A Randomized Trial of Visual Attention of Preterm Infants Fed Docosahexaenoic Acid Until Two Months[1]

Susan E. Carlson[a–c,*] and Susan H. Werkman[a,b]

Departments of [a]Pediatrics, [b]Obstetrics and Gynecology, and [c]Biochemistry, The University of Tennessee, Memphis, Memphis, Tennessee 38163

ABSTRACT: This was a randomized, double-blind trial to determine if a nutrient-enriched (preterm) formula supplemented with 0.2% docosahexaenoic acid (DHA, 22:6n-3) from a low eicosapentaenoic acid (0.06%) source of marine oil would enhance visual novelty preference and attention of preterm infants. Both the standard and experimental formulas contained 3% of total fatty acids as linolenic acid (18:3n-3) and were fed from approximately three days of age to two months past term. After two months, both diet groups were fed a commercially-available term formula with linolenic acid as the only source of n-3 fatty acid. At 12 mo visual recognition memory (novelty preference) and visual attention (number and duration of discrete looks) were determined with the Fagan Test of Infant Intelligence. The DHA-supplemented group compared with the control group had more and shorter duration looks in comparisons of familiar and novel stimuli, confirming earlier evidence that DHA can increase information processing speed of preterm infants who otherwise are receiving good intakes of linolenic acid. Because supplementation was stopped at two months and the effects seen at 12 mon, this study demonstrates for the first time that a relatively short period of DHA supplementation can produce significant effects on later visual attention.
Lipids 31, 85–90 (1996).

Earlier we tested the hypothesis that preterm infants fed an infant formula supplemented with a marine oil source of docosahexaenoic acid (DHA) would have enhanced visual and neural development compared with infants fed linolenic acid as their sole source of n-3 fatty acids. The DHA-supplemented group had higher preferential looking grating acuity at two and four months (1,2) and more (3,4) and shorter duration looks (4) during paired comparisons of novel and familiar stimuli at 6.5, 9, and 12 mon. Both higher visual acuity (5) and shorter look duration during paired comparisons of familiar and novel stimuli (6) are analogous to observations made in monkey infants with better DHA status, i.e., those fed linolenic acid-replete compared with linolenic acid-deficient diets. A major difference between the monkey infant studies and our randomized trial in preterm infants, however, was that the group of infants with poorer DHA status were fed good intakes of linolenic acid, i.e., 1.2 and 2.4% of energy intake before and after two months of age, respectively.

Although these data suggested that DHA was conditionally essential for normal visual and neural outcomes of preterm infants, growth, another planned outcome of the trial, was adversely affected by long-term DHA supplementation (7). DHA supplementation decreased plasma and red blood cell (RBC) phospholipid arachidonic acid (AA) (20:4n-6) (8), and plasma phosphatidylcholine AA, a marker of AA status, was highly correlated with first-year growth (9). The current trial provided the DHA-supplemented group with a lower eicosapentaenoic acid (EPA, 20:5n-3) source of marine oil DHA for a shorter period of time than our first trial (4), with the intent of minimizing the effect of n-3 long-chain polyunsaturated fatty acids on AA status and growth (10). As a result, the experimental group in this study received formula with the same amount of DHA (0.2%) but with only half as much long-chain n-3 fatty acid (0.26% instead of 0.5%). Infants were fed their assigned formulas until two months past term, and the effects of DHA supplementation on visual attention later in infancy are reported here.

EXPERIMENTAL PROCEDURES

Subject selection. Fifty-nine infants randomly assigned to treatment constituted the final study population in this, our second, double-blind study of the effects of DHA supplementation on preterm infants. The selection criteria for infants in the total sample have been reported in detail (10). Briefly, this was a group of infants weighing between 747 and 1275 g at birth who met the strict criteria for eligibility used in our earlier trial (4), except for having an incidence of bronchopulmonary dysplasia (BPD) or chronic lung disease of ~40%, typical of infants in this birth weight range. The diagnosis of BPD was based on a continuous requirement for supplemental oxygen at 28 d of age and the presence of characteristic radiologic signs of BPD. At 12 mon, a subset of 27 of these infants (12 control, 15 DHA-supplemented) received the same version of the Fagan Test of Infant Intelligence administered in our earlier trial. Their results are included in this report, and their neonatal/perinatal characteristics are shown in Table 1.

