Impact of Repeated Dietary Counseling Between Infancy and 14 Years of Age on Dietary Intakes and Serum Lipids and Lipoproteins

The STRIP Study

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Background—Atherosclerosis development might be delayed or prevented by dietary measures. The aims of the present study were to evaluate the effect of low-saturated-fat, low-cholesterol dietary counseling on fat intakes, growth, serum cholesterol values, and pubertal development in children and adolescents.

Methods and Results—In the randomized prospective Special Turku Coronary Risk Factor Intervention Project (STRIP), a low-saturated-fat, low-cholesterol diet was introduced to intervention infants (n = 540) at 7 months of age, and control children (n = 522) received an unrestricted diet. Dietary intakes, serum cholesterol values, somatic growth, and development were followed up throughout childhood and adolescence. Saturated fat intakes, serum total cholesterol, and low-density lipoprotein cholesterol values were lower (P < 0.001) in the intervention than in control children during the 14 years, whereas high-density lipoprotein cholesterol values in the 2 study groups showed no difference. Boys had lower total and low-density lipoprotein cholesterol concentrations than girls throughout childhood (P < 0.001), and the intervention effect on serum cholesterol concentration was larger in boys than girls. The 2 study groups showed no difference in growth, body mass index, pubertal development, or age at menarche (median, 13.0 and 12.8 years in the intervention and control girls, respectively; P = 0.52). The cholesterol values decreased as puberty progressed. Mean concentrations of total and high-density lipoprotein cholesterol decreased from ≈4.5 and ≈1.4 mmol/L, respectively, in Tanner stage 1 (prepubertal) boys to ≈3.9 and ≈1.1 mmol/L in Tanner stage 4 (late pubertal) boys.

Conclusions—Repeated dietary counseling remains effective in decreasing saturated fat and cholesterol intake and serum cholesterol values at least until 14 years of age. Puberty markedly influences serum cholesterol concentrations. (Circulation. 2007;116:1032-1040.)

Key Words: cholesterol • coronary disease • nutrition • pediatrics • prevention

Atherosclerosis develops as a result of a lifelong process often leading to coronary heart disease. Extensive dietary-fat–oriented and other lifestyle recommendations have been delivered to the general community to manage this epidemic. However, fears that low intake of saturated fat and cholesterol might influence growth and cognitive development have led to the exclusion of infants and young children from these recommendations, although numerous arguments support early-onset prevention of children’s exposure to environmental coronary heart disease risk factors. Dietary fat intake, fat quality, and cholesterol intake regulate values of serum lipids in children the same way they do in adults. Children with high serum cholesterol and low-density lipoprotein (LDL) cholesterol values are predisposed to early atherosclerotic changes in large arteries. Exposure to high LDL cholesterol values in childhood is associated with increased carotid artery atherosclerosis measured decades later. A lifestyle with an emphasis on avoiding atherosclerosis risk factors might be most easily adopted, as well as most effective in the long run, if introduced in early childhood.
introduced to healthy infants in the intervention group before their 1-year birthdays. We showed previously that such an early-onset counseling of saturated fat- and cholesterol-restricted diet decreased serum cholesterol concentrations successfully up to early school age with no assessable adverse effects. However, age >7 years creates new challenges in nutrition counseling because school-aged children and adolescents consume progressively more of their nutrient intakes away from home and peer pressure starts to influence food consumption. Furthermore, most children enter puberty at or around 11 years of age, which significantly modifies serum lipid and lipoprotein values in boys and girls. It is also worth noticing that cholesterol is a precursor of sex hormones, and indeed, in the Dietary Intervention Study in Children (DISC), serum estradiol and other sex hormone concentrations were lower in adolescent girls receiving dietary counseling to reduce intake of saturated fat and cholesterol than in control subjects.

We have now investigated of the effects of low-saturated-fat, low-cholesterol dietary counseling on dietary intakes, growth, and serum lipid, lipoprotein, and apolipoprotein values until 14 years of age. We also prospectively measured the effect of such counseling and of the induced dietary changes on pubertal development. Finally, we examined in detail the serum lipid and lipoprotein changes occurring during progression of the pubertal stages between 10 and 14 years of age.

