0031-3998/84/1812-1233$02.00/0
PEDIATRIC RESEARCH

Vol. 18, No. 12, 1984
Printed in U.S.A.

Indices of Fatness and Serum Cholesterol at Age Eight Years in Relation to Feeding and Growth during Early Infancy

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ABSTRACT. During the early months of life, gains in length and weight are more rapid by formula-fed than by breast-fed infants and we and others have speculated that the greater gains of the formula-fed infants are the result of greater food intake. If overfeeding during early infancy resulted in establishment of habits of overeating, or if, for any other reason, diet-induced fatness in infancy persisted into childhood, we might be able to demonstrate differences in fatness in childhood related to mode of feeding (breast or bottle) during infancy. We therefore examined at age 8 years 469 children born in 1966–1971 who had been studied intensely in our unit from 8 to 112 days of age. At age 8 years there were no differences in indices of fatness related to mode of feeding during infancy.

Serum concentrations of cholesterol at age 8 years were also of interest because of reports from animal studies that differences in feeding during early life may be responsible for subsequent differences in cholesterol homeostasis. Cholesterol concentrations at age 8 years did not demonstrate significant differences related to mode of feeding during infancy. It is possible, however, that age 8 years is too early for an effect to be demonstrated. (*Pediatr Res* 18:1233–1238, 1984)

We have reported that formula-fed infants gain weight more rapidly than do breast-fed infants (16). Although Dine *et al.* (8) and several other investigators cited by them failed to detect such a difference, the weight of evidence indicates greater rates of gain by formula-fed infants (23–25, 33, 38, 40). If weight gain by breast-fed infants as a group is considered adequate or normal, a greater weight gain by formula-fed infants may be considered excessive. A probable explanation for the greater weight gain by formula-fed infants is a greater intake of energy and/or other nutrients by these infants than by breast-fed infants. The data of Hofvander *et al.* (22) appear to offer some support for the hypothesis that energy intakes are greater by formula-fed than by breast-fed infants, although weighing infants before and after feedings appears to be a quite crude method of determining intake (7, 41).

On the basis of animal experiments (*e.g.* 2, 10, 26), it appears possible that excessive energy intake during infancy is somehow associated with greater fatness later in life. Human studies relating energy intake in infancy to later indices of fatness have not been reported, and it is difficult to imagine a completely satisfactory design for such a study. There are, however, a number of reports relating body size or gains in weight, weight for length, or skinfold thickness in infancy with fatness later in life. A number of these studies have been identified previously (8, 13). Mellbin and Vuille (34–36), Hernesniemi *et al.* (21), and Dine *et al.* (8) have demonstrated that significant "tracking" of relative weight is present between infancy and childhood, and Charney *et al.* (5) have demonstrated that significant tracking occurs between infancy and adulthood.

Whether indices of fatness in childhood or adulthood are appreciably influenced by mode of feeding (by breast or bottle) during infancy is uncertain. Dine *et al.* (8) reported no significant differences in indices of fatness during infancy or childhood to age 5 years in relation to mode of feeding during early infancy. However, the report is difficult to interpret because the eligibility criteria for the breast-fed and formula-fed groups are not given and the comparison of data for breast-fed and formula-fed groups was not carried out on a sex-specific basis. Marmot *et al.* (31) reported that body weight at age 32 years was significantly greater for 57 men who had been exclusively breast-fed during the first 5 months of life than for 20 men who had been bottle-fed during the first 5 months of life. No such difference was found in women of the same age (68 initially breast-fed, 27 initially bottle-fed). Socioeconomic differences between the groups were poorly defined.

Although several of the more important studies mentioned had not yet been reported in 1971 when we decided to undertake our study, the general nature of the problem was already evident. We therefore decided to carry out a follow-up study as a test of the hypothesis that indices of fatness are greater in children who had been fed formula in infancy than in those who had been breast-fed. We identified a cohort of subjects whom we had studied between 8 and 112 days of age and examined them at age 8 years. The age of 8 years was selected because we wished to avoid the onset of the adolescent growth spurt.