[1]Based on a presentation at the AOCS Annual Meeting & Expo in San Antonio, Texas, May 7–11, 1995.

*To whom correspondence should be addressed at Newborn Center, Room 201, 853 Jefferson Ave., Memphis, TN 38163.

Abbreviations: AA, arachidonic acid; BPD- bronchopulmonary dysplasia; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; PE, phosphatidylethanolamine; PMA, postmenstrual age; RBC, red blood cell.

TABLE 1
Neonatal and Perinatal Characteristics of Infants Randomly Assigned to Receive Commercially Available Formulas (control) or These Formulas with Added Marine Oil–Docosahexaenoic Acid (DHA-supplemented)

Variable	Control (n = 12)	DHA-supplemented (n = 15)
Birth weight (g)	1050 ± 149[a]	1027 ± 153
Gestational age (wk)	28.2 ± 1.5	27.9 ± 1.5
Black/white	10/2	15/0
Male/female	7/5	8/7
Apgar at 5 min	7.0 ± 1.6	7.1 ± 1.4
Gravida (number)[a]	3.1 ± 1.2	2.5 ± 1.2
Mother's education (yr)	11.9 ± 1.4	12.0 ± 1.0
Father's education (yr)	12.0 ± 1.4	12.2 ± 1.3
Ventilator (h)[b]	72 ± 5	65 ± 10
Total oxygen (h)[b]	261 ± 6	154 ± 9
First formula (h)	86 ± 72	92 ± 33
Age at enrollment (d)	3 ± 1	3 ± 1
Weight at enrollment (d)	1001 ± 189	965 ± 160
Two-month RBC PE DHA[c,d]	3.9 ± 0.7	7.6 ± 0.9
Weight at two months (kg)	4.93 ± 0.8	4.56 ± 0.5

[a]Mean ± SD.
[b]Because ventilator and total oxygen were not normally distributed, the individual values were transformed to $\log_{10}$ to approximate a normal distribution. The log hours ($X \pm$ SD) were calculated for each dietary group and the antilog taken to reach $X \pm$ SD (h).
[c]Red blood cell phosphatidylethanolamine (RBC PE) DHA at two months as a percent of total fatty acids (g/100 g).
[d]$P < 0.05$ for a difference between diet groups.

TABLE 2
Formula Fatty Acid Composition (g/100 g total fatty acids)[a]

	Preterm formula		Term formula
	Control	DHA-supplemented	
Fatty acid	3 d to 2 mon	3 d to 2 mon	2–12 mon
8:0	28.1	28.0	2.6
10:0	15.9	15.7	2.1
12:0	7.8	7.8	17.5
14:0	3.3	3.3	7.2
16:0	6.5	6.5	10.2
18:0	3.2	3.2	4.2
18:1	11.0	11.0	16.1
18:2n-6	21.2	21.2	34.3
18:3n-3	2.4	2.4	4.8
20:5n-3	—	0.06	—
22:6n-3	—	0.2	—

[a]The preterm formulas contained 812 kcal/L and were fed until two months past expected term when infants weighed ~4.8 kg. All infants received an unsupplemented term formula with 676 kcal/L from 2 until 12 mon past expected term. Abbreviation as in Table 1.

Experimental design. Consent for the study was obtained according to a protocol approved by the Institutional Review Board of The University of Tennessee, Memphis. Only parents who stated that they planned to feed infant formula were approached for permission to enroll their infant in this study. Infants were randomly assigned to a diet group by opening the next available envelope assigned to their gender. Each envelope contained a number identifying the formula, and the randomization was done in sequential series of eight. Each formula-gender appeared twice in each set of eight envelopes. The infants were enrolled when they were ready to start enteral feeding between two and five days of age. A preterm formula (Similac Special Care; Ross Products Division, Abbott Laboratories, Columbus, OH) was fed to the control group. The experimental formula was prepared by substituting a small amount of marine oil for an equivalent amount of the fat blend in the preterm formula. Otherwise, the experimental formula was identical to the commercially available preterm formula. Compared with most sources of marine oil, the source of marine oil added to the experimental formula had a relatively high ratio of DHA to EPA. The fatty acid composition of the two preterm formulas is shown in Table 2.

The preterm formula was designed especially for the higher nutrient needs of preterm as compared with term infants. Both diet groups received a low-iron version of the formula containing 24 kcal/oz (11) with or without a low EPA source of marine oil from enrollment until 2 mon past term. Infants received a daily supplement of 5 mg of iron from ferrous sulfate, beginning when they weighed 1.8 kg body weight and ending when they were two months past term. From 2 to 12 mon, infants from both groups were provided with a commercially-available formula (Similac with Iron) (11) designed for the nutrient requirements of infants born at term. The formulas were provided free to parents and without restriction. Compared with a group of ~60 term infants in the same hospital, the preterm infants in this study at 12 mon had slightly lower normalized weights but identical normalized lengths (12), evidence that they were well-nourished.

The gestational age of each infant was determined at birth by a combination of obstetric and pediatric assessments. The 52-wk (12 mon) Fagan Test was administered at 92 wk postmenstrual age (PMA) (12 mon) to all who returned for this visit.

Visual behavior testing. The method used to measure visual recognition memory and attention at 12 mon was the same as has been described (4). All tests were done by the same investigator, who was unaware of the infants' diets at the time of testing.

Statistical methods. This study was designed to test several hypotheses, including the hypothesis that visual novelty preference and attention of preterm infants during paired comparisons of novel and familiar stimuli would be enhanced by DHA supplementation. The power analysis for the trial was based on the number of infants needed to reject the null hypothesis for an effect of DHA supplementation on growth. Based on this analysis, 30 infants per group were planned.

At 12 mon, approximately half of the infants in each diet group were tested with a newer version of the Fagan Test that yielded data for look duration and number significantly different from the older version of the Fagan Test (Carlson, S.E., unpublished data). Because only the results obtained with the older version of the Fagan Test could be compared directly with those from our earlier study, only the scores of infants tested with that version are reported in Tables 3 and 4, where they are contrasted with results from that study. Many comparisons between diets (Table 4) suggest the null hypothesis

TABLE 3
Total Number of Discrete Looks During Familiarizations by Infants Fed a Commercial Formula (control, n = 12) or the Same Formula with a Marine Oil Source of DHA[a]

	Diet	12 mon	12 mon[b]
Total looks (#)	Control	37.1 ± 2.1	38.4 ± 1.6
	DHA-supp.	38.9 ± 1.5	38.9 ± 1.7
Looks left (#)	Control	19.3 ± 1.2	20.2 ± 1.1
	DHA-supp.	21.1 ± 1.1	19.4 ± 1.1
Looks right (#)	Control	17.8 ± 1.1	18.2 ± 0.9
	DHA-supp.	17.8 ± 0.7	19.5 ± 1.0
Time/total look (s)	Control	1.41 ± 0.08	1.39 ± 0.06
	DHA-supp.	1.33 ± 0.06	1.34 ± 0.06
Time/look left (s)	Control	1.37 ± 0.10	1.36 ± 0.08
	DHA-supp.	1.25 ± 0.08	1.37 ± 0.08
Time/look right (s)	Control	1.48 ± 0.09	1.54 ± 0.07
	DHA-supp.	1.45 ± 0.06	1.37 ± 0.08

[a]DHA-supplemented, n = 15. Mean ± SEM; supp., supplemented; (#), number; (s), second.
[b]Twelve-month looks and look duration in infants fed control and DHA-supplemented formula in our earlier randomized trial (Ref. 4).

cannot be accepted because of Type II error that resulted from the unplanned loss of power.

The effects of diet on 12-mon visual attention were determined by Student's *t*-test. A *post hoc* two-way analysis of variance for diet and BPD was used to look for an effect of BPD, as well as diet. These analyses were done on a MacIntosh IIcx computer with StatView software (Abacus Concepts, Inc., Berkeley, CA). A P value of <0.05 was considered statistically different.

TABLE 4
Visual Attention During Paired Comparisons by Infants Fed a Commercially Available Formula (control, n = 12) or the Same Formula with a Marine Oil Source of Docosahexaenoic Acid[a]

		12 mon	12 mon[b]
Novel time (% total)	Control	64.0 ± 1.9	64.6 ± 1.2
	DHA-supp.	59.7 ± 1.7	60.5 ± 1.3[c]
Total time (s)	Control	50.0 ± 1.6	48.9 ± 1.4
	DHA-supp.	50.8 ± 1.7	51.2 ± 1.4
Time to novel (s)	Control	33.1 ± 1.4	32.6 ± 1.2
	DHA-supp.	31.5 ± 1.5	31.9 ± 1.2
Time to familiar (s)	Control	16.9 ± 1.0	16.3 ± 0.8
	DHA-supp.	19.3 ± 0.9	19.3 ± 0.9[c]
Total looks (#)	Control	40.4 ± 2.7	42.4 ± 1.3
	DHA-supp.	46.8 ± 2.7	47.7 ± 1.4[d,e]
Looks to novel (#)	Control	22.9 ± 1.5	23.6 ± 0.8
	DHA-supp.	25.3 ± 1.6	26.0 ± 0.8[c,e]
Looks to familiar (#)	Control	17.5 ± 1.4	18.8 ± 0.8
	DHA-supp.	21.5 ± 1.3[c]	21.7 ± 0.8[c,e]
Time/look (s)	Control	1.30 ± 0.10	1.18 ± 0.05
	DHA-supp.	1.13 ± 0.07	1.11 ± 0.05[e]
Time/novel look (s)	Control	1.49 ± 0.09	1.43 ± 0.07
	DHA-supp.	1.28 ± 0.06[c]	1.27 ± 0.07[e]
Time/familiar look (s)	Control	1.04 ± 0.11	0.85 ± 0.05
	DHA-supp.	0.95 ± 0.08	0.91 ± 0.05

[a]DHA-supplemented, n = 15. Mean ± SEM. Abbreviations as in Table 3.
[b]Visual attention at 12 mon in infants fed control and DHA-supplemented formula in an earlier trial (Ref. 4).
[c]Different from control infants of the same study age, $P < 0.05$ by Student's *t*-test.
[d]Different from control infants of the same study age, $P < 0.01$.
[e]Diet effect ($P < 0.05$) with repeated measures analysis of variance including tests at 6.5, 9, and 12 mon.

RESULTS

Age at test. The actual test ages in weeks from term (mean ± SD) and the numbers of infants tested with the original 52-wk version of the Fagan Test in each diet group were, respectively, 52.6 ± 1.2 (n = 12) for the control group and 52.4 ± 1.0 (n = 15) for the DHA-supplemented group. This age is described throughout the paper as 12 mon. The mean test age of the diet groups did not differ.

Neonatal and perinatal characteristics of the infants. The infants in each diet group are described in Table 1. The groups were similar in all respects except that the group fed DHA-supplemented formula had higher RBC phosphatidylethanolamine (PE) DHA at two months compared with the control group as a result of receiving a DHA-supplemented diet from birth until that age. After the DHA supplement was discontinued at two months, RBC PE DHA (g/100 g total fatty acid) declined progressively over the next few months. At 12 mon, the groups could not be distinguished from each other on the basis of their RBC PE DHA (10).

Effect of diet on visual attention during familiarization. During familiarization, infants in the two diet groups had similar numbers of looks at each study age, and the total number of looks was divided nearly equally between the infants' left and right (Table 3). Both the number of looks and look duration at 12 mon were similar to the results of our earlier randomized trial (Table 3).

Infants with BPD differed from those without BPD in that they had significantly fewer total looks during familiarization with the Fagan Test (Table 5, $P < 0.02$). Because all infants were required to look for the same amount of time during familiarization, a lower number of looks was directly related to a significantly longer look duration in infants with BPD compared with infants without BPD ($P < 0.01$).

Effect of diet on visual attention during paired comparisons. Both diet groups had a significant preference for the novel stimuli during paired comparison tests (Table 4), but DHA-supplemented compared with control infants had significantly more discrete looks to the familiar stimuli during paired comparison testing ($P < 0.05$). A comparison of the 12-month data from this trial with that from our earlier trial (shown in the last column of Table 4) indicates similar increases in the numbers of total looks, looks to novel, and looks to familiar with DHA supplementation, and remarkably similar looking times and novelty preferences. At 12 mon the average time/novel look (s) was lower in DHA-supplemented infants ($P < 0.05$), and the average time/look (s) tended in the same direction. Again, the average times/novel look for the control and DHA-supplemented infants in this study were practically the same as for their respective groups in our earlier study (Table 4).

At 12 mon, infants who developed BPD compared with those without BPD had a longer average time/look ($P < 0.03$),

average time/novel look ($P < 0.02$), and average time/familiar look ($P < 0.06$) (Table 5). Although the numbers in each diet-BPD group were small, longer look duration in infants with BPD appeared to be due to higher look duration in the BPD infants fed control formula because the means for the DHA-supplemented infants with and without BPD were similar. Novelty preference determined during paired comparison tests was not affected by BPD (Table 5).

DISCUSSION

While subjects of this study compared with our earlier study (4) had similar birth weights and gestational ages and were fed experimental and control formulas with the same amounts of DHA and linolenic acid, respectively, the studies also differed in several ways: (i) The source of marine oil was lower in EPA in the second compared with the first study (0.06 vs. 0.3%). (ii) The experimental formula with DHA was fed until two months instead of nine months past term. (iii) Infants in the second randomized trial were fed a nutrient-enriched, energy-concentrated (24 kcal/oz) preterm formula instead of a 20 kcal/oz term formula from 36 to 48 wk PMA. (iv) The infants in the second trial had a 40% incidence of BPD, usual for this weight range, whereas practically no infants with BPD were included in our first study (3 of 67) (7).

This study confirmed that preterm infants fed DHA have shorter look durations to novel stimuli on paired comparison tests compared with infants fed linolenic acid as their sole source of n-3 fatty acid. In addition, the outcomes for visual recognition memory and attention (number and duration of looks) of control and DHA-supplemented infants were numerically similar to the responses observed earlier despite the smaller than intended sample size and several differences in design that could have decreased the response of the experimental group (Table 4).

For example, the shorter period of DHA supplementation might have been expected to decrease or to eliminate the effect of DHA supplementation on number and duration of discrete looks during the test. This did not appear to happen.

Because the effects of DHA supplementation on visual attention were found ten months after DHA was removed from the diet, the data suggested that the early diet had a long-term effect on the neural pathways responsible for differences in look duration. The idea is plausible, given that human milk feeding, which provides DHA, has been shown to increase DHA in the central nervous system compared with DHA-free infant formulas (13,14).

What cannot be concluded from this study is whether or not this short interval of DHA supplementation interacted with the prolonged feeding of nutrient-enriched formula to produce the effects of short-term DHA feeding on 12-month look duration shown here. A comparison of the outcomes at 12 mon for control infants without BPD in this study (Table 5) with controls in our earlier study suggests, however, that prolonged use of a nutrient-supplemented formula in this trial neither enhanced novelty preference nor shortened look duration.

Among preterm infants, it is well known that those with BPD are at higher risk for poorer neurodevelopmental outcomes than those without BPD. The reasons for this are not entirely clear. Because novelty preference has predictive validity for performance on standardized intelligence tests in childhood (15,16), we might have anticipated that infants with BPD would have had a lower novelty preference than those without BPD. Instead, the infants with BPD in this study had the same visual recognition memory (novelty preference) as infants without BPD (Table 5).

Compared with infants without BPD, however, infants with BPD had longer looks during the paired comparison (novelty) tests. When the look durations to the novel stimuli and familiar stimuli were considered independently, BPD infants also had significantly longer duration looks to both novel stimuli and familiar stimuli. The data in Table 5 suggest that the higher look duration seen in the analysis of variance was due to a higher look duration among infants with BPD fed the control diet. Infants with BPD who received the DHA-supplemented diet appeared to have the same look du-

TABLE 5
Effect of DHA Supplementation on 12-Month Novelty Preference and Visual Attention in Preterm Infants without or with Bronchopulmonary Dysplasia (BPD)

	Control		DHA-supplemented		Diet	BPD	Diet × BPD
Infant Looking at objects during test	No BPD (n = 7)	BPD (n = 5)	No BPD (n = 9)	BPD (n = 6)			
Familiarization							
Total Looks	40.6 ± 1.9[a]	32.2 ± 3.2	40.3 ± 1.8	36.7 ± 2.6	N.S.[b]	$P < 0.02$	N.S.
Time/look (s)	1.26 ± 0.06	1.62 ± 0.14	1.27 ± 0.06	1.41 ± 0.11	N.S.	$P < 0.01$	N.S.
Paired comparisons							
Novelty time (%)	64.9 ± 2.2	62.6 ± 3.5	59.2 ± 2.3	60.4 ± 2.5	N.S.	N.S.	N.S.
Total looks (#)	42.8 ± 3.0	37.0 ± 4.9	46.2 ± 2.6	47.7 ± 6.1	$P < .10$	N.S.	N.S.
Looks to novel (#)	24.6 ± 2.0	20.6 ± 2.2	24.9 ± 1.6	25.8 ± 3.4	N.S.	N.S.	N.S.
Looks to familiar (#)	18.3 ± 1.4	16.4 ± 2.8	21.3 ± 1.1	21.8 ± 2.9	$P < 0.04$	N.S.	N.S.
Time/look (s)	1.12 ± 0.05	1.55 ± 0.19	1.11 ± 0.07	1.16 ± 0.13	$P < 0.07$	$P < 0.03$	N.S.
Time/novel look (s)	1.32 ± 0.05	1.73 ± 0.17	1.25 ± 0.07	1.32 ± 0.11	$P < 0.02$	$P < 0.02$	N.S.
Time/familiar look (s)	0.85 ± 0.05	1.31 ± 0.22	0.94 ± 0.09	0.98 ± 0.16	N.S.	$P < 0.06$	N.S.

[a]Mean ± SEM. Abbreviations as in Table 3.
[b]N.S., not significant.

ration as DHA-supplemented infants without a history of BPD. Larger numbers of infants would need to be studied to determine if this is the case.

The familiarization interval for the Fagan Test is long and appears to be insensitive to known differences between groups of infants, e.g., the longer period of familiarization needed by preterm compared with term infants to demonstrate a novelty preference (17). Just as we found earlier (4), dietary DHA increased look number and decreased look duration during paired comparisons but not during familiarizations. Infants with BPD compared with those without BPD, however, had significantly fewer looks (and the reciprocal, longer look duration) during familiarizations, regardless of diet, suggesting poorer ability to shift attention.

In summary, the data from this randomized trial confirmed an earlier report (4) that preterm infants fed DHA have shorter look duration during paired comparison tests than infants fed linolenic acid as their sole dietary source of n-3 fatty acids. These data are analogous to those from monkey infants fed diets with, compared to without, adequate linolenic acid in that the group with better DHA status had a shorter look duration (6). Like novelty preference, shorter visual fixation in infancy is related to superior performance in infancy and childhood (18–20). Longer look duration has been suggested to be evidence of slower visual information processing (21,22), slower ability to disengage attention (23), or increased reactivity. If this is so, preterm infants fed DHA for only a short interval after birth may have more rapid visual information processing or more mature attention months after DHA is removed from their diet.

ACKNOWLEDGMENTS

This study was supported by grants from the National Eye Institute (RO1-EY08770), the National Institute of Child Health and Human Development (RO1-HD31329), and a gift from Ross Products Division, Abbott Laboratories (Columbus, OH). The authors wish to thank Rosalind Griffin for assistance with publication of this manuscript and Dr. Sydney Reisbick for many helpful comments about the original version of the manuscript.

REFERENCES

1. Carlson, S.E., Cooke, R., Werkman, S., and Peeples, J. (1989) Docosahexaenoate (DHA) and Eicosapentaenoate (EPA) Supplementation of Preterm (PT) Infants: Effects on Phospholipid DHA and Visual Acuity, *FASEB J. 3*, A1056.
2. Carlson, S.E., Werkman, S.H., Rhodes, P.G., and Tolley, E.A. (1993) Visual Acuity Development in Healthy Preterm Infants: Effect of Marine Oil Supplementation, *Am. J. Clin. Nutr. 58*, 35–42.
3. Carlson, S.E. (1993) Lipid Requirements of Very Low Birth Weight Infants for Optimal Growth and Development, in *Lipids, Learning and the Brain: Fats in Infant Formula, Report of the 103rd Ross Conference on Pediatric Research* (Dobbing, J., and Benson, J.D., eds.) pp. 188–214, Ross Laboratories, Columbus.
4. Werkman, S.H., and Carlson, S.E. (1996) A Randomized Trial of Visual Attention of Preterm Infants Fed Docosahexaenoic Acid Until Nine Months, *Lipids 31*, 91–97.
5. Neuringer, M., Connor, W.E., Van Petten, C., and Barstad, L. (1984) Dietary Omega-3 Fatty Acid Deficiency and Visual Loss in Infant Rhesus Monkeys, *J. Clin. Invest. 73*, 272–276.
6. Reisbick, S., Neuringer, M., and Gohl, E. (1994) Increased Look Duration in Paired Comparisons by Rhesus Monkey Infants with n-3 Fatty Acid Deficiency (n-3 FAD), *Soc. Neurosci. Abstr. 20*, 1696.
7. Carlson, S.E., Cooke, R.J., Werkman, S.H., and Tolley, E.A. (1992) First Year Growth of Preterm Infants Fed Standard Compared to Marine Oil n-3 Supplemented Formula, *Lipids 27*, 901–907.
8. Carlson, S.E., Cooke, R.J., Rhodes, P.G., Peeples, J.M., Werkman, S.H., and Tolley, E.A. (1991) Long Term Feeding of Formulas High in Linolenic Acid and Marine Oil to Very Low Birth Weight Infants: Phospholipid Fatty Acids, *Pediatr. Res. 30*, 404–412.
9. Carlson, S.E., Werkman, S.H., Peeples, J.M., Cooke, R.J., and Tolley, E.A. (1993) Arachidonic Acid Status Correlates with First Year Growth in Preterm Infants, *Proc. Natl. Acad. Sci. (U.S.A.) 90*, 1073–1077.
10. Carlson, S.E., Werkman, S.H., and Tolley, E.A. (1996) The Effect of Long Chain n-3 Fatty Acid Supplementation on Visual Acuity and Growth of Preterm Infants with and without Bronchopulmonary Dysplasia, *Am. J. Clin. Nutr.* in press.
11. Ross Laboratories (1992) *Ross Laboratories Product Handbook*, pp. 36–37, 44–45, Ross Laboratories, Columbus.
12. Carlson, S.E., Koo, W.W.K., and Werkman, S.H. (1995) Omega-3 and Omega-6 Supplementation of Infants: Biochemistry, Visual Development and Growth, *Proceedings from the Scientific Conference on Omega-3 Fatty Acids in Nutrition, Vascular Biology, and Medicine*, pp. 47–59, American Heart Association, Dallas.
13. Farquharson, J., Cockburn, F., Patrick, W.A., Jamieson, E.C., and Logan, R.W. (1992) Infants Cerebral Cortex Phospholipid Fatty-Acid Composition and Diet, *Lancet 340*, 810–813.
14. Makrides, M., Neumann, M.A., Byard, R.W., Simmer, K., and Gibson, R.A. (1994) Fatty Acid Composition of Brain, Retina and Erythrocytes in Breast-Fed and Formula-Fed Infants, *Am. J. Clin. Nutr. 60*, 189–194.
15. Fagan, J.F., and Singer, L.T. (1983) Infant Recognition Memory as a Measure of Intelligence, *Advances in Infancy Research* (Lipsitt, L.P., ed.), Vol. 2, pp. 31–72, Ablex, Norwood.
16. Rose, S.A., and Wallace, I.F. (1985) Cross-Modal and Intramodal Transfer as Predictors of Mental Development in Full Term and Preterm Infants, *Dev. Psychol. 21*, 949–962.
17. Rose, S.A. (1983) Different Rates of Visual Information Processing in Full-Term and Preterm Infants, *Child Dev. 54*, 1189–1198.
18. Colombo, J., Mitchell, D.W., and Horowitz, F.D. (1988) Infant Visual Attention in the Paired-Comparison Paradigm: Test-Retest and Attention-Performance Relations, *Child Dev. 59*, 1198–1210.
19. Mitchell, D.W., and Colombo, J. (1989) Fixation Time as a Predictor of 3- and 4-Month-Olds' Learning, Retention, and Transfer, *Abstr. Soc. Res. Child Dev. 6*, 321.
20. Rose, D.H., Slater, A., and Perry, H. (1986) Prediction of Childhood Intelligence from Habituation in Early Infancy, *Intelligence 10*, 251–263.
21. Colombo, J., and Mitchell, D.W. (1990) Individual Differences in Early Visual Attention: Fixation Time and Information Processing, *Individual Differences in Infancy: Reliability, Stability, and Prediction* (Colombo, J., and Fagan, J., eds.) pp. 193–227, Erlbaum, Hillsdale.

22. Colombo, J., Mitchell, D.W., Coldren, J.T., and Freeseman, L.J. (1991) Individual Differences in Infant Visual Attention: Are Short Lookers Faster Processors or Feature Processors?, *Child Dev. 62*, 1247–1257.
23. Johnson, M.H., Posner, M.I., and Rothbart, M.K. (1991) Components of Visual Orienting in Early Infancy: Contingency Learning, Anticipatory Looking, and Disengaging, *J. Cognitive Neurosci. 3*, 335–344.

[Received August 25, 1995; Revision accepted November 30, 1995]