Special Turku Coronary Risk Factor Intervention Project for Babies (STRIP)[1–3]

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ABSTRACT

Background: Introducing nutritional and lifestyle principles to children in late infancy may permanently improve their adherence to a low-saturated fat, low-cholesterol diet, thus reducing of coronary risk factors, but worries about possible effects on growth and development have hampered such an approach.

Objective: The Special Turku Coronary Risk Factor Intervention Project for Babies (STRIP) aimed to decrease exposure to known environmental atherosclerosis risk factors in children 7–36 mo of age.

Design: Repeated, individualized counseling aimed at promoting a fat intake of 30% of energy and a 1:1:1 ratio of saturated to monounsaturated to polyunsaturated fat intake was provided (*n* = 540 intervention children; 284 boys). Nutrition was discussed superficially with the families of the control children (*n* = 522; 266 boys) and food intake was recorded at 3–6-mo intervals by use of 3–4-d food diaries. Serum lipids were measured at 6–12-mo intervals and growth was monitored regularly.

Results: Fat intake of the intervention (control) children provided 29.5% (29.4%) of energy at the age of 8 mo, 26.6% (28.5%) of energy at 13 mo, 30.5% (33.5%) of energy at 24 mo, and 31.5% (33.5%) of energy at 36 mo. The intervention children consistently consumed less saturated fat than did the control children ($P < 0.0001$). Recommended intakes of other nutrients (except vitamin D and occasionally iron) were reached irrespective of the amount and type of dietary fat. Serum cholesterol, non-HDL cholesterol, and HDL-cholesterol concentrations were 3–6% lower in the intervention children than in the control children. The intervention had no effect on height, weight, or head circumference gain. Fat intake did not predict children's growth patterns.

Conclusion: Repeated, individualized counseling in early childhood aimed at reducing consumption of saturated fat and cholesterol was effective and feasible and did not restrict growth in circumstances in which children were regularly monitored. *Am J Clin Nutr* 2000;72(suppl):1316S–31S.

KEY WORDS Energy intake, fat intake, nutrient intake, growth, children, infants, coronary heart disease, STRIP, Finland

INTRODUCTION

The most important risk factors of coronary heart disease (CHD) are hyperlipemia, obesity, hypertension, and smoking—all of which are modifiable through changes in lifestyle. Dietary fats regulate serum lipid concentrations in adults and in children: an excess intake of saturated fat increases, yet a diet rich in polyunsaturated and monounsaturated fats decreases total serum and LDL-cholesterol concentrations (1–4). Although feeding with breast milk or formula during infancy probably does not influence future serum lipid values (5–7), prevention of CHD through intervention in early childhood is supported by the fact that dietary habits and food preferences are formed early in life and that diets consumed by families tend to persist in the new generation (8). Atherosclerotic mechanisms already function in early childhood because clusters of macrophage foam cells are found in arterial intima in young children, which are followed later by the development of localized fatty streaks and fibrous plaques (9, 10). Progression of preatherosclerotic lesions also depends on serum cholesterol concentrations during childhood (11, 12) and on attempts to delay atherosclerosis development in children (13–15). Early intervention is supported by the studies of Law et al (16) who showed that the earlier serum lipid values decrease in adults, the better the prognosis. Further, reduction of serum cholesterol concentration diminishes CHD morbidity and mortality in primary (17) and secondary (18) prevention and in subjects with average serum cholesterol concentrations (19).

Despite apparent benefits of reducing serum cholesterol values in adults via use of polyunsaturated and monounsaturated fats, manipulation of fat content in the diets of children has been strongly opposed and dietary guidelines for CHD prevention have excluded children <2–3 y of age (14, 20). Such stringent exclusion of the youngest age groups is based on fears that low-fat diets might cause growth failure in some children because of inadequate energy supply (21, 22).

In the randomized, prospective Special Turku Coronary Risk Factor Intervention Project for Babies (STRIP), a low saturated-fat, low-cholesterol diet was introduced at an exceptionally young age, ie, at the age of 7 mo (23). We evaluated the effects
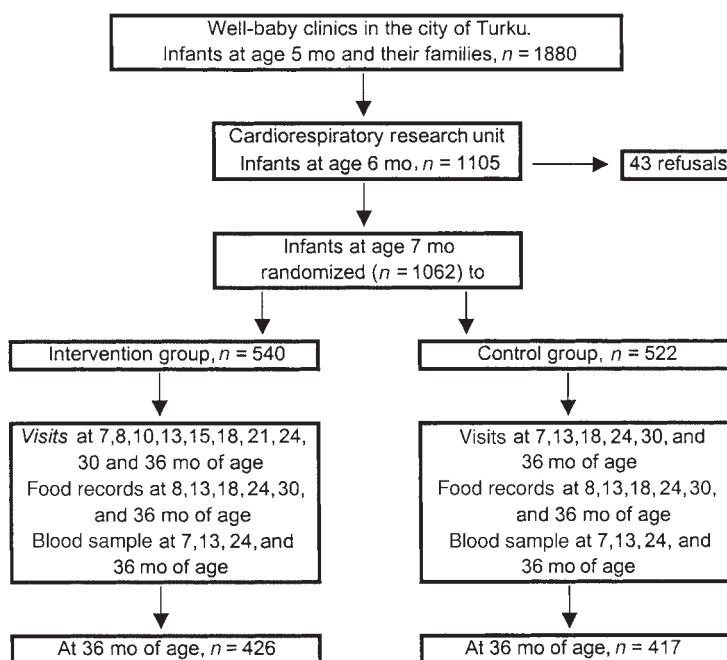
FIGURE 1. The flow-chart of the STRIP trial.

of such dietary intervention on the intake of fat and other nutrients, serum lipid and lipoprotein values, and growth of children during the first 3 y of life.

SUBJECTS AND METHODS

Design and subjects

Nurses at the well-baby clinics in the city of Turku, Finland, began recruiting children to STRIP in March 1990; recruitment ended in May 1992. The study comprised 1054 voluntary families with 1062 infants (8 twin pairs) (56.5% of the 1880 eligible infants). At the infant's age of 6 mo, a pediatrician explained the design and purpose of the trial to the families (n = 1105); 43 families refused then to participate. After informed consent was received from the remaining parents, the children were allocated by random numbers to an intervention group (n = 540; 284 boys; 3 twin pairs), or a control group (n = 522; 266 boys; 5 twin pairs). The number of participating children grew equally in both groups, which helped to avoid the confounding effects of the seasonal variation in serum lipid concentrations (24, 25). The intervention families visited the counseling team when the child was 7, 8, 10, 13, 15, 18, 21, 24, 30, and 36 mo old; the control families were not invited when the child was 8, 10, 15 and 21 mo old (**Figure 1**). Nonfasting blood samples were drawn at the ages of 7, 13, 24, and 36 mo for measurement of serum cholesterol, HDL cholesterol, and apolipoproteins (apo) A-I and B; lipoprotein(a), apo E phenotypes, and serum cholesterol ester fatty acids were also determined but are not discussed here. The actual date of blood sampling differed from the calendar age by 7 ± 11 d and 9 ± 12 d in the intervention and control groups, respectively, at 7 mo of age. The respective numbers were 2 ± 8 (1 ± 7) days at

13 mo, 3 ± 12 (0 ± 11) days at 24 mo, and 3 ± 18 (2 ± 14) days at 36 mo. Food consumption of the children was recorded at 8, 13, 18, 24, 30, and 36 mo of age. After the age of 3 y, the trial has continued with visits at 6-mo intervals and yearly blood draws.

All children continued to visit the well-baby clinics for vaccinations, growth and development follow-up, and basic health education. Daily supplementation of 400 μg (1000 IU) retinol palmitate (vitamin A) and 10 μg (400 IU) ergocalciferol (vitamin D_2) was recommended until the age of 2 y; continued supplementation until the age of 6 y during the winter months depended on the family. Solid foods were introduced between the ages of 3 and 5 mo. Breastmilk was the only milk source in infants of both groups for 5 ± 4 mo($\bar{x}$ ± SD) (**Table 1**). For other children, commercial cow milk–based formulas were recommended to the age of 12 mo. The energy density of the formulas used was 2.8 kJ/g. Fat accounted for 47% of energy, protein for 9% of energy, and carbohydrates for 44% of energy. Of the formula fat, 67% was from milk fat and 33% was from vegetable fat; 54% of formula fat was saturated. After 12 mo of age, all infants used cow milk as their milk source (except the few children allergic to cow milk). Only a few children received any breast milk after the age of 12 mo (Table 1). At 3 y, 114 intervention children (21.1%) and 105 control children (20.1%) had discontinued participation (**Table 2**).

Counseling

Five pediatricians, 3 dietitians, and 1 registered nurse participated in the counseling. The pediatrician recorded the child's past history, measured growth parameters, examined the child, and evaluated the child's development by questions and clinical examination. Possible current health problems were discussed. A nutritionist recorded the child's dietary history and taught the parents how to accurately record the child's food consumption.

TABLE 1
Characteristics of study children and their parents

	Intervention group (n = 284 boys, 256 girls)	Control group (n = 266 boys, 256 girls)
Birth weight of boys (g)	3630 ± 520	3630 ± 560
Birth weight of girls (g)	3490 ± 480	3460 ± 540
Birth weight ≤2500 g (n)	11	27
Duration of breast-feeding[1] (mo)	5.3 ± 3.7[2]	4.9 ± 3.7
Duration of breast-feeding[1] (mo)	5[3]	4
Any breast milk >12 mo (n)	31	29
Weaned to formula before 1 mo of age (n)	15	23
Mother's age at 7-mo visit (y)	30 ± 5	30 ± 5
Father's age at 7-mo visit (y)	33 ± 6	32 ± 6
Midparental BMI at 7-mo visit (kg/m^2)	24.0 ± 2.7	23.9 ± 2.7
Smokers at 7-mo visit, mothers (%)	15	19
Smokers at 7-mo visit, fathers (%)	31	34

[1] Breast milk as only milk source.
[2] $\overline{x}$ ± SD.
[3] Median.