Methods

Study Design, Counseling of the Families, and Food Recording

In the prospective, randomized STRIP project, families were recruited to the study at the well-baby clinics in Turku, Finland, at the infants’ 5-month visits between 1990 and 1992 as described. The infants at 7 months of age were randomly assigned either to receive individualized counseling aimed at controlling environmental coronary heart disease risk factors (n=540) or to a control group (n=522). The intervention families visited the counseling team at 1- to 3-month intervals until the child reached 2 years of age and twice a year thereafter; the control families were seen by the same team twice a year until the child reached 7 years of age and once a year after that age. The Joint Commission on Ethics of the Turku University and the Turku University Central Hospital approved the STRIP study.

A nutritionist provided dietary counseling to the intervention families, and the child and family had an active role in the counseling sessions. The intervention was individualized for each child and aimed at achieving a fat intake of 30% to 35% of daily energy (E%), with a ratio of saturated to monounsaturated plus polyunsaturated fatty acid of 1:2 and cholesterol intake <200 mg/d. Breastfeeding or formula was advised during the first year of life; then, 0.5 to 0.6 L skim milk daily was recommended. To maintain adequate fat intake, the parents were taught to add daily 2 or 3 teaspoonfuls (10 g) of soft margarine or vegetable oil, mainly low-erucic-acid rapeseed oil, to the child’s food from 12 to 24 months of age. Change in the type of milk was the major subject matter of the intervention during the first months of the trial. Because the counseling was individualized, the nutritionist used the child’s recent food record as a basis for suggestions. The families were encouraged to gradually change the child’s diet toward better fat composition. Ample use of vegetables, fruits, berries, and whole grain products was encouraged.

During the first years, the counseling was given primarily to the parents. However, beginning at 7 years of age, progressively more dietary information and suggestions were given directly to the child. The counseling was based on the age and cognitive ability of the child. Most of the material used was specially developed for the project because ready-made counseling materials for children are sparse. The parents were carefully informed about the counseling session and were encouraged to discuss the same food-related topics with the child at home.

The control children were seen biannually until 7 years of age and annually thereafter. They received the basic health education routinely given at Finnish well-baby clinics and through school health care. At 12 months of age, cow’s milk with 1.9% (1.5% after May 1995) fat was recommended for daily use. Dietary issues were discussed only superficially with control families.

Food consumption data were obtained through annual 4-day food records (3-day food records before 2 years of age). After a nutritionist reviewed the food records for accuracy, the nutrient intakes were calculated with software (Micro Nutrica, Turku, Finland) based on the Food and Nutrient Database of the Social Insurance Institution.

Serum Lipid and Apolipoprotein Determinations

A venous blood sample was drawn for measurement of serum lipid and apolipoprotein concentrations at 7 months, 13 months, and 2 years of age and annually thereafter. All serum analyses were done at the laboratory of the National Public Health Institute in Turku, Finland.

After clotting at room temperature and low-speed centrifugation (at 3400g for 12 minutes), serum was separated and stored at -25°C for up to a few weeks. Serum cholesterol concentration was measured with a fully enzymatic cholesterol oxidase-p-aminophenazone method (CHOD-PAP, Merck, Darmstadt, Germany) in an AU 510 automatic analyzer (Olympus, Hamburg, Germany) or, after January 2001, an AU 400 analyzer. Calibration runs were performed for cholesterol, high-density lipoprotein (HDL) cholesterol, and apolipoprotein concentrations, and the results for samples analyzed before 2001 were corrected as follows: s-cholesterol=s-cholesterol (before 2001)×1.0207+0.0526; s-HDL-cholesterol=s-HDL-cholesterol (before 2001)×1.031–0.0083; s-ApoA-I=s-ApoA-I (before 2001)×1.0239+0.0991; and s-ApoB=s-ApoB (before 2001)×1.0239+0.0991, where s indicates serum and ApoA-I and ApoB indicate apolipoprotein A-I and B. Serum HDL cholesterol concentration was measured after precipitation of LDL and very LDL with dextran sulfate 500 000. The inter assay (intra-assay) coefficients of variation for total cholesterol and HDL cholesterol were 2.0% (1.5%) and 1.9% (1.2%), respectively. ApoA-I and ApoB were determined immunoturbidometrically with ApoA-I and B kits (Orion Diagnostica, Helsinki, Finland). The inter assay (intra-assay) coefficients of variation of the ApoA-I and ApoB determinations were 3.0% (1.8%) and 4.5% (3.3%), respectively. Serum triglyceride values were analyzed with the colorimetric GPO-PAP method (Merck, Darmstadt, Germany) in an automatic Olympus AU 510 analyzer or, after January 2001, with an AU 400 analyzer; earlier values were corrected as follows: s-triglyceride=s-triglyceride (before 2001)×1.0247+0.0191.