In the pursuit of our main hypothesis, it was evident that we would also be able to determine the extent to which parameters of fatness at age 8 years are predictable from gain in weight between 8 and 112 days of age and from parameters of fatness at age 112 days.

A vexing problem in all studies comparing performance of breast-fed and formula-fed infants is the impossibility of random assignment of infants to feeding groups. Thus, with mothers selecting the mode of feeding, the environment and, perhaps, other intrinsic parameters may differ between the groups and serve as confounding factors. No design will eliminate this difficulty but we believed that in a university community the tendency toward higher socioeconomic and educational status of families of breast-fed infants (32) would be minimized.

In addition to the anthropometric phase of the study, we realized that it would be possible to determine the relation between type of feeding during early infancy and subsequent

Received January 2, 1984; accepted May 15, 1984.

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This work was supported in part by United States Public Health Service Grant MC-R-190260.

serum concentration of cholesterol. Studies of several animal species have shown that nutritional influences during early life can permanently alter varius aspects of cholesterol metabolism (see "Discussion"). Data concerning this possibility in humans are sparse and equivocal. Because we had determined serum cholesterol concentrations during infancy, we were also able to examine the relationship between serum cholesterol concentration in infancy and during childhood.

MATERIALS AND METHODS

The study cohort was defined at the outset to include subjects born between January 1, 1966 and December 31, 1971 who had completed as planned the study between 8 and 112 days of age. All such infants were to be included except those fed formulas containing butterfat or differing appreciably in composition from commercially available formulas (one formula providing 133 kcal/dl, several formulas providing approximately 1.5 g protein/100 kcal or providing protein in the form of a protein hydrolysate). In drawing up our list of subjects we overlooked the fact that the formula, NAN (Nestlé, Vevey, Switzerland), contained 80% of fat in the form of butterfat. Thirty other infants fed formulas containing butterfat were excluded. The initially identified study cohort therefore included 471 subjects, including 15 subjects fed NAN.

Through the efforts of two of the investigators (R. R. R and L. N. T.) all but two of the subjects were located. Of the two not located, one had been placed for adoption during infancy and, at the request of the mother, no attempt was made to locate the child. Of the 469 children located, none refused participation and all but four were examined within 61 days of the eighth birthday. The exceptions were four subjects who were examined 63, 69, 148, and 214 days, respectively, after the eighth birthday. Thus, data concerning 465 children examined within 61 days of the eighth birthday were available for analysis.

In an attempt to achieve a reasonably homogeneous population of the initially formula-fed subjects, certain groups were excluded from analysis, including exclusion from results of anthropometric measurement of 33 female subjects who had been fed between 8 and 112 days of age formulas with relatively low (54 kcal/dl) or relatively high (100 kcal/dl) energy density (14). There were therefore 156 children (73 males and 83 females) who had been breast-fed during infancy and 276 children (171 males and 105 females) who had been fed formulas during infancy. The energy density of the formulas fed during infancy was 67 kcal/dl.

Excluded from analysis of the serum cholesterol data were 15 females who had been fed NAN (80% of the fat from butterfat) and 15 males who had been fed a formula providing 40% of the fat in the form of medium-chain triglyceride oil. The data were excluded because during infancy serum cholesterol concentrations were greater in these infants than in infants fed formulas with vegetable oils. Thus, the subjects included for the analysis of serum cholesterol data were either breast-fed during infancy or were fed formulas with fat from vegetable oils.

We have previously presented detailed descriptions of the methods used in studying breast-fed (15, 18) and formula-fed (16) infants. Data concerning each of the breast-fed infants and many of the formula-fed infants included in the present study have been presented in the appendices of those reports. A number of the breast-fed infants received some formula, and some breast-fed and some formula-fed infants received beikost (foods other than milk or formula). For breast-fed infants born after January 1, 1969, the quantities of such foods consumed have been reported (18). Each infant was enrolled in the study between birth and 9 days of age and was measured within 2 days of ages 8, 14, 28, 42, and 56 days and within 4 days of ages 84 and 112 days. Lengths and weights of the infants were determined as described elsewhere (11).

Examination of the 8-year-old children was performed in the home or at another convenient location (school, church) in the presence of at least one parent. With few exceptions, examinations were performed by one investigator (R. R. R.) and most of the remaining examinations were made by individuals trained by this investigator. Weight of the 8-year-old children was determined with the children wearing undergarments. Measurements were recorded to the nearest 0.01 kg using a portable beam scale which was calibrated at 3-month intervals. Standing height and skinfold thickness at the triceps and subscapular sites were measured (with a Lange caliper) as described previously (12). Self-reported information about the heights and weights of both parents was gathered for 400 of the 432 subjects, but it was not feasible to verify this information. If both the subject and the parent(s) agreed, a sample of venous blood (5 ml) was drawn from an antecubital vein. Blood was obtained without reference to the time of food consumption. The blood was allowed to clot and was then centrifuged by use of a portable hand-operated centrifuge; serum was harvested and was not refrigerated until it reached the laboratory up to 40 h later. In the laboratory, serum was kept refrigerated until analyzed, which occurred within 2 wk.

Until March 1969, determinations of serum cholesterol were performed manually using the method of Carr and Drekter (4). Since that time, serum cholesterol has been determined by an automated (Technicon Auto-Analyzer I) modification of the method of Levine and Zak (28). As discussed previously (18), values obtained with the manual method were generally somewhat greater than those obtained with the automated method. Only values obtained with the automated method are included in this report.

Duplicate determinations of cholesterol with the two members of each pair determined on separate days were done with 181 serum samples between 1975 and 1979. The coefficient of variation for these duplicates was 7.6%. In this same period the coefficients of variation obtained with Versatol (General Diagnostics, Morris Plains, NJ), a commercially available lyophilized reference serum, was 6.5%.

The protocols for the infant studies and for the study of 8-year-old children were reviewed and approved by the University of Iowa Committee on Human Experimentation. The studies were discussed with one or both parents and with the 8-year-old children and written consent was obtained from the parents and the 8-year-old children.

Comparisons between breast-fed and formula-fed groups were performed by two-tailed t test unless otherwise noted. Other statistical analyses are indicated in the text.

RESULTS

Anthropometric findings. Specific socioeconomic data about the families of the subjects were not accumulated and, in any case, would have been difficult to interpret because of the preponderance (55.7%) of student families. Comparison of the occupations of the fathers of the subjects (Table 1) suggests that the makeup of the two groups is generally similar except for the greater percentage of fathers of the breast-fed group (14.7%) than of the formula-fed group (4.4%) who were members of the university faculty.

As is generally the case with infants (3), males in our study were somewhat larger than females at birth and gained more rapidly in weight and length during early infancy (Table 2). Both in males and in females, weight and weight/length^2 at 112 days of age were significantly greater for formula-fed than for breast-fed infants. Similar feeding-related differences existed for length at 112 days of age and for gains in weight and length, but the differences were statistically significant only for males (Table 2).

Among the formula-fed males, gain in length was significantly ($p < 0.01$) greater by those fed soy-based than by those fed milk-based formulas (data not shown). This finding must be interpreted with caution because comparisons of larger groups of infants fed milk-based and soy-based formulas has shown growth to be similar (17). There were no other significant differences in

anthropometric parameters between infants fed soy-based and those fed milk-based formulas.

Anthropometric data at age 8 years are summarized in Table 2. There were no statistically significant differences, on a sex-specific basis, between subjects who had been breast-fed during infancy and those who had been fed formulas.

Simple Pearson correlation coefficients between parameters determined at age 8 years and those determined during infancy are presented in Table 3. With few exceptions, the strongest correlations were between weight, height, and weight/height^2 at age 8 years and the corresponding parameters at age 112 days. These correlations were statistically significant in each sex-feeding category. The correlations were weaker between weight and height at age 8 years and weight and length, respectively, at age 8 days. Surprisingly, correlations between weight and height at age 8 years and gain in weight and height, respectively, between 8 and 112 days of age were also relatively low. Correlation coefficients for formula-fed subjects were higher than corresponding coefficients for breast-fed subjects. The differences were substantial in a number of instances, although there were differences in the opposite direction also. In both feeding categories, correlation coefficients tended to be considerably lower in females than in males.

Table 1. *Occupations of fathers*

	Breast-fed		Formula-fed	
	Number	%	Number	%
University of Iowa				
Students	81	51.9	161	58.3
Faculty	23	14.7	12	4.4
Nonfaculty administrative, professional, & technical	21	13.5	28	10.1
Support personnel*	2	1.3	12	4.4
Nonuniversity				
Professional & clergy	3	1.9	1	0.4
Teachers	7	4.5	15	5.4
Businessmen	3	1.9	10	3.6
Other†	16	10.3	37	13.4
Total	156		276	

* Category includes carpenter, computer terminal operator, draftsman, maintenance worker, security officer.

† Category includes farmer, military enlisted man or officer, maintenance worker, policeman, fireman, construction worker.

Using a stepwise regression procedure as described in the SAS User's Guide (39), we determined the effect of four independent variables (birth weight, length at 8 days, midparental height, and midparental weight) on anthropometric parameters at age 8 years as dependent variables. These regressions were calculated on a sex-specific but not feeding-specific basis. For each dependent variable, those independent variables were identified which contributed significantly (F test, $p < 0.05$) in the stepwise regression model. We then used these independent variables as adjustors in the calculation of partial correlation coefficients and have presented these on a sex-specific and feeding-specific basis in Table 4. The correlations concern the 400 subjects for whom self-reported heights and weights were obtained for both parents.

As may be seen from a comparison of Tables 3 and 4, the partial correlation coefficients tended to be lower than the corresponding simple correlation coefficients. In some cases (*e.g.* height at age 8 years with length at age 112 days), the difference was quite large in all sex-feeding categories, whereas in other cases the difference was trivial; in some cases, the partial correlation coefficients were higher than the corresponding simple ones. As with the simple correlation coefficients, partial correlation coefficients tended to be less for breast-fed than for formula-fed and for female than for male subjects.

Serum concentrations of cholesterol. As previously mentioned, data on serum concentrations of cholesterol are restricted to determinations performed in March 1969 and subsequently. At each age during infancy, serum cholesterol concentrations of breast-fed infants were greater than those of formula-fed infants (analysis of variance, $p < 0.01$ for each sex), whereas at age 8 years serum cholesterol concentrations of children who had been breast-fed during infancy did not differ from those of children who had been fed formulas during infancy (Table 5). During

Table 2. *Anthropometric parameters**

	Males		Females	
	Breast-fed (73)	Formula-fed (171)	Breast-fed (83)	Formula-fed (105)
Parameters during infancy				
W (kg)				
Birth	3.460 ± 0.398	3.519 ± 0.411	3.287 ± 0.387	3.341 ± 0.379
8 d	3.411† ± 0.408	3.552† ± 0.418	3.286 ± 0.384	3.358 ± 0.376
112 d	6.545‡ ± 0.687	6.938‡ ± 0.729	6.025† ± 0.582	6.190† ± 0.523
L (cm)				
8 d	51.3 ± 1.6	51.6 ± 1.7	50.6 ± 1.7	50.6 ± 1.6
112 d	62.7‡ ± 1.7	63.4‡ ± 2.0	61.3 ± 1.7	61.5 ± 1.8
W/L^2 (g/cm^2)				
8 d	0.866 ± 0.084	0.882 ± 0.083	0.872 ± 0.087	0.887 ± 0.082
112 d	1.663‡ ± 0.138	1.723‡ ± 0.138	1.600† ± 0.124	1.637† ± 0.108
Gain 8–112 d				
W (g/day)	30.1‡ ± 5.9	32.6‡ ± 5.8	26.3 ± 5.1	27.2 ± 5.1
L (mm/day)	1.10‡ ± 0.10	1.13‡ ± 0.11	1.03 ± 0.11	1.05 ± 0.10
Parameters at age 8 years				
W (kg)	26.73 ± 3.64	26.66 ± 3.47	27.11 ± 4.19	26.35 ± 4.42
H (cm)	128.5 ± 5.2	128.6 ± 4.9	128.8 ± 5.9	127.7 ± 5.0
W/H^2 (g/cm^2)	1.614 ± 0.149	1.608 ± 0.142	1.629 ± 0.180	1.610 ± 0.194
SF (mm)				
Triceps	8.1 ± 2.8	8.0 ± 3.1	10.9 ± 4.1	11.1 ± 3.9
Subscapular	5.2 ± 1.6	5.5 ± 1.9	6.9 ± 3.2	6.8 ± 2.8
Sum	13.3 ± 4.1	13.5 ± 4.8	17.8 ± 7.0	18.0 ± 6.5

* W, weight; L, length; H, height; SF, skinfold thickness; d, days of age. Same superscript on same line indicates a feeding group-related difference within the same sex: † $p < 0.05$, ‡ $p < 0.01$. Values are mean ± SD. Numbers of subjects are in parentheses.

Table 3. *Selected simple correlation coefficients between anthropometric parameters measured at age 8 years and parameters measured during infancy**

	Males		Females	
	Breast-fed (73)	Formula-fed (171)	Breast-fed (83)	Formula-fed (105)
Weight at age 8 years				
BW	0.235	0.322	0.130	0.263
W at 112 d	0.352	0.522	0.257	0.330
Gain W at 8–112 d	0.191	0.393	0.191	0.184
L at 8 d	0.287	0.278	0.207	0.194
L at 112 d	0.437	0.338	0.263	0.260
Gain L at 8–112 d	0.249	0.168	0.093	0.138
W/L^2 at 112 d	0.173	0.411	0.130	0.191
Height at age 8 years				
BW	0.166	0.354	0.233	0.278
W at 112 d	0.237	0.441	0.237	0.375
Gain W at 8–112 d	0.117	0.295	0.081	0.209
L at 8 d	0.399	0.437	0.479	0.328
L at 112 d	0.550	0.574	0.581	0.492
Gain L at 8–112 d	0.256	0.336	0.176	0.333
W/L^2 at 112 d	−0.045	0.124	−0.129	0.045
Weight/height^2 at age 8 years				
BW	0.218	0.159	0.065	0.172
W at 112 d	0.314	0.379	0.181	0.196
Gain W at 8–112 d	0.177	0.321	0.200	0.107
L at 8 d	0.079	0.022	−0.095	0.054
L at 112 d	0.167	0.000	−0.103	0.021
Gain L at 8–112 d	0.141	−0.030	−0.019	−0.048
W/L^2 at 112 d	0.295	0.489	0.303	0.228

* BW, birth weight; other abbreviations as in Table 2. Underlined values are statistically significant at $p < 0.05$. Numbers of subjects are in parentheses.

Table 4. *Partial correlation coefficients between anthropometric parameters measured at age 8 years and parameters measured during infancy**

	Males		Females	
	Breast-fed (69)	Formula-fed (156)	Breast-fed (80)	Formula-fed (95)
Weight at age 8 years adjusted for	BW, MP-H, MP-W		L 8 d, MP-W	
W at 112 d	0.249	0.437	0.180	0.228
Gain in W at 8–112 d	0.187	0.426	0.213	0.180
W/L^2 at 112 d	0.144	0.404	0.138	0.196
Height at age 8 years adjusted for	L 8 d, MP-H		BW, L 8 d, MP-H	
L at 112 d	0.363	0.376	0.271	0.295
Gain in L at 8–112 d	0.365	0.377	0.274	0.298
Weight/height^2 at age 8 years adjusted for	BW, L 8 d, MP-W		MP-H, MP-H	
W at 112 d	0.224	0.403	0.275	0.153
Gain in W at 8–112 d	0.167	0.360	0.272	0.199
W/L^2 at 112 d	0.228	0.454	0.305	0.068

* MP-H, midparental height; MP-W, midparental weight; other abbreviations as in Tables 2 and 3. Each of the variables used exerted a significant effect in the stepwise regression procedure (see text). Underlined values are significant at $p < 0.05$. Numbers of subjects are in parentheses.

infancy, males tended to have lower serum cholesterol concentrations than did females. At age 8 years, this tendency was less marked.