She also suggested changes to the composition, amounts, and preparation of foods for the intervention children.

The intervention families received intensive individualized health education aimed at decreasing the child's exposure to known environmental atherosclerosis risk factors. Special attention was paid to dietary fat content and quality. The optimal diet for a child between 1 and 3 y of age was defined to contain energy ad libitum, fat as 30–35% of energy and a ratio of polyunsaturated to monounsaturated to saturated fat of 1:1:1, protein as 10–15% of energy, and carbohydrates as 50–60% of energy. The advantages of low salt intake were discussed briefly. The mothers were encouraged to breast-feed. Breast milk or formula was recommended until the age of 12 mo, and later, 0.5–0.6 L skim milk was recommended daily. The mothers of the intervention children were advised to replace the missing milk fat in the child's diet (2–3 teaspoons = 10–15 g) with vegetable oil (usually low–erucic acid rapeseed oil; 100 g contains 6 g saturated fatty acids, 57 g monounsaturated fatty acids, and 32 g polyunsaturated fatty acids) or soft margarine. The aim was to maintain the fat intake of the intervention children at the same amount as in children who consume milk with 1.9% fat. The use of oil or soft margarine in food preparation was encouraged. Detailed suggestions were made to replace saturated fat–containing products, eg, leaner meat products, low-fat cheese, and nondairy ice cream. The consumption of vegetables was encouraged and although the daily use of candy or simple sugars was discour-

aged, no foods were prohibited. Fish was recommended as a constituent of main meals once or twice a week. Two to 3 tablespoons (25–45 g) of meat, chicken, or fish were advised to be eaten daily before the age of 2 y, with a gradual increase to 4–5 tablespoons (50–75 g) at the age of 3–4 y. Particularly during the winter months, ≤50% of the children took multivitamin supplements because of their family's own choice.

In practice, at each visit the nutritionist suggested small changes in the child's diet that she thought would be deemed acceptable by the family. These suggestions were formed on the basis of a detailed dietary history of the child and family. Furthermore, the dry chemistry cholesterol values (*see* Laboratory methods below) obtained at every visit were used in counseling. A fixed diet was never ordered but the families were encouraged to make small changes that would lead toward an optimal diet. Issues concerning smoking prevention in the family and benefits of regular physical activity were also discussed.

The control children received the basic health education routinely given at Finnish well-baby clinics. Breast-feeding was encouraged. At the age of 12 mo, cow milk with ≥1.9% fat was recommended for daily use. No suggestions on the use of fats were given and dietary issues were discussed only superficially. Recommendations about vitamin supplementation were similar to those given to the intervention families.

The project was approved by the Joint Commission on Ethics of the Turku University and Turku University Central Hospital. Informed consent was obtained from the parents. Data from the 3 children with familial hypercholesterolemia were excluded from the analyses.

Dietary recording

When the child was 8, 13, and 18 mo of age, the parents (mainly the mother; if pertinent, the personnel at the daycare center) recorded the child's food consumption for 3 consecutive days. As the diet became more diversified, the food records covered 4 consecutive days at 24, 30, and 36 mo of age. The records, which included at least one weekend day, were evenly distributed throughout the year in the intervention and control families. The timing of the food records was changed if the child had an acute illness. At the age of 8 mo, 43% of the children still received breast milk. Consequently, an analysis of nutrient intakes was then limited to totally weaned infants, but later analyses included all children.

The nutritionists instructed the parents on how to properly record food intake. Written instructions and drawings of some ordinary food sizes were given. The personnel of the daycare centers were informed of the methods used. Household measures or home scales were used.

TABLE 2
Baseline characteristics of study participants who continued until the age of 3 y (n = 843) and of those who dropped out before the 3-y visit (n = 219)[1]

	Intervention group		Control group	
	Continued until age 3 y (n = 426)	Dropped out (n = 114)	Continued until age 3 y (n = 417)	Dropped out (n = 104)
Boys (%)	52	52	51	51
Weight at 7 mo (kg)	8.6 ± 1.0	8.6 ± 0.8	8.5 ± 1.0	8.6 ± 1.0
Height at 7 mo (cm)	70.5 ± 2.4	70.3 ± 2.2	70.3 ± 2.5	70.4 ± 2.6
Cholesterol at 7 mo (mmol/L)	3.98 ± 0.79	4.04 ± 0.82	3.99 ± 0.71	3.92 ± 0.81
Fat intake at 8 mo (% of energy)	29 ± 5	29 ± 5	29 ± 4	29 ± 5

[1] $\overline{x}$ ± SD.

The food records were evaluated by a nutritionist at each visit and the brand names and food preparation methods were clarified if necessary. The data were transferred to a computer by an experienced dietitian. Nutrient compositions were analyzed by using a MICRO NUTRICA PC program (26). This program, which is continuously updated, uses the nutrient database of the Social Insurance Institution of Finland as the source (27). It calculates 62 nutrients in >650 of the most commonly used foods, including baby foods and infant formulas, and provides a reasonably accurate estimation of the intake of most nutrients, including fats (26).

Laboratory methods

After cutaneous analgesia with lidocaine and prilocaine creme (EMLA, Astra, Södertälje, Sweden), ≈8 mL of blood was drawn from the antecubital vein of each child by using minimal stasis. Because of the young age of the subjects, the samples were nonfasting, and serum triacylglycerol values are not presented. Thus, instead of using the Friedewald formula to calculate LDL-cholesterol values (28), non-HDL-cholesterol values are shown. Fasting has no significant effect on serum cholesterol concentration and its effect on HDL-cholesterol concentration is modest, whereas the calculated LDL-cholesterol concentrationis strongly influenced by meals (29). Backup aliquots (2×0.5 mL serum at each time point) were stored at $-70\,°C$. If the blood draw was not successful on the first attempt, only a dry chemistry cholesterol measurement was obtained. The samples were drawn throughout the year at the time of day most convenient to the family, usually between 0900 and 1800.

Lipids, lipoproteins, and apolipoproteins were measured at the Research and Development Unit of the Social Insurance Institution, Turku, Finland. The laboratory cross-checked the lipid determinations with the World Health Organization reference laboratory in Prague, the Czech Republic, 2–4 times/y. Blood samples were allowed to clot at room temperature for 30–60 min. Serum was separated with low-speed centrifugation ($1500 \times g$, for 10 min, $5\,°C$) and stored at $-25\,°C$ for 2 wk. Storage ≤ 3 mo at $-20\,°C$ does not significantly alter measurement of cholesterol and HDL-cholesterol concentrations (30). Serum cholesterol was measured by using fully enzymatic cholesterol oxidase-p-aminophenazone methods (CHOD-PAP; Merck, Darmstadt, Germany) (31) in an AU 510 automatic analyzer (Olympus, Hamburg, Germany), except for the samples analyzed before November 20, 1990, which were measured by using a Boehringer CHOD-PAP kit (32) and OLLI analyzer (Kone, Helsinki). Serum HDL-cholesterol concentration was measured after precipitation of LDL and VLDLs with dextran sulfate 500 000 (33). The results of the samples analyzed before November 1990 were corrected according to calibration runs. For serum cholesterol, the corrective equation was: serum cholesterol = 1.068859 × serum cholesterol (during 1990) − 0.317158. For serum HDL cholesterol the equation was: serum HDL cholesterol = 1.066248 × serum HDL cholesterol (during 1990) − 0.030667. Apolipoprotein A-I and B were measured immunoturbidimetrically by using Apolipoprotein A-I and B kits (34) (Orion Diagnostica, Helsinki). The apolipoprotein measurements were standardized against World Health Organization International Reference Materials SP1–01 for apo A-I and SP3–07 for apo B. Results of samples analyzed before September 1993 were corrected according to the following equations: corrected apo A-I = 1.022726 × apo A-I (during 1990–1993) + 0.047643 and corrected apo B = 1.056093 × apo B (during 1990–1993) + 0.041142. The interassay (intraassay) CUs of cholesterol, HDL cholesterol, and apo A-I and B determinations were 2.0% (1.5%), 1.9% (1.2%), 3.0% (1.8%), and 4.5% (3.3%), respectively.

Dry chemistry cholesterol values (Reflotron, Behringer Mannheim, Mannheim, Germany) were measured in all venous blood samples available and used for counseling of the intervention families. If the venous blood draw was unsuccessful, only a fingertip sample was taken for dry chemistry analysis of capillary cholesterol. The detection limit of the dry chemistry measurement was 2.59 mmol/L. The Reflotron cholesterol concentrations were 3–4% lower than the CHOD-PAP cholesterol concentrations at 7 mo of age and 1–2% lower at 36 mo of age. When dry chemistry and CHOD-PAP cholesterol results were compared, the 95% CIs of the mean differences between groups in the increase of cholesterol concentrations from 7 to 36 mo were comparable in both sexes, implying that at the group level, the serum and dry chemistry cholesterol measurements gave similar results.

Measurement of growth

Weight of children to the nearest 0.01 kg was measured until the age of 15 mo by using a baby scale (Seca 725; Seca, Hamburg, Germany) and then by using an electronic scale to the nearest 0.1 kg (Soehnle S10; Soehnle, Murhardt, Germany). Length of children to the nearest 1.0 mm was measured horizontally by using a baby board (Bekvil, Paljerakenne, Helsinki) until the age of 21 mo. Thereafter, standing height was measured using the Harpenden stadiometer (Holtain, Crymych, United Kingdom). Head circumference (to the nearest 1.0 mm) was measured by using a flexible measuring tape. Height or length, relative height (deviation of height in SD units from the mean height of healthy Finnish children of the same age and sex), weight, and relative weight [deviation of weight (as a percentage) from the mean weight of healthy Finnish children of the same height and sex] and head circumference were recorded (35). The weights and heights of parents were measured with an electronic scale and stadiometer. The measurements were performed by using similar procedures by the members of the counseling team. The scales were calibrated regularly.

Statistical methods

The required sample size was predicted to show a 0.2-mmol/L true difference in the change in serum cholesterol concentration between the intervention and control groups at the 1% significance level with 80% power. The results are shown as $\bar{x} \pm$ SD values with 95% CIs when appropriate. The SAS program (release version 6.08, 1990; SAS Institute Inc, Cary NC, 1990) and the BMDP version 1990 (36) were used. Differences were considered significant at $P < 0.05$.

Serum lipid values were normally distributed. To selectively analyze the effects of intervention, values were adjusted for the baseline situation (7-mo lipid values). Longitudinal serum lipid concentrations were analyzed with unbalanced repeated measures analysis of covariance (37) with the 7-mo lipid value as a covariate. The sexes were analyzed together and also separately. Children with the baseline and at least one later lipid measurement were included in the analysis. Analyses using values of children with complete data were also conducted ($n = 527$). Apolipoprotein and dry chemistry cholesterol values were available in 688 and 942 children, respectively.

Heights, relative heights, weights, and relative weights measured at 7, 13, 18, 24, 30, and 36 mo and head circumferences

measured at 7, 13, and 24 mo of age were normally distributed. Longitudinal data were analyzed by using analysis of variance for unbalanced-measures design with one between factor (study group) and one within factor (time). The sexes were analyzed separately. Children with ≥2 measurements during the trial were included in the growth analyses (n = 1002, 997, 887, and 842 at 7, 13, 24, and 36 mo of age, respectively).

To analyze the growth of children with different fat intakes, the children were categorized on the basis of fat intake: <25% of energy, 25–30% of energy, and >30% of energy at 13, 24, and 36 mo, respectively. The growth data of children in these fat intake groups were compared by using one-way analysis of variance. Growth of children who were continuously (ie, at 13, 24, and 36 mo of age) in the lowest fat intake quartile was then compared with growth of children with higher fat intakes by using unbalanced repeated measures analysis of variance.

To investigate the differences between children growing at different rates, the relative height and relative weight of each child at each time point between 7 and 36 mo was recorded and linear regression lines of relative height and relative weight on age using all available data points for each child were formed. The children with ≥5 measurements (ie, ≥2 y follow-up) were included in these analysis. The 2 children with Down syndrome were excluded. Children of both sexes were then divided separately into 5 groups by using the following criteria: *1*) children with decreasing relative height (ie, the lowest 5% of the regression line, the "slow height gain" children), *2*) children with consistently low relative height (ie, the "short" children; mean relative height <5%), *3*) children growing normally (ie, the "normal" children, 80% of all), *4*) children with increasing relative height (ie, the highest 5% of the regression slope, the "rapid height gain" children), and *5*) children with consistently high relative height (ie, the "tall" children, mean relative height >95%,). Similar criteria were used for relative weight but the children with decreasing relative weight who were still above the mean weight-for-height and sex at 36 mo of age were included in the group of normally growing children, if not included in the "obese" group (by definition: mean relative weight >95%). The intervention and control children were combined, but when categorizing children who were growing differently into groups, we separated the sexes. Thus, each group of children growing at a different rate included both sexes evenly. Boys and girls were combined when analyzing the dietary variables of these groups. The dietary variables of these 5 groups were analyzed by using one-way analysis of variance, and, further, polychotomous logistic regression analysis was used to determine the influence of the child's food record data at 8, 13, 24, and 36 mo energy intake, relative energy intake (kJ/kg body wt), fat intake, and protein intake, and of parental anthropometric measures [midparental height and body mass index (BMI)] in predicting the growth pattern of the children.

RESULTS

Dietary intakes

Food intake was first recorded at the age of 8 mo, when dietary intervention had still been minimal. Because it was not feasible to quantitate ingested breast milk in a large group of 8-mo-old children, dietary results comprise only data of the weaned infants at this age (≈60% of all).

At 8 mo, the energy intake of the formula-fed intervention children was 4.5% lower than that of the formula-fed control infants (P = 0.0039; **Table 3**). Neither fat intake, polyunsaturated-to-saturated fat ratio (P-S), unsaturated-to-saturated ratio, nor intake of cholesterol differed between the 2 study groups (P = 0.38–0.76). Between 13 and 36 mo of age, the mean daily energy intake was slightly lower in the intervention than the control children (P = 0.050–0.13) (Table 3). Similarly, relative energy intake was 8–13 kJ/lower per kilogram body weight body weight lower in the intervention children than in the control children through the trial. The energy density, calculated as energy intake per amount of food eaten, was slightly lower in the intervention children than in the control children from age 13 mo. During the intervention, intake of fat, saturated fatty acids, and cholesterol were lower, but the P-S and unsaturated-to-saturated fat ratios were consistently higher in the intervention children than in the control children. The difference in the P-S fat ratio between the 2 study groups was largest at 13 mo of age, but thereafter it continuously decreased slightly (Table 3).

Absolute and relative energy intake was within the reference range (3800–7100 kJ/d) (38) in both groups of children during the trial. However, fat intake in both groups was markedly lower than what has been recommended for these ages. The difference was particularly striking at the age of 8 mo (29.4% in all STRIP children combined compared with 35–45% of children in the Nordic Nutrition Recommendations) (38). Mean fat intake was still below the recommendation (30–35% of energy) at 13 mo of age in both groups (intervention children: 26.4% of energy, control children: 28.5% of energy), but at 2 and 3 y of age, the mean fat intake was within the recommended range in both groups. Protein intake in both groups was higher than recommended throughout the trial. No consistent differences between the intervention and control children in vitamin and mineral intakes were found (data not shown). Inter- and intraindividual day-by-day variations in dietary intakes were large.

Serum lipids, lipoproteins, and apolipoproteins

Children who had the baseline measurement and at least one later lipid measurement were included in these statistical analyses. Serum cholesterol and HDL-cholesterol concentrations (**Figure 2**) and other lipid, lipoprotein, and apolipoprotein values (**Table 4** and **Table 5**) were similar in the intervention and control children at baseline. At baseline, girls had higher cholesterol, non-HDL-cholesterol, and apo B values than did the boys (P > 0.0001 for all), while the HDL ratio (P = 0.0002) and the ratios of apo A-I to apo B (P < 0.0001) were higher in boys. Concentrations of apo A-I and apo B did not differ between the sexes.

Intervention influenced serum lipid and lipoprotein concentrations markedly (Figure 2, Table 4, and Table 5). Serum cholesterol concentrations increased more in the control children than in the intervention children between 7 and 36 mo of age (P < 0.0001, 95% CI for the difference between baseline-adjusted means of the intervention and control children: −0.27, −0.12 mmol/L, sexes combined). The difference between the baseline-adjusted means of the 2 groups of children remained stable during this period (P = 0.28 for group-by-time interaction). When the children were divided by sex, the difference was significant only in boys. The 95% CIs indicated that the baseline-adjusted serum cholesterol concentration of the intervention boys was ≤0.39 mmol/L and ≥0.20 mmol/L lower than that of the control boys, whereas the intervention girls had ≤

TABLE 3
Daily energy and nutrient intakes by the intervention and control children at 8, 13, 24, and 36 mo of age (at the age of 8 mo, the data are from formula-fed children only)[1]

	Intervention children	Control children	P (95% CI)[2]
8 mo (n = 221 intervention children, 215 control children)			
Energy (kJ)	3360 ± 511	3515 ± 616	0.0039 (−264, −50)
Fat (% of energy)	29.0 ± 4.7	28.8 ± 4.1	0.67 (−0.6, 1.0)
P:S	0.39 ± 0.08	0.40 ± 0.15	0.38 (−0.03, 0.01)
U:S	1.08 ± 0.21	1.10 ± 0.26	0.51 (−0.06, 0.03)
Protein (% of energy)	12.1 ± 2.1	12.2 ± 1.7	0.89 (−0.4, 0.3)
Carbohydrates (% of energy)	58.8 ± 4.6	59.0 ± 4.2	0.72 (−1.0, 0.7)
Cholesterol (mg/1000 kJ)	21 ± 6	21 ± 7.9	0.76 (−1, 1)
13 mo (n = 488 intervention children, 464 control children)			
Energy (kJ)	4048 ± 763	4143 ± 779	0.050 (−197, −0)
Energy (kJ/kg body wt)	393 ± 79	406 ± 79	0.017 (−21, −4)
Fat (% of energy)	26.2 ± 6.0	27.9 ± 4.9	<0.0001 (−2.4, −1.0)
P:S	0.64 ± 0.41	0.33 ± 0.25	<0.0001 (0.26, 0.35)
U:S	1.75 ± 0.82	1.07 ± 0.41	<0.0001 (0.60, 0.77)
Protein (% of energy)	17.6 ± 2.9	17.1 ± 2.6	0.015 (0.1, 0.8)
Carbohydrates (% of energy)	56.3 ± 5.6	55.0 ± 5.4	0.0002 (0.6, 2.0)
Cholesterol (mg/1000 kJ)	22 ± 10	26 ± 9	<0.0001 (−5, −3)
24 mo (n = 424 intervention children, 436 control children)			
Energy (kJ)	4714 ± 829	4802 ± 863	0.13 (−197, 25)
Energy (kJ/kg body wt)	369 ± 67	377 ± 71	0.014 (−21, −2)
Fat (% of energy)	29.9 ± 5.0	32.8 ± 4.8	<0.0001 (−3.6, −2.2)
P:S	0.52 ± 0.21	0.33 ± 0.15	<0.0001 (0.17, 0.22)
U:S	1.52 ± 0.46	1.10 ± 0.30	<0.0001 (0.37, 0.48)
Protein (% of energy)	17.0 ± 2.4	16.1 ± 2.3	<0.0001 (0.5, 1.2)
Carbohydrates (% of energy)	53.1 ± 5.1	51.0 ± 5.3	<0.0001 (1.4, 2.8)
Cholesterol (mg/1000 kJ)	28 ± 10	33 ± 12	<0.0001 (−6, −3)
36 mo (n = 392 intervention children, 398 control children)			
Energy (kJ)	5070 ± 905	5191 ± 980	0.070 (−251, 8)
Energy (kJ/kg body wt)	339 ± 63	348 ± 67	0.0095 (−21, −4)
Fat (% of energy)	30.8 ± 4.9	33.2 ± 4.6	<0.0001 (−3.1, −1.7)
P:S	0.48 ± 0.17	0.33 ± 0.13	<0.0001 (0.12, 0.17)
U:S	1.38 ± 0.37	1.08 ± 0.24	<0.0001 (0.25, 0.34)
Protein (% of energy)	16.0 ± 2.2	15.4 ± 2.3	0.0002 (0.3, 0.9)
Carbohydrates (% of energy)	53.1 ± 4.9	51.3 ± 5.1	<0.0001 (1.1, 2.5)
Cholesterol (mg/1000 kJ)	28 ± 10	33 ± 11	<0.0001 (−6, −3)

[1] $\bar{x}$ ± SD. P:S, ratio of polyunsaturated to saturated fat; U:S, ratio of unsaturated to saturated fat.
[2] 95% CI for the difference of the group means.

0.21 mmol/L lower and ≤0.01 mmol/L higher serum cholesterol concentration than the control girls. Serum cholesterol concentrations were higher in girls than in boys (P = 0.03) throughout the trial (39). The mean change in serum cholesterol concentration from 7 to 36 mo was 0.25 mmol/L (6%) [0.14 mmol/L (3%)] greater in the control boys (girls) than in the intervention boys (girls). The results remained almost unchanged when only children with complete data (n = 527) were included in the analyses.

Serum non-HDL-cholesterol concentration increased more in the control children than in the intervention children (P < 0.0001, 95% CI: −0.22, −0.08 mmol/L, sexes combined), but, as for the total cholesterol concentration, the difference was not significant in girls. The difference between group means did not change during the follow-up (P = 0.29). The mean change in serum non-HDL-cholesterol concentration was 0.18 mmol/L (6%) [0.11 mmol/L (3%] greater in the control boys (girls) than in the intervention boys (girls). Girls had higher non-HDL-cholesterol concentrations than boys (P = 0.02).

The dry chemistry cholesterol concentration also increased more in the control boys and girls than in the intervention boys

and girls. The mean increase from 7 to 36 mo in dry chemistry cholesterol value was 0.28 mmol/L (0.19 mmol/L) greater in the control boys (girls) than in the intervention boys (girls) (95% CI: 0.43, 0.12 mmol/L and 0.36, 0.02 mmol/L, respectively).

Serum HDL-cholesterol concentration increased more in the control children than in the intervention children during the trial (P < 0.0001, 95% CI for the mean difference: −0.07, −0.03 mmol/L, sexes combined) (Figure 2). This difference between the study means did not change during the follow-up (P = 0.60). Between 7 and 36 mo, HDL-cholesterol concentrations increased 0.07 mmol/L (6 %) more in the control boys than in the intervention boys [in girls, concentrations increased 0.03 mmol/L (3%)]. Sex had no significant influence on HDL-cholesterol concentrations.

The HDL ratios showed no differences between the intervention and control children in either sex (P = 0.59, 95% CI: −0.007, 0.004, sexes combined). The HDL ratio increased with age (P < 0.0001). The boys had higher mean HDL ratios than did the girls throughout the study (P = 0.02).

Apo A-I concentrations increased in the control children more than in the intervention children in both sexes (P < 0.0001,
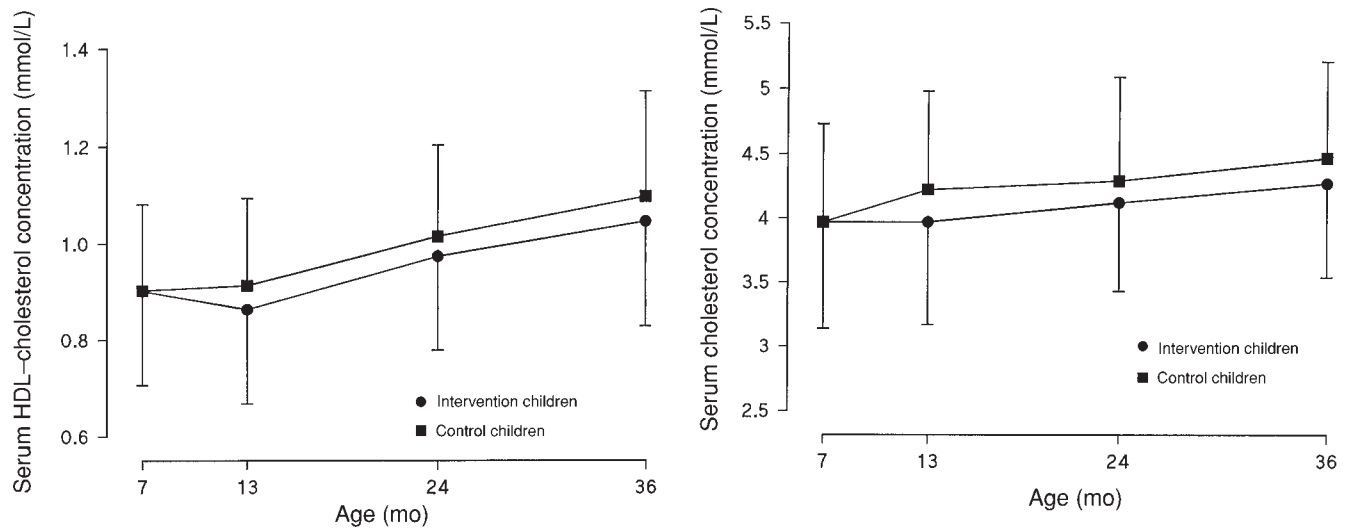
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FIGURE 2. Mean (±SD) serum cholesterol and HDL-cholesterol concentrations in the intervention and control children at 7 and 36 mo of age. The data comprise values of children of both sexes. From 13 to 36 mo of age, the baseline-adjusted mean cholesterol concentration was lower in the intervention children than in the control children ($P < 0.0001$, 95% CI of the mean difference: -0.27, -0.12 mmol/L). The mean HDL-cholesterol concentration was also lower in the intervention children than in the control children ($P < 0.0001$, 95% CI: -0.07, -0.03 mmol/L).

95% CI for the mean difference between intervention and control children sexes combined: -0.05, -0.02 g/L) between 7 and 36 mo of age (Tables 4 and 5). Apo A-I concentrations increased with age ($P < 0.0001$) but sex had no influence on apo A-I concentrations ($P = 0.35$). The intervention children had lower serum concentrations of apo B than did the control children ($P = 0.013$; 95% CI: -0.04, -0.005 g/L, sexes combined). As for the serum cholesterol and non-HDL-cholesterol values, the difference was significant only in boys. Girls had higher apo B values than did boys ($P = 0.002$). The ration of apo A-I to apo B was lower in girls than in boys ($P = 0.01$) but the intervention had no influence on the ratio in either sex ($P = 0.45$, 95% CI: -0.06, 0.03, sexes combined).

Growth

In the beginning of the trial, the mean heights, weights, and BMIs of the intervention and control parents were very similar. The birth weights and lengths of the intervention boys (girls) and control boys (girls) were almost identical. Birth weights of the boys ranged from 850 to 5460 g and those of the girls from 1860 to 5260 g. The birth weights of 37 children were <2500 g (4% of the cohort; 11 and 26 in the intervention and control groups, respectively) (Table 1). In the beginning of the trial, height, relative height, weight, and relative weight of the boys and girls were similar in the intervention and control groups. Therefore, the intervention and control children were expected to grow similarly.

In the analysis of growth, the interactions between study group and time were not significant. Consequently, despite the smaller mean intake of energy and fat by the intervention children (Table 3), the children in both groups grew equally (**Table 6** and **Table 7**).

The intervention boys (girls) were as tall and as heavy as the control boys (girls) at 36 mo of age. Head circumference of the children of both sexes increased normally in the intervention and control groups.

At 7 mo of age, 67 children had a relative weight of $\leq -10\%$ on the growth charts of healthy Finnish children. Of these children, 35 belonged to the intervention group (6.8% of the whole intervention group) and 32 (6.6%) belonged to the control group. Similarly, the relative weights were $\leq 10\%$ of 65 children at 13 mo [32 intervention children (6.3%) and 33 control children (6.8%)], of 78 children at 24 mo [34 intervention children (7.6%) and 44 control children (10.1%)], and of 74 children at 36 mo [35 intervention children (8.2%) and 39 control children (9.4%)].

At 13 mo of age, 35% of all children had a fat intake of <25% of energy, 36% had a fat intake of 25–30% of energy, and 29% had a fat intake of >30% of energy. At 24 mo of age, the proportion of children with these respective fat intakes were 11%, 27%, and 62%, and at 36 mo, intakes were 7% , 26%, and 67%. The relative heights and relative weights of children whose fat intakes were <25% of energy, 25–30% of energy, or >30% of energy at 13, 24, or 36 mo of age were very similar. The relative heights and relative weights of the 35 children who belonged consistently to the lowest relative fat intake quartile were similar to those of the children with a higher fat intake (**Table 8**). Those children with low fat intake grew 5.5 ± 1.4 cm and gained 1.3 ± 0.5 kg between 13 and 18 mo of age, whereas the respective values were 5.4 ± 1.4 cm and 1.3 ± 0.5 kg in the other children (NS). The height and weight gain velocities were also similar between children with a consistently low intakes of fat and the other children between the ages of 18 and 24 mo, 24 and 30 mo, and 30 and 36 mo.

