age	Diet × Age
n-6 series												
18:2	2.7 ± 0.1	3.5 ± 0.5	2.7 ± 0.2	4.9 ± 0.4^{b}	9.2 ± 0.5^{a}	7.3 ± 0.6^{a}	6.2 ± 0.5^{b}	10.2 ± 0.4^{a}	9.0 ± 0.5^{a}	<0.001	<0.001	<0.001
18:3	0.2 ± 0.1	0.2 ± 0.0	0.2 ± 0.1	0.1 ± 0.0	0.3 ± 0.1	0.2 ± 0.0	0.2 ± 0.1	0.2 ± 0.0	0.2 ± 0.1	NS	NS	NS
20:2	0.1 ± 0.0	0.1 ±0.0	0.1 ± 0.0	0.2 ± 0.0	0.2 ± 0.1	0.1 ± 0.0	0.1 ± 0.0	0.2 ± 0.1	0.2 ± 0.0	NS	NS	NS
20:3	1.5 ± 0.1	1.7 ± 0.1	1.7 ± 0.1	1.2 ± 0.1^{b}	1.5 ± 0.1^{a}	1.7 ± 0.2^{a}	1.3 ± 0.1^{b}	1.9 ± 0.1^{a}	1.8 ± 0.2^{a}	<0.01	<0.05	NS
20:4	24.0 ± 0.9	24.3 ± 0.9	24.5 ± 1.2	23.0 ± 0.7	20.0 ± 1.2	22.3 ± 1.1	22.3 ± 0.7	22.4 ± 1.0	23.4 ± 0.6	NS	<0.01	NS
22:4	7.9 ± 0.3	7.8 ± 0.5	8.2 ± 0.4	7.5 ± 0.2^{a}	6.3 ± 0.4^{b}	8.3 ± 0.4^{a}	7.3 ± 0.2^{b}	7.1 ± 0.3^{b}	9.1 ± 0.4^{a}	<0.01	NS	<0.01
22:5	3.1 ± 0.2	3.0 ± 0.3	3.0 ± 0.2	2.8 ± 0.2	2.4 ± 0.3	2.7 ± 0.2	2.5 ± 0.2	2.0 ± 0.2	2.5 ± 0.2	NS	<0.01	NS
n-3 series												
18:3	0.5 ± 0.0	0.5 ± 0.1	0.5 ± 0.1	0.5 ± 0.1	0.6 ± 0.1	0.4 ± 0.6	0.6 ± 0.1	0.7 ± 0.2	0.5 ± 0.0	NS	NS	NS
18:4	0.1 ± 0.0	0.1 ± 0.0	0.1 ± 0.0	0.1 ± 0.0	0.2 ± 0.1	0.1 ± 0.0	0.2 ± 0.1	0.2 ± 0.1	0.0 ± 0.0	NS	NS	NS
20:5	0.5 ± 0.1	0.6 ± 0.1	0.6 ± 0.1	0.5 ± 0.1	0.7 ± 0.1	0.4 ± 0.1	0.7 ± 0.1	0.5 ± 0.1	0.5 ± 0.01	NS	<0.05	<0.10
22:4	0.8 ± 0.1	0.6 ± 0.1	0.6 ± 0.1	0.9 ± 0.1	0.9 ± 0.2	0.7 ± 0.1	0.9 ± 0.1	0.6 ± 0.1	0.6 ± 0.1	NS	NS	NS
22:5	1.0 ± 0.1	1.0 ± 0.1	1.0 ± 0.1	1.5 ± 0.1^{a}	1.2 ± 0.1^{a,b}	1.1 ± 0.1^{b}	2.3 ± 0.2^{a}	2.3 ± 0.2^{a}	1.5 ± 0.2^{b}	<0.01	<0.01	<0.01
22:6	9.0 ± 0.3	7.9 ± 0.7	8.9 ± 0.6	8.4 ± 0.3^{a}	6.1 ± 0.4^{b}	7.4 ± 0.4^{a,b}	8.0 ± 0.4^{a}	5.2 ± 0.3^{b}	6.1 ± 0.4^{b}	<0.001	<0.05	<0.10

* Values are expressed as g/100 g (means ± SEM). Values with like superscripts are not significantly different and refer only to diet effects at the time point indicated. Age effects are discussed in thet text.

6) in the plasma phospholipids of the CORN compared with the breast-fed group at wk 8.

DISCUSSION

The primary focus of analysis in this study was comparison of (n-3) and (n-6) fatty acids in the circulating lipids of healthy term infants fed a formula containing CORN oil or SOY oil as the source of unsaturated fat in relation to breast-fed infants. The fatty acid composition of plasma and RBC phospholipids is often used in clinical studies to assess possible essential fatty acid status. The relationship of the percentage of content of AA and DHA in plasma or RBC phospholipid fatty acids to that in CNS membranes, or to CNS functions, such as visual acuity, learning, or other cognitive processes, has not been fully established. Reduced levels of DHA have been found in RBC and plasma phospholipids, as well as in CNS lipids, of animals fed diets containing very low amounts of 18:3(n-3) (5, 6, 11–13, 32). It is known that RBC phospholipids and their fatty acids turn over during the lifetime of the mature cell in the circulation. This turnover is the result of exchange of intact phospholipids, which occurs on the outer membrane surface, and fatty acid turnover by deacylation-reacylation, which occurs predominantly on the inner membrane surface (33). PC is mainly found on the outer membrane surface of the RBC (76% of the total RBC PC), whereas PE is found predominantly on the cytosolic surface (80% of the total RBC PE) (33). Compatible with this are the results of these studies, which show that diet-related changes in circulating lipid fatty acids of infants in relation to HM or formula feeding were reflected first in the plasma phospholipid, which is almost entirely PC, then in the RBC PC, followed by the RBC PE.

Competition between 18:2(n-6) and 18:3(n-3) for desaturation to AA and DHA, respectively, is known (34). Despite the 6-fold difference in the formula supply of 18:3(n-3) and difference in 18:2(n-6)/18:3(n-3) ratio of 39:1 in the CORN and 7:1 in the SOY formula, the plasma phospholipid, RBC PE, and RBC PC levels of 20:4(n-6) did not differ between the two groups of formula-fed infants. Lower blood lipid levels of DHA in formula-fed infants than in breast-fed infants have been reported by others (15–20). This study confirmed this and found no difference in the circulating lipid levels of DHA as a result of the difference in 18:3(n-3) content of the CORN and SOY formulas. These results, therefore, suggest that the formula intake of 18:3(n-3) or 18:2(n-6)/18:3(n-3) ratio over the range of 7:1 to 39:1 studied is not a significant determinant of the circulating lipid levels of AA or DHA in formula-fed infants.

The lower RBC PE percentage of DHA found in infants fed the SOY and CORN formulas than in infants in the HM group suggests that a preformed source of DHA is needed in formula to achieve circulating lipid levels of DHA similar to that of infants fed HM. Whether or not plasma or RBC levels of DHA in infants are an accurate index of the amount of DHA deposited in growing membrane lipids or of the conversion of 18:3(n-3) to DHA in important organs is a subject of controversy. Lower blood lipid levels of DHA similar to or possibly even lower than that in formula-fed infants have been found in breast-fed infants whose mothers followed vegan diets lacking in preformed DHA rather than mixed diets with DHA (26). Functional measures, such as ERG or acuity card testing of visual function or other measures of cognitive development have not been reported for infants fed HM of varying DHA content. No information is available to suggest any deleterious effect on infant growth and development due to the low levels of DHA in some HM.

Studies in rhesus monkeys have shown impaired visual transduction, evidenced by delayed peak latency and response recovery in ERG recordings, and reduced visual acuity as a result of feeding a semipurified diet containing safflower oil from before conception throughout pregnancy and infancy. The safflower oil diet provided about 0.08% total energy as 18:3(n-3) and led to lower plasma, erythrocyte, retina, and brain phospholipid levels of DHA than those in monkeys fed the soy oil (control) diet with about 2.12% total energy as 18:3(n-3), with no preformed DHA. Studies in developing rodents have also found visual abnormalities and altered learning behavior as a result of feeding diets with 0.08% kcal 18:3(n-3) through two generations (11). Diets supplying 0.3% or more energy as 18:3(n-3), however, seemed adequate to support maximum assimilation of DHA in the developing rat brain (11), which in comparison to the human brain is very immature at birth (35). The CORN and SOY formulas fed to the term gestation infants from birth in this study provided about 0.4% and 2% kcal as 18:3(n-3), respectively.

An increase in 22:5(n-6) in CNS and other organ phospholipids is a characteristic finding in nonhuman primates, piglets, and rodents fed diets deficient in 18:3(n-3) (5, 6, 11–13, 36). No increase in 22:5(n-6) was found in the circulating lipids of infants fed the formulas in this study. The plasma phospholipid levels of DHA in rhesus monkeys with visual abnormalities were 0.23 ± 0.03 and 0.14 ± 0.02% fatty acids at 8 and 12 wk of age, respectively (5). The plasma phospholipid percentage of DHA was 2.3 ± 0.2 and 2.2 ± 0.3% fatty acids, respectively, in infants

fed the SOY and CORN formula for 8 wk. These levels are similar to those of the 2.67 ± 0.18% DHA in the plasma phospholipids of the monkeys fed the SOY formula diet and which exhibited apparently normal visual function and ERG patterns (5, 6). In the study reported here, the RBC PE percentage of DHA in formula-fed infants was 5.2 to 6.1% total fatty acids and, in the breast-fed infants, was about 8.0% fatty acids. It seems possible that the decrease in circulating lipid DHA found during the course of feeding infants with the formulas may therefore be explained by exchange of the RBC lipids fatty acids with absorbed formula fat. There are at present no data on the levels of 18:3(n-3) or DHA needed in circulating lipids to support optimum uptake and accumulation of (n-3) fatty acids in the developing CNS.

Studies in other species have suggested that 18:3(n-3) given in sufficient quantities can support adequate tissue synthesis and acylation of DHA (5, 6, 11–13). Preformed dietary 20:5(n-3) and DHA, however, seem to be quantitatively more effective than 18:3(n-3) as a source of DHA for developing brain, retina, and liver (37). This is most likely explained by efficient mitochondrial oxidation of 18:3(n-3) (38) and preferential acylation of DHA into structural lipids. Oxidation of 20:5(n-3) and DHA is known to occur in peroxisomes (39, 40), and the activity of the mitochondrial carnitine acyltransferase with these fatty acids is low (41). A factor to equate the bioactivity of dietary 18:3(n-3) with DHA has not yet been established. Because the available information seems to suggest that circulating lipid levels of DHA reflect the diet intake of preformed DHA and are not necessarily a reflection of the synthesis of DHA in organs after different intakes of 18:3(n-3), it will be difficult to determine dietary requirements for 18:3(n-3) from fatty acid analyses of plasma or RBC lipids. Combined biochemical and functional tests seem to be needed to establish the adequacy of the n-3 fatty acid content of formula feedings and the dietary requirements of infants for particular n-6 and n-3 fatty acids.

Conclusion. There were no statistically significant differences in the percentages of DHA in the plasma or RBC PC and PE between infants fed formula with 4.8% 18:3(n-3) (2.0% energy) from SOY oil and infants fed formula with 0.8% 18:3(n-3) (0.4% energy) from CORN oil. Infants fed formula had significantly lower plasma and RBC DHA than infants fed HM. The biologic significance of the lower plasma and RBC DHA levels in term gestation formula-fed infants compared with breast-fed infants is unknown. The results suggest preformed DHA will need to be added to formula fats if levels of DHA in the circulating lipids of formula-fed infants similar to those in breast-fed infants are to be achieved. However, the extent of desaturation-elongation of 18:3(n-3) to DHA in tissues of infants fed the CORN and SOY formulas is not known. The need for preformed DHA in infant diets remains an important question. Evaluation of the adequacy of the n-3 fatty acid content of formulas, however, requires functional as well as biochemical measures.

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Announcement

Annual Meeting of the Society for Adolescent Medicine

The Society for Adolescent Medicine, a multidisciplinary professional organization, will hold its annual meeting March 18–21, 1993, at the Hilton Hotel, Chicago, IL. The theme of the meeting will be "Interfacing of Health and Education." In addition to addressing this topic, the meeting will present new material on a broad range of issues important to adolescent physical and emotional health, including AIDS and HIV medical management, teenage sexuality, eating disorders, depression, and risk taking behaviors such as drug and alcohol use and abuse. Meeting presentations include all-day institutes, 3-hour clinically oriented workshops, luncheon seminars, scientific research paper presentations and poster sessions, as well as the prestigious Gallagher Lecture Series. CME/CEUs are available. *For additional information, contact* the Society for Adolescent Medicine, Suite 120, 19401 E. U.S. Highway 40, Independence, MO 64055, (816) 795-8336.