The relationship between average cholesterol concentrations during infancy and cholesterol concentrations at age 8 years was examined by calculating Pearson correlation coefficients. As may be seen from Table 6, data for males demonstrated considerably higher correlation coefficients than data for females. The correlations were statistically significant ($p < 0.01$) for formula-fed males only.

DISCUSSION

The quantity of milk consumed by an infant is the consequence of a complex interaction between the infant and the mother or other individual responsible for the feeding. Whether a woman feeds her infant by breast or bottle, the frequency of feeding will to a large extent be determined by her ability to interpret the signals from the infant and her willingness to respond to them. Once the feeding process has begun, a further interaction occurs between the infant and the mother, and in this interaction little is known about the extent to which the mother influences the quantity of milk or formula consumed by the infant. In seems likely that most mothers attempt to influence their infant's food consumption and that the influence, at least during the early months of life, is exerted in the direction of increasing rather than decreasing intake. Greater intakes may be perceived as beneficial to the health of the infant and, at the same time, advantageous for the mother. For example, the

Table 5. *Serum cholesterol concentration (mg/dl) in relation to sex, feeding, and age**

Age	Males		Females	
	Breast-fed	Formula-fed	Breast-fed	Formula-fed
28 days	136 ± 27 (15)	104 ± 18 (41)	140 ± 33 (28)	106 ± 20 (36)
56 days	121 ± 18 (15)	100 ± 23 (74)	135 ± 43 (30)	105 ± 28 (61)
84 days	119 ± 18 (13)	100 ± 22 (57)	133 ± 24 (26)	105 ± 25 (34)
112 days	127 ± 24 (16)	107 ± 23 (80)	143 ± 49 (30)	107 ± 23 (63)
Infancy average				
1 or more values	126 ± 20 (22)	103 ± 20 (100)	138 ± 28 (39)	107 ± 23 (81)
2 or more values	128 ± 19 (20)	102 ± 17 (83)	138 ± 27 (35)	105 ± 18 (67)
8 years†	158 ± 23 (70)	163 ± 26 (148)	167 ± 30 (76)	166 ± 30 (105)

* Numbers of subjects are in parentheses. For each sex at each age during infancy, concentrations of cholesterol were significantly greater ($p < 0.05$) in the breast-fed than in the formula-fed group; at age 8 years, the differences were not significantly different.

† One-sided t test, breast-fed *vs.* formula-fed males; $t = 1.52$, $p = 0.13$.

Table 6. *Simple correlation coefficients between average serum cholesterol concentrations in infancy and at age 8 years**

	Males				Females			
	Breast-fed		Formula-fed		Breast-fed		Formula-fed	
	n	*r*	*n*	*r*	*n*	*r*	*n*	*r*
Infancy average								
1 or more values	21	0.393	98	0.272	34	0.232	71	0.130
2 or more values	19	0.391	81	0.487	31	0.282	59	0.200

* Underlined values significant at $p < 0.01$.

mother may reason that a larger intake at a feeding will permit a longer interval between feedings.

Although a mother's motivation to influence the infant's food consumption may be similar whether she feeds her infant by breast or bottle, we and others have speculated that the ability of the mother to influence food consumption is greater with bottle feeding. A difference in energy intake seems to us the most likely explanation for the greater weight gains of formula-fed than of breast-fed infants (16). The greater fatness of formula-fed infants might persist into childhood either because habits of overeating had been established during infancy or because of other poorly defined nongenetic relationships between fatness in infancy and subsequently. We therefore wished to test the hypothesis that parameters of fatness at age 8 years would be greater in children who had been formula-fed during infancy than in those who had been breast-fed. The choice of age 8 years for the measurements was somewhat arbitrary but represented an age well beyond infancy and before the onset of the adolescent growth spurt. The data we obtained (Table 2) failed to provide support for the hypothesis. There was no suggestion that parameters of fatness were greater at age 8 years in chldren who had been formula-fed than in those who had been breast-fed.

In relating parameters measured during infancy to parameters measured in childhood, several investigators (9, 34–36) have focused their attention on the relationship between gain in weight during infancy and subsequent indices of fatness. In our study, the rate of gain in weight from 8 to 112 days of age generally demonstrated a relatively low correlation with weight or weight/height^2 at age 8 years.

Studies suggesting that nutritional factors operating during early infancy may influence response to an atherogenic diet during adulthood have been reviewed by several authors (13, 19, 37). The more important bits of information are the following. 1) When rat pups were weaned prematurely (day 18) or normally (day 30), were fed rat chow until reaching adulthood, and then were challenged with an atherogenic diet, the prematurely weaned rats demonstrated higher serum concentrations of cholesterol (20). This exaggerated response of the prematurely weaned pups to the atherogenic diet could be prevented by feeding a high-fat diet from weaning to adulthood. 2) Male guinea pigs fed a cholestyramine-containing diet from 1 to 7 weeks of age and subsequently challenged with an atherogenic diet fed from 13 to 17 weeks of age demonstrated lower serum concentrations of cholesterol than did controls similarly challenged. Adult animals that had been fed cholestyramine excreted more bile acids and had larger bile acid pools than did controls (29, 30). 3) The responses of serum concentrations of high density lipoprotein cholesterol and apolipoprotein A-1 of juvenile (4- to 6-year-old) baboons challenged with a diet high in saturated fat or a diet high in polyunsaturated fat differed in relation to mode of feeding during infancy. Baboons that had been breast-fed during infancy demonstrated greater serum concentrations of high density lipoprotein cholesterol and apolipoprotein A-1 when challenged with the diet high in polyunsaturated fat whereas baboons fed any of several formulas during infancy demonstrated greater serum concentrations of these substances when challenged with the diet high in saturated fat (37).

These animal studies all suggest that early nutritional management influences subsequent cholesterol homeostasis. Possibly the mechanism of the effect is in regulation of cholesterol catabolism, as suggested by Li *et al.* (29, 30).

Human studies thus far have failed to demonstrate that dietary factors operating during infancy influence subsequent serum concentrations of cholesterol. Although Marmot *et al.* (31) reported greater serum concentrations of cholesterol in young women who had been formula-fed during infancy than in those who had been breast-fed, the number of subjects was small and the mean serum concentrations of cholesterol were surprisingly high (209 mg/dl for those who had been breast-fed and 229 mg/dl for those who had been formula-fed). As summarized by several authors (13, 19, 37), studies of children have failed to demonstrate that mode of feeding (breast or formula) during infancy influences subsequent serum concentrations of cholesterol. Our findings (Table 5) are therefore in agreement with findings of other investigators. However, childhood (age 10 years or younger) may be too early to demonstrate an effect (19). It is, of course, possible that there may have been differences in cholesterol fractions as well as in concentrations of apolipoproteins, none of which would necessarily be reflected in serum total cholesterol concentration.

Serum concentrations of cholesterol at birth (cord blood), at 7 to 9 months of age, and at 14 to 19 months of age have been correlated by Andersen *et al.* (1) with concentrations at 3 to 4 years of age in 64 children. The correlation coefficient was not significant ($r = -0.144$) for cord serum but was significant for serum at 7 to 9 months of age ($r = 0.450$) and at 14 to 19 months of age ($r = 0.517$). Somewhat higher values have been reported by several groups of investigators for the correlations between serum concentrations of cholesterol determined at 7 to 14 years of age and those obtained 3 to 6 years later (6, 27, 42). Our data appear to be the first to present correlations between values obtained during the early months of life and those obtained in school-age children. The observation that these values are sig-

nificant in males but not in females is surprising. Such a sex-related difference in tracking of serum cholesterol concentrations has not previously been described.

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