The children ($n = 38$) who were consistently in the lowest serum cholesterol concentration quartile at 7, 13, 24, and 36 mo of age grew in the same way as the children with higher serum cholesterol concentrations. For example, at 7 mo of age the relative heights and relative weights were +0.25 SD and +0.24 SD ($P = 0.93$) and +2.6% and 2.3% ($P = 0.84$) in children in the lowest serum cholesterol concentration quartile and for the other children with higher concentrations, respectively. The respective values were +0.28 SD and +0.18 SD ($P = 0.51$) and +0.3% and 0.0% ($P = 0.82$) at 3 y. Similarly, no differences in growth were seen between children who were consistently in the lowest decile in serum cholesterol concentrations ($n = 12$) and children with higher cholesterol concentrations ($n = 530$). At 3 y of age, the relative height was +0.44 SD and the relative

TABLE 4
Serum lipid, lipoprotein, and apolipoprotein concentrations in the intervention and control boys[1]

	7 mo	13 mo	24 mo	36 mo	7–36 mo[2]	P (95% CI)[3]
Cholesterol (mmol/L)						
Intervention boys (n = 201)	3.79 ± 0.74	3.74 ± 0.60	3.95 ± 0.59	4.12 ± 0.63	0.32 ± 0.76	<0.0001 (−0.39, −0.20)
Control boys (n = 187)	3.87 ± 0.69	4.16 ± 0.76	4.24 ± 0.83	4.44 ± 0.79	0.57 ± 0.65	
Non-HDL cholesterol (mmol/L)						
Intervention boys (n = 201)	2.89 ± 0.72	2.87 ± 0.57	2.98 ± 0.56	3.07 ± 0.60	0.17 ± 0.71	<0.0001 (−0.33, −0.14)
Control boys (n = 187)	2.97 ± 0.68	3.24 ± 0.73	3.21 ± 0.80	3.32 ± 0.75	0.35 ± 0.59	
HDL cholesterol (mmol/L)						
Intervention boys (n = 201)	0.90 ± 0.20	0.87 ± 0.20	0.97 ± 0.21	1.05 ± 0.23	0.15 ± 0.23	0.0001 (−0.08, −0.03)
Control boys (n = 187)	0.91 ± 0.19	0.92 ± 0.19	1.03 ± 0.19	1.12 ± 0.22	0.21 ± 0.19	
HDL ratio						
Intervention boys (n = 201)	0.24 ± 0.07	0.24 ± 0.06	0.25 ± 0.06	0.26 ± 0.06	0.01 ± 0.07	0.76 (−0.01, 0.01)
Control boys (n = 187)	0.24 ± 0.05	0.23 ± 0.05	0.25 ± 0.05	0.26 ± 0.05	0.02 ± 0.05	
Apolipoprotein A-I (g/L)						
Intervention boys (n = 184)	1.10 ± 0.14	1.05 ± 0.16	1.09 ± 0.15	1.13 ± 0.16	0.02 ± 0.16	0.0007 (−0.06, −0.02)
Control boys (n = 167)	1.11 ± 0.12	1.09 ± 0.14	1.12 ± 0.15	1.18 ± 0.17	0.07 ± 0.15	
Apolipoprotein B (g/L)						
Intervention boys (n = 184)	0.72 ± 0.18	0.75 ± 0.16	0.74 ± 0.14	0.75 ± 0.16	0.03 ± 0.19	0.0021 (−0.06, −0.01)
Control boys (n = 167)	0.73 ± 0.17	0.81 ± 0.18	0.78 ± 0.18	0.79 ± 0.18	0.06 ± 0.15	
Ratio of apolipoprotein A-I to apolipoprotein B						
Intervention boys (n = 184)	1.65 ± 0.56	1.47 ± 0.47	1.54 ± 0.46	1.59 ± 0.51	−0.07 ± 0.47	0.87 (−0.06, 0.05)
Control boys (n = 167)	1.60 ± 0.42	1.41 ± 0.38	1.51 ± 0.42	1.56 ± 0.43	−0.03 ± 0.36	

[1] $\bar{x}$ ± SD.

[2] Individual changes from 7 to 36 mo.

[3] Analysis of covariance; 95% CI of the difference between group means from 13 to 36 mo of age adjusted for baseline (the 7-mo value).

weight was −0.6% in children with lower serum cholesterol concentrations, whereas in the children with higher concentrations, the respective values were +0.18 SD and 0.0% (P = 0.35 and P = 0.78), respectively.

On the basis of the development of the height-for-age (weight-for-height) scores, the children were categorized into 5 growth pattern groups (*see* Methods; **Table 9** and **Table 10**). For children between 7 and 36 mo of age, short children grew an average of 24.0 ± 2.0 cm, slow height gain children grew an average of 23.1 ± 1.6 cm, rapid height gain children grew an average of 29.7 ± 2.0 cm, tall children grew an average of 29.5 ± 2.1 cm, and normal children grew an average of 26.5 ± 2.1 cm (P < 0.001 between groups). Between 7 and 36 mo of age, the thin children gained an average of 5.6 ± 0.6 kg, whereas the slow weight gain children gained an average of 4.9 ± 0.6 kg, the rapid weight gain children gained an average of 9.2 ± 1.6 kg, the obese children gained an average of 7.6 ± 1.3 kg, and the normal children gained an average of 6.5 ± 1.0 kg (P < 0.001 between the groups).

Energy intakes and relative energy intakes (kJ/kg body weight) differed in children with different growth patterns (P always < 0.05) (Tables 9 and 10). The thin and the short children consumed less energy throughout the trial than did those with normal growth, but the relative energy intakes of the thin and the short children were higher than those of the children with normal growth. The obese and the tall children had the lowest relative energy intakes. At 13 mo of age, the children with slow height gain consumed relatively less energy than the children with normal growth (P = 0.02), but these slow height gain children were at that time considerably taller (mean relative height +1.2 SD) than the normal growth children (mean relative height +0.45 SD). Fat intake was similar in all height gain

groups throughout the trial (P = 0.14–0.77). At 13 and 24 mo of age, the thin children had the highest relative fat intakes.

Polychotomous logistic regression analysis, used to evaluate the influence of dietary parameters and parental anthropometric measures on the child's growth pattern, showed that the midparental height (P < 0.001) and relative energy intake of the child (P = 0.008–0.025) predicted the child's height gain patterns at 8, 13, 24, and 36 mo of age. The results were similar when total daily energy intake instead of relative energy intake was used as the predicting variable, except that at 13 mo of age relative fat intake (P = 0.012) and relative zinc intake (P = 0.019) predicted the child's growth pattern. Energy intake as such was a significant predictor of the child's growth pattern from 13 to 36 mo of age. The variables that predicted the child's weight gain pattern were, at 13 mo, the midparental BMI (P < 0.001), relative energy intake (P = 0.002), and fat intake as percentage of energy (P = 0.015); at 24 mo, midparental BMI (P < 0.001) and relative energy intake (P < 0.001); and at 36 mo, mid-parental BMI (P < 0.001) and relative zinc intake (P = 0.048). Furthermore, energy intake as such was a significant predictor of a child's weight gain pattern from 13 to 36 mo of age.

Polychotomous logistic stepwise regression analysis of the data at 13 and 36 mo of age showed that an increase in the midparental height of 1 cm increased the possibility of the child belonging to the tall group than to the normal group by 1.1-fold, and a 10-cm increase in midparental height increased the possibility by 4-fold. Similarly, at 3 y of age, an increase of 42 kJ/kg (≈10 kcal/kg) in relative energy intake decreased the possibility of the child belonging to the thin group than to the normal group by 1.6-fold. According to the model, one can predict that an

TABLE 5
Serum lipid, lipoprotein, and apolipoprotein concentrations in the intervention and control girls[1]

	7 mo	13 mo	24 mo	36 mo	7–36 mo[2]	P (95% CI)[3]
Cholesterol (mmol/L)						
Intervention girls (n = 173)	4.19 ± 0.88	4.23 ± 0.91	4.32 ± 0.74	4.45 ± 0.80	0.23 ± 0.82	0.089 (−0.21, 0.01)
Control girls (n = 187)	4.08 ± 0.81	4.29 ± 0.77	4.34 ± 0.77	4.49 ± 0.69	0.37 ± 0.76	
Non-HDL cholesterol (mmol/L)						
Intervention girls (n = 173)	3.28 ± 0.86	3.37 ± 0.89	3.34 ± 0.69	3.40 ± 0.77	0.09 ± 0.78	0.26 (−0.17, 0.05)
Control girls (n = 187)	3.18 ± 0.79	3.38 ± 0.76	3.33 ± 0.73	3.42 ± 0.64	0.20 ± 0.71	
HDL cholesterol (mmol/L)						
Intervention girls (n = 173)	0.91 ± 0.19	0.86 ± 0.20	0.98 ± 0.18	1.05 ± 0.20	0.15 ± 0.20	0.0068 (−0.07, −0.01)
Control girls (n = 187)	0.90 ± 0.17	0.91 ± 0.17	1.00 ± 0.18	1.08 ± 0.21	0.18 ± 0.20	
HDL ratio						
Intervention girls (n = 173)	0.22 ± 0.06	0.21 ± 0.05	0.23 ± 0.04	0.24 ± 0.05	0.02 ± 0.06	0.26 (−0.01, 0.00)
Control girls (n = 187)	0.23 ± 0.05	0.22 ± 0.05	0.24 ± 0.05	0.24 ± 0.05	0.02 ± 0.05	
Apolipoprotein A-I (g/L)						
Intervention girls (n = 152)	1.11 ± 0.13	1.05 ± 0.15	1.08 ± 0.14	1.13 ± 0.15	0.01 ± 0.17	0.0011 (−0.06, −0.02)
Control girls (n = 161)	1.11 ± 0.13	1.09 ± 0.15	1.11 ± 0.14	1.17 ± 0.15	0.06 ± 0.13	
Apolipoprotein B (g/L)						
Intervention girls (n = 152)	0.81 ± 0.19	0.87 ± 0.21	0.82 ± 0.16	0.83 ± 0.18	0.02 ± 0.20	0.72 (−0.03, 0.02)
Control girls (n = 161)	0.79 ± 0.19	0.86 ± 0.18	0.82 ± 0.18	0.84 ± 0.16	0.04 ± 0.18	
Ratio of apolipoprotein A-I to apolipoprotein B						
Intervention girls (n = 152)	1.46 ± 0.41	1.26 ± 0.34	1.35 ± 0.29	1.41 ± 0.36	−0.04 ± 0.40	0.089 (−0.10, 0.01)
Control girls (n = 161)	1.48 ± 0.39	1.33 ± 0.36	1.42 ± 0.35	1.45 ± 0.33	−0.02 ± 0.33	

[1] $\overline{x}$ ± SD.

[2] Individual changes from 7 to 36 mo.

[3] Analysis of covariance; 95% CI of the difference between group means from 13 to 36 mo of age adjusted for baseline (the 7-mo value).

increase in the midparental BMI (measured at the beginning of the trial) of 1 kg/m^{2} increased the possibility of the child belonging to the obese group than to the normal group by 1.2-fold and an increase in the midparental BMI of 10 kg/m^{2} by 6-fold. The results were virtually the same if the study group was expanded to include children with ≥3 available growth measurements during the study (n = 950; data not shown).

Finally, we analyzed whether the intervention children more often showed deviant growth patterns than did the control children. Of the slow height gain children, 22 belonged to the intervention group and 21 to the control group, and of the slow weight gain children, 15 belonged to the intervention group and 28 to the control group. The fat intakes of the 3 children (all from the control group) who belonged to both the slow height gain and slow weight gain groups varied from 33% of energy to 35% of energy at 13 mo, from 26% of energy to 39% of energy at 24 mo, and from 37% of energy to 39% of energy at 36 mo of age. The relative weights and relative heights did not differ at any age between the children who were included in the regression analysis (n = 848) and those children who had fewer measurements during the follow-up periods and had thus been excluded from this analysis (data not shown).

DISCUSSION

Because only 56.5% of the eligible age cohort participated in this project, it is possible that the participating families were more health-conscious than the nonparticipating families. It is also possible that children with growth or other health-related problems in infancy did not participate in the trial as frequently as did children with no previous or current health problems. According to phone contact with families who had decided not to participate in the trial (n = 417), no bias was found in the socioeconomic status or health beliefs between the participating and nonparticipating families. The most common reasons for not participating were difficulties in arranging the office visits and unwillingness to change the diet. A remarkably small number of families (20%) had left the trial before the 3-y visit. There were no differences in the number of the dropouts between the intervention and control groups and no significant differences were observed in baseline serum cholesterol concentration, fat intake, and growth between the study participants and dropouts. Because only minor differences between the trial participants and nonparticipants were found and the drop-out rate of the participants did not differ between the 2 study groups, the results are probably valid in the whole age cohort in the Turku area.

Dietary intakes

Intake of energy was slightly lower and intake of saturated fat markedly lower in the intervention children than in the control children. Intake of polyunsaturated fat and the P-S ratio of the diet in the intervention children were higher than those in the control children, even though the targeted low intake of saturated fat (one-third of all fat) was not reached.

The daily energy and fat intakes of the intervention and control children were lower than what had been reported previously in the United States [7900 kJ with 39% of energy from fat at 24 mo of age, and 9200 kJ with 38% of energy from fat at 36 mo of age in Louisiana (40) and from 4600 to 7500 kJ in children aged 26–62 mo (41)]. The Bogalusa Study results are not fully comparable with our results because of the different race and socioeconomic status of the study populations. However, a study applying doubly labeled water as a tracer suggested that energy expenditure has previously been slightly overestimated and that the mean

TABLE 6
Height, relative height, weight, and relative weight of the intervention and control boys at 7–36 mo of age[1]

Age (mo)	Height			Relative height			Weight			Relative weight		
	Intervention	Control	P2	Intervention	Control	P2	Intervention	Control	P2	Intervention	Control	P2
	cm			SD			kg			%		
7 (n = 269 intervention, 248 control boys)	71.2 ± 2.2	71.2 ± 2.3	0.62 (−0.57, 0.34)	0.17 ± 0.94	0.15 ± 1.02	0.53 (−0.19, 0.10)	8.8 ± 0.9	8.8 ± 1.0	0.87 (−0.22, 0.19)	2.8 ± 8.4	3.0 ± 8.4	0.86 (−1.1, 1.3)
13 (n = 268 intervention, 246 control boys)	78.7 ± 2.5	78.7 ± 2.6		0.35 ± 0.92	0.40 ± 1.00		10.6 ± 1.1	10.7 ± 1.1		1.4 ± 7.6	2.0 ± 8.1	
18 (n = 241 intervention, 210 control boys)	84.0 ± 2.8	84.1 ± 2.8		0.27 ± 0.92	0.34 ± 0.94		11.9 ± 1.3	11.8 ± 1.2		1.0 ± 7.8	0.6 ± 7.2	
24 (n = 235 intervention, 221 control boys)	89.0 ± 2.8	88.9 ± 2.8		0.25 ± 0.83	0.23 ± 0.84		13.1 ± 1.4	13.0 ± 1.3		1.3 ± 7.6	0.7 ± 7.3	
30 (n = 228 intervention, 211 control boys)	93.1 ± 3.2	93.3 ± 3.1		0.03 ± 0.90	0.09 ± 0.86		14.2 ± 1.5	14.2 ± 1.4		1.5 ± 7.3	0.7 ± 6.7	
36 (n = 225 intervention, 215 control boys)	97.2 ± 3.5	97.4 ± 3.3		0.18 ± 0.93	0.23 ± 0.88		15.3 ± 1.6	15.2 ± 1.6		1.5 ± 7.1	0.5 ± 7.3	

[1] $\bar{x}$ ± SD.
[2] 95% CI for the difference in group means in parentheses.

TABLE 7
Height, relative height, weight, and relative weight of the intervention and control girls at 7–36 mo of age[1]

Age (mo)	Height			Relative height			Weight			Relative weight		
	Intervention	Control	P2	Intervention	Control	P2	Intervention	Control	P2	Intervention	Control	P2
	cm			SD			kg			%		
7 (n = 245 intervention, 240 control girls)	69.4 ± 2.3	69.3 ± 2.3	0.19 (−0.16, 0.77)	0.34 ± 1.02	0.21 ± 1.04	0.21 (−0.06, 0.28)	8.3 ± 0.9	8.2 ± 0.9	0.11 (−0.04, 0.42)	4.5 ± 9.0	3.3 ± 8.9	0.17 (−0.4, 2.3)
13 (n = 242 intervention, 241 control girls)	77.2 ± 2.5	76.8 ± 2.5		0.56 ± 1.09	0.45 ± 1.11		10.0 ± 1.1	9.9 ± 1.1		2.9 ± 8.0	2.3 ± 8.3	
18 (n = 216 intervention, 223 control girls)	82.6 ± 2.8	82.5 ± 2.6		0.53 ± 1.10	0.46 ± 1.05		11.4 ± 1.3	11.2 ± 1.2		2.4 ± 8.4	1.1 ± 8.0	
24 (n = 212 intervention, 219 control girls)	87.8 ± 2.8	87.5 ± 2.8		0.49 ± 0.99	0.37 ± 0.97		12.8 ± 1.5	12.5 ± 1.5		2.2 ± 8.6	0.9 ± 9.3	
30 (n = 207 intervention, 205 control girls)	92.1 ± 3.3	91.8 ± 3.1		0.17 ± 1.01	0.07 ± 0.96		13.9 ± 1.7	13.7 ± 1.8		1.6 ± 8.6	0.4 ± 9.3	
36 (n = 200 intervention, 202 control girls)	96.6 ± 3.5	96.0 ± 3.5		0.24 ± 1.00	0.09 ± 1.00		15.0 ± 1.8	14.7 ± 2.0		0.8 ± 8.4	−0.1 ± 9.8	

[1] $\bar{x}$ ± SD.
[2] 95% CI for the difference in group means in parentheses.

TABLE 8
Relative height and relative weight of the children who consistently belonged to the lowest relative fat intake quartile (at 13 mo <23.4 % of energy, at 24 mo <27.7 % of energy, and at 36 mo <28.7 % of energy from fat) compared with other trial children[1]

	Relative height			Relative weight		
	Low fat intake ($n = 35$)	Other ($n = 705$)	P[2]	Low fat intake ($n = 35$)	Other ($n = 705$)	P[2]
	SDS			%		
Age (mo)						
7	0.22 ± 1.0	0.22 ± 1.0	0.93	2 ± 9	3 ± 9	0.81
13	0.47 ± 1.2	0.41 ± 1.0		1 ± 7	2 ± 8	
24	0.30 ± 0.9	0.32 ± 0.9		1 ± 8	1 ± 8	
36	0.18 ± 1.0	0.16 ± 0.9		1 ± 7	1 ± 8	

[1] $\overline{x} \pm$ SD. Relative height is expressed as deviation in SD scores (SDS) from the mean height of healthy Finnish children of the same age and sex. Relative weight is expressed as deviation in percentages from the mean weight of healthy Finnish children of the same height and sex.
[2] P for difference between the 2 groups of children by unbalanced analysis of variance of repeated measurements.

intake is >10% below the currently recommended values (42). The secular changes in habitual levels of physical activity may be responsible for the reduced amounts of energy intake. The mean energy expenditure was ≈4500 kJ at 2 y of age and 5060 kJ at 3 y of age, whereas in STRIP, the respective intakes were 4780 kJ and 5100 kJ. In a study of 140 Australian children, the mean energy intake according to 7-d food records in different fat intake groups was ≈4300–4950 kJ at 2 y of age (43), ie, quite comparable with the values in our study. In the National Diet and Nutrition Survey in the United Kingdom (44), the mean energy intake was 4380 kJ at 2 y and 4860 kJ at 3 y of age. The Nordic Nutrition Recommendations suggest that fat should comprise 30–35% of energy in children's diets and that daily energy intake should be 5400 kJ (range: 3800–7100 kJ) between 1 and 3 y of age (38, 39). The daily energy intake recommendations were met in the STRIP trial, but the mean relative fat intake at 13 mo of age (26% of energy and 28% of energy in the intervention and control children, respectively) was far less than what was recommended.

It is a common belief that relative fat intake is high (35–55% of energy) during the first year of life, but that the intake decreases toward adult values (30–35% of energy) during subsequent years. A striking finding in the STRIP study was that the fat intake was markedly lower than what was expected in children during the first 2 y of life and the nadir of the relative fat intake was reached during the second year of life. As early as 8 mo of age, the mean fat intake of formula-fed infants was 29% of energy, and variation in intakes between individuals was large.

Formulas contain ≈35 g fat/L, whereas the fat content of human milk is 41 g/L (27). In theory, if an 8-mo-old child consumes 600 mL formula daily and then changes back to breast milk, fat intake would increase by 3–4 g (110–150 kJ/d; 3–4% of daily energy intake). Note that complementary foods in infants' diets contain surprisingly small amounts of fat. Fat accounts for only 12% of energy in infants' complementary foods at the age of 7 mo and 25% of energy at the age of 1 y (45). In STRIP, only by 2–3 y of age did the fat intake reach values suggested by the current recommendations. Reports of very low and variable fat intakes by young, healthy well-nourished and normally growing infants and children have also been published also by other investigators (46, 47). In the 1980s, healthy Swedish infants received 28% of energy from fat at 9 mo of age (48). The mean fat intake of 5-y-old Japanese boys in the Tokyo metropolitan area was only 12.6% of energy in 1952 and 20.9% of energy in 1960, but in 1982 it had risen to 32% (49). As reported previously, the dietary energy and nutrient composition of 1–2-y-old

Finnish children varies widely (50). The mean daily energy intake was 4900 kJ: 33% of energy from fat (range: 20–50%) and 16% of energy from protein. The mean dietary P-S ratio was 0.33, ie, exactly the same as in the STRIP control group. In that study, the low-fat diet was not associated with lower-than-average intakes of energy or of any essential nutrients whereas high-fat diets (>40% of energy from fats) contained several nutrients in less than recommended amounts. Thus, the dietary results of STRIP are probably fairly reliable because parental reports of the child's food intake using food records represent habitual intakes rather well, whereas in pubertal children food records tend to underestimate true intake (51).

Serum lipids, lipoproteins, and apolipoproteins

In STRIP, 3–6% lower serum cholesterol concentrations persisted ≤3 y of age when a low-saturated fat, low-cholesterol diet was introduced during infancy. In addition to a decrease in serum total cholesterol concentration, non-HDL-cholesterol concentrations, and apo B, HDL-cholesterol, and apo A-I concentrations decreased concurrently, but the HDL ratio and the ratio apo A-I to apo B were continuously similar in the intervention and control children.

The intervention partially inhibited age-related increases in serum cholesterol concentrations in both sexes, although when the sexes were analyzed separately, the effect was significant only in the boys. Later in life, boys are at a far greater risk for CHD than girls and the possible CHD becomes evident in males about one decade earlier than in females. It is tempting to hypothesize that the intervention parents, who are well aware that CHD is far more common in males, may be more careful of the diets of their sons than of their daughters. Comparison of dietary intakes of intervention boys with intervention girls gave some, albeit very weak, evidence of such a phenomenon.

A crucial question is whether the reduction in concentrations of total cholesterol, non-HDL cholesterol, and apo B is beneficial if HDL cholesterol and apo A-I decrease concurrently, as happened in this trial. Clearly, HDL-cholesterol concentration is inversely related to CHD incidence (52–54). Concentration of HDL cholesterol decreases if a low-fat diet or a diet rich in polyunsaturated fatty acids is used because apo A-I synthesis diminishes (55). Vegetarians (56) and Seventh-day Adventists (57, 58) have low HDL-cholesterol concentrations and a low risk of CHD. Furthermore, HDL-cholesterol concentrations are higher in countries where the mean serum cholesterol concentrations and CHD mortality are higher. The HDL ratios between coun-

TABLE 9
Daily energy and nutrient intakes and midparental height of children with different height gain patterns[1]

	Short (n = 41)	Slow height gain (n = 43)	Normal (n = 683)	Rapid height gain (n = 43)	Tall (n = 38)	P[2]
Energy intake (kJ)						
8 mo	3226 ± 549	3180 ± 499	3423 ± 570	3247 ± 515	3721 ± 582[3]	0.024
13 mo	3784 ± 750[3]	4071 ± 934	4094 ± 750	4194 ± 792	4299 ± 729	0.036
24 mo	4500 ± 1039	4525 ± 834	4747 ± 834	4793 ± 679	5103 ± 817[3]	0.015
36 mo	4579 ± 997[3]	5351 ± 1030	5120 ± 921	5191 ± 876	5596 ± 750[3]	0.001
Energy intake/kg						
13 mo	503 ± 84[3]	372 ± 71[3]	402 ± 80	423 ± 92	360 ± 67[3]	<0.001
24 mo	410 ± 92[4]	351 ± 63	373 ± 67	369 ± 63	344 ± 54[3]	<0.001
36 mo	360 ± 75	360 ± 75	344 ± 63	335 ± 63	314 ± 54[3]	0.012
Fat intake (% of energy)						
8 mo	31 ± 3	28 ± 5	29 ± 4	29 ± 5	29 ± 5	0.14
13 mo	29 ± 5	27 ± 5	27 ± 6	27 ± 6	26 ± 5	0.16
24 mo	32 ± 5	31 ± 6	31 ± 5	31 ± 5	31 ± 5	0.77
36 mo	33 ± 4	31 ± 5	32 ± 5	32 ± 6	32 ± 5	0.77
Protein intake (% of energy)						
8 mo	13 ± 3	12 ± 1	12 ± 2	12 ± 2	11 ± 1	0.17
13 mo	17 ± 3	17 ± 3	17 ± 3	17 ± 3	17 ± 2	0.54
24 mo	17 ± 2	16 ± 2[3]	17 ± 2	17 ± 3	17 ± 3	0.035
36 mo	16 ± 2	15 ± 3	16 ± 2	16 ± 2	16 ± 1	0.12
Zinc intake (mg)						
8 mo	4.0 ± 1.5	3.5 ± 1.1	3.9 ± 1.3	3.8 ± 1.1	4.2 ± 1.2	0.69
13 mo	5.8 ± 1.7	6.0 ± 1.7	6.3 ± 1.6	6.3 ± 1.8	6.4 ± 1.4	0.27
24 mo	6.5 ± 1.7	6.2 ± 1.6[3]	6.8 ± 1.6	7.2 ± 1.8	7.2 ± 1.3	0.014
36 mo	6.3 ± 1.7[3]	7.1 ± 2.0	7.1 ± 1.6	7.2 ± 1.5	7.7 ± 1.3	0.006
Midparental height (cm)	168 ± 4[4]	173 ± 4	173 ± 4	174 ± 5	176 ± 5[4]	<0.001

[1] $\bar{x} \pm$ SD. Children are categorized into different groups by computing the linear regression lines of relative heights on age between 7 and 36 mo for each child. Values given at 8 mo of age are from the formula-fed infants only.

[2] Analysis of variance; overall difference between groups of children showing different growth patterns.

[3,4] Significantly different from children with normal height gain pattern: [3] $P = 0.01$–0.05, [4] $P < 0.001$.

tries show smaller differences, but, interestingly, this ratio tends to be low in countries where CHD mortality is low, eg, in Asia (59). Certainly, not all persons with low HDL-cholesterol values are at increased risk of CHD. For example, vegetarians are actually protected against CHD, probably because of low LDL-cholesterol concentrations (60). The concentrations of both total cholesterol and HDL cholesterol may increase when a Western diet, which contains a large proportion of food of animal origin, is consumed. Thus, the higher the concentration of LDL cholesterol, the more HDL cholesterol is needed. As reported by Knuiman et al (59), the concentration of HDL cholesterol in boys from countries with low rates of CHD mortality is lower than in countries with high rates of CHD mortality. It therefore appears that total cholesterol concentration is the best predictor of population differences in rates of mortality from CHD. We believe that decreasing total cholesterol and LDL-cholesterol concentrations are the most important aims in reducing the risk of CHD, although a decrease in HDL cholesterol may slightly diminish the preventive effect.

A 6% reduction in serum cholesterol was achieved in 3-y-old children consuming a low-saturated-fat, low-cholesterol diet (3). A 15% decrease in serum cholesterol and a 17% decrease in HDL-cholesterol concentrations was found when 36 healthy 8–18-y-old children in eastern Finland consumed a diet for 12 wk, which increased the P-S ratio from 0.18 to 0.61 (4). In studies of hypercholesterolemic children, 10–15% reductions in serum cholesterol values were achieved by dietary intervention (61–64). In STRIP, the reduction was smaller, but the children

were healthy and normocholesterolemic. In the Dietary Intervention Study in Children (65), a 7–8% reduction in serum cholesterol concentration was achieved in 8–10-y-old hypercholesterolemic children in both the intervention and usual care groups, but the net effect of intervention on serum cholesterol was only ≈0.08 mmol/L (2%) over 3 y. In STRIP, as in many other studies, the blood samples were drawn from the control children as often as from the intervention children and the parents were informed of the results. This approach may have caused some changes in the nutrition of the control families, especially if the cholesterol values were high. However, the P-S ratio and proportional fat intake (as a percentage of energy) in the control group closely paralleled the respective values found in 1–2-y-old children in Helsinki, in 1988 (52). Comparison of the lipid concentrations of the control children with those of children in the general population is impossible because the current cholesterol values of healthy young Finnish children, apart from the findings in our trial, are not known.

The diets consumed by families tend to be quite consistent over the years because nutrient intakes at the age of 2 y correlate with intakes at the age of 4 y (8). An effect on serum cholesterol concentrations was achieved already during the first 6 mo of intervention in our trial (23), but after the age of 13 mo, serum cholesterol concentrations began to increase even in the intervention children. A slight dilution of the intervention effect was evident in food records because the P-S ratio decreased and the intake of saturated fat (as a percentage of energy) increased in the intervention children over time. Thus, frequent, continuous counseling is

TABLE 10
Daily energy and nutrient intakes and midparental BMI of children with different weight gain patterns[1]

	Thin ($n = 42$)	Slow weight gain ($n = 43$)	Normal ($n = 682$)	Rapid weight gain ($n = 43$)	Obese ($n = 38$)	P[2]
Energy intake (kJ)						
8 mo	3150 ± 373[3]	3406 ± 670	3402 ± 578	3523 ± 532	3750 ± 557[3]	0.024
13 mo	3708 ± 608[4]	4043 ± 959	4098 ± 754	4349 ± 817[3]	4169 ± 704	0.003
24 mo	4311 ± 649[4]	4734 ± 1043	4734 ± 809	5120 ± 867[4]	5007 ± 1102	<0.001
36 mo	4898 ± 1249	4735 ± 804[4]	5133 ± 888	5321 ± 863	5501 ± 1316[3]	0.002
Energy intake by weight (kJ/kg body wt)						
13 mo	436 ± 67[4]	410 ± 92	402 ± 79	415 ± 88	344 ± 50[5]	<0.001
24 mo	394 ± 54[3]	402 ± 79[4]	372 ± 67	356 ± 75	331 ± 71[5]	<0.001
36 mo	390 ± 101[5]	356 ± 54	344 ± 59	297 ± 63[5]	314 ± 79[4]	<0.001
Fat intake (% of energy)						
8 mo	30 ± 5	29 ± 5	29 ± 4	28 ± 4	28 ± 3	0.43
13 mo	30 ± 7[4]	28 ± 5	27 ± 5	26 ± 6	27 ± 5	0.008
24 mo	33 ± 4[4]	32 ± 5	31 ± 5	32 ± 5	30 ± 5	0.027
36 mo	33 ± 5	31 ± 5	32 ± 5	31 ± 5	32 ± 4	0.47
Protein intake (% of energy)						
8 mo	12 ± 2	12 ± 1	12 ± 2	12 ± 2	12 ± 1	0.74
13 mo	16 ± 2[3]	17 ± 3[3]	17 ± 3	17 ± 3	17 ± 3	0.059
24 mo	16 ± 3	16 ± 3	17 ± 2	17 ± 3	17 ± 3	0.66
36 mo	16 ± 3	15 ± 2	16 ± 2	16 ± 2	15 ± 2	0.27
Zinc intake (mg)						
8 mo	3.6 ± 1.3	3.7 ± 1.5	3.8 ± 1.2	4.5 ± 1.4[5]	4.4 ± 1.3	0.064
13 mo	5.4 ± 1.3[4]	5.9 ± 1.5	6.3 ± 1.7	7.0 ± 1.7[4]	6.7 ± 1.5	<0.001
24 mo	6.1 ± 1.5[4]	6.7 ± 1.9	6.8 ± 1.5	7.8 ± 1.9[5]	7.1 ± 1.8	<0.001
36 mo	6.7 ± 1.6	6.4 ± 1.6[4]	7.1 ± 1.5	7.9 ± 1.6[4]	7.4 ± 2.0	0.001
Midparental BMI	22.7 ± 2.6[3]	23.5 ± 3.0	23.9 ± 2.6	26.1 ± 4.4[5]	25.3 ± 2.3[4]	<0.001

[1] $\overline{x} \pm$ SD. Children were categorized into different groups by computing the linear regression lines of relative weights on age between 7 and 36 mo for each child. Values given at 8 mo of age are from the formula-fed infants only. Midparental BMI is the mean of mother's and father's BMI.

[2] Analysis of variance; overall difference between the groups of children showing different growth patterns.

[3–5] Significantly different from the children with normal weight gain: [3] $P = 0.01–0.05$, [4] $P = 0.001–0.01$, [5] $P < 0.001$.

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needed if cholesterol concentrations are expected to remain persistently within a low range. It is not known how a 3–6% reduction in serum cholesterol concentration in childhood, if maintained, associates with the incidence of CHD in adulthood. If the results of Klag et al (66) and meta-analysis of studies in adults (16) are extrapolated to children, the benefit should be substantial.

Children's growth

Maintenance of normal growth during infancy and childhood may be crucial in the prevention of atherosclerosis because the incidence of CHD is higher in men with low birth weight or low weight at 1 y of age (67, 68). The intervention children in the STRIP trial showed no evidence of delayed growth during the first 3 y of life. The heights and weights of the intervention and control children increased according to the growth standards of Finnish children and were comparable with the respective values in other European countries (69).

In further analysis of the growth data, all children followed for >2 y were divided into 5 groups, gaining weight or growing height at different rates. Each group included an equal number of children of both sexes to make comparison of the dietary intake variables of the different groups possible. If the sexes had not been separated when dividing the children into groups growing differently, an excess of either sex in any group would have led to a bias in interpreting the influence of dietary intakes on growth, ie, at all ages, the boys as a group ate more than the girls. Interestingly, in this cohort, when the current growth charts were used, variation in the relative growth was wider in girls than in boys. We found no evidence supporting the hypothesis that low fat intake (as a percentage of energy) retards children's growth, even though fat intake, especially during the first 2 y of life, was lower than currently recommended. Growth may indeed be more directly related to protein intake than to fat intake (70). Energy intake was higher in obese children and in children gaining weight rapidly than in normally growing children, but relative energy intake (kJ/kg) was lower in children who weighed more. The short (and thin) children consumed more energy per kilogram body weight than did their normal-sized peers, although their total daily energy intake was lower. The variables that best predicted that a child would have a certain growth pattern were midparental height in height gain and midparental BMI in weight gain. Relative fat intake poorly predicted the child's growth pattern. The obese children were likely to have obese parents. Thus, prevention of obesity is particularly important in the offspring of obese parents.

The children with low fat intakes grew as well as with the children with higher fat intakes. Furthermore, no differences in growth were seen between the children who consistently belonged to the lowest quartile or even the lowest decile of serum cholesterol concentration and the other study children. This implies that even though malnutrition is a possible cause of hypocholesterolemia (71), in an otherwise healthy population of children, low serum cholesterol values are not associated with poor growth but are instead more likely to be caused by genetic factors.

The importance of dietary fat intake for growth before the age of 5 y has remained controversial. No significant associations between fat intake (as a percentage of energy) and growth were

found in 6–12-mo-old infants in the Copenhagen Cohort Study (47). Shea et al (72) found that 3–5-y-old children whose relative fat intake was in the lowest quintile grew in the same way as did the children in the highest fat intake quintile. Fat intake in the lowest quintile was 27% percent of energy, considerably less than the current recommendation (30–35% of energy). Children in the lowest fat intake quintile consumed less calcium and phosphorus than the children in other quintiles. In our study, the intervention children consumed as much calcium and phosphorus as the control children (data not shown) because the amounts of calcium and phosphorus are equal in 1.9%-fat milk and skim milk (1.2 g Ca and 860–890 mg P/L). Thus, eating less fat was not equal to drinking less milk. In a study that included 140 children followed from infancy to 8 y of age, no differences were found in the growth of children with different fat intakes, although the total energy intake was lower in the low-fat group at 2 and 4 y of age (73).

Nicklas et al (40) reported no significant differences in any growth variable between children in different fat intake groups, although the daily energy intake was considerably lower (7500 kJ compared with 10 000 kJ) in 10-y-old children with fat intakes <30% of energy than in children consuming >30% of energy as fat.

Several other studies also suggest that fat restriction does not result in growth failure (3, 61, 62, 74). If energy and protein intakes remain at acceptable levels, low dietary fat intake does not seem to result in growth retardation. However, height-for-age and weight-for-age decreased by 0.4 SD in 30 children who were on a fat-reduced diet, whereas these SD scores were not affected by treatment with diet and cholestipol (75). Detailed dietary records were not reported in that study and there was a possible bias introduced by the fact that some children were followed through puberty. Growth failure was also reported in 8 of the 40 children who were treated with an unsupervised fat-reduced diet for hypercholesterolemia (22). In that study, the mean fat intake was 30% of energy, whereas in the 8 poorly growing children, the intake was 25.4% of energy, and in the 3 most growth-retarded children only 20.6% of energy. The diet of the growth-retarded children was also deficient in zinc and many other nutrients. One of the main differences in the foods consumed by the children who grew at a normal or a delayed rate was that the children with poor growth consumed less meat and fish. Food consumption was estimated by using 24-h dietary recall and assessing eating patterns and preferences, but no food records were used. Parental health beliefs may also compromise children's growth (21). Food records of 4 children, in-hospital energy intake records of 2 children, and an unstructured interview of 1 poorly growing child suggested that their energy intakes were low (63–94% of recommended dietary allowances) and that fat intakes varied between 25% and 37% of energy. Obvious feeding errors were found, eg, one child was breast-fed almost exclusively for ≈2 y and one mother diluted formula with water. However, no reports indicate that growth might be impaired if fat quality rather than fat quantity in the child's diet is changed (76, 77).

Fat is an important source of energy, especially for fast-growing infants. During the first weeks and months of life when a great part of daily energy is used for growth, a high fat intake (≤40–55% of energy) is probably essential. The amount of energy required for growth has been estimated to decrease from 120 to 170 $kJ \cdot kg^{-1} \cdot d^{-1}$ during the first months of life to 8–13 $kJ \cdot kg^{-1} \cdot d^{-1}$ after the age of 1 y. Thus, in an older child, other components of energy expenditure, ie, the basal metabolic rate, thermoregulation, and, above all, physical activity, become more important. Interestingly, some studies suggest that the energy expenditure of young children is markedly below previous estimates (42). The total daily energy expenditure in 1.5–2.5-y-old children averages only 350–360 kJ/kg body wt. In our trial, only obese and tall children had mean relative energy intakes below these values. In conclusion, the growth data of the STRIP trial support the safety of a low-saturated-fat, low-cholesterol diet administered to infants aged >7 mo and continued through the first years of life.

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