The blood samples drawn before 5 years of age were nonfasting. From 5 years of age on, fasting blood samples were drawn, and the Friedewald formula was used to calculate the LDL cholesterol concentrations.

Anthropometric Measurements and Recording of the Pubertal Status

Weights of the children were measured to the nearest 0.1 kg and height to the nearest 0.1 cm. Recumbent lengths were recorded until 2 years of age; thereafter, standing heights were measured with a Harpenden stadiometer (Holtain, Crymych, UK). Weights and heights were plotted on the Finnish growth charts. Body mass index (BMI) was calculated as kilograms per meter squared. Pubertal status was recorded beginning at the age of 9 years. Breast tissue diameter and testicular length were measured with a ruler, and pubic hair development was estimated visually. The respective pubertal stages (M1 through M5 and P1 through P5 in girls; G1 through G5
and P1 through P5 in boys) were recorded according to well-established criteria.14 M2 stood for breast budding; G2 indicated testicular length of >20 mm (corresponding volume >3 mL). For dividing subjects to pubertal and prepubertal, children with P1/G1 or P1/M1 were considered prepubertal, and all others were considered pubertal. For allocating children to Tanner stages 1 through 5, Tanner stage 1 corresponded to G1 and M1, Tanner stage 2 for G2 and M2, Tanner stage 3 for G3 and M3, Tanner stage 4 for G4 and M4, and Tanner stage 5 for G5 and M5 in boys and girls, respectively.

Statistical Analyses
Repeated-measures ANOVA was conducted for lipid values, food intakes, and growth measures across the age points 7 months to 14 years. Multivariate repeated-measured ANCOVA models were used to adjust the intervention effect on serum lipid values with energy intake, saturated fatty acid intake (as E%), height (SD), and BMI. Lipid values from 10 to 14 years of age also were analyzed with repeated-measures ANOVA with Tanner puberty stage as the repeat factor. Because of skewed distribution, triglycerides, weight, and BMI were analyzed after logarithmic transformation. If a child stayed in a certain puberty stage for several years, his/her lipid values were averaged within the puberty stage for analyses. Sex and intervention group–with-interaction terms were included in all analyses; interactions with an observed significance level >0.1 were excluded from the final models. In case of significant interactions, pairwise comparisons between groups were accomplished by Bonferroni-corrected t tests to avoid the increase in type I error risk. For interaction containing age, the pairwise comparisons between groups and/or sexes were done at 9 and 14 years of age (ApoA-I and ApoB at 9 and 13 years), with 9 years representing prepubertal and 13 to 14 years representing pubertal age.

Differences in the proportion of pubertal children (puberty ongoing/prepubertal) between the intervention and control groups were analyzed with Cochran-Mantel-Haenszel method for general association stratified by sex. This same method also was used to examine whether M2 preceded P2 in girls’ pubertal development. Survival analysis was assessed for the age of menarche of the girls studied, with log-rank test for the pairwise comparison between intervention and control groups.

Results were considered statistically significant at values of \( P<0.05 \). Statistical analyses were performed with the SAS software for Windows, release 9.1 (SAS Institute, Cary, NC).

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Results
Dietary Intakes
The intervention children had lower fat and saturated fat intakes (both \( P<0.001 \); Figure 1) than control children, whereas the protein and carbohydrate intakes (Table 1) were higher in intervention than control children (both \( P<0.001 \)).

Intervention effect on saturated fatty acid intake was similar in both sexes (\( P=NS \)). The energy intake of the intervention children, especially of the boys, also was slightly lower than that of the control children throughout the study (Table 1). Fat intake (as E%) did not differ between genders (\( P=0.37 \)), but the girls had lower energy (\( P<0.001 \)) and higher saturated fat (as E%; \( P=0.035 \)) intakes than boys.

Growth and Pubertal Progression
There were no differences in heights (\( P=0.44 \)), weights (\( P=0.27 \)), or BMIs (\( P=0.28 \)) between the intervention and control groups (Table 1 and Figure 1). About 60% of the children had entered puberty by 11 years of age (Table 2). No differences existed in the pubertal progression between the study groups (\( P=0.19 \) in boys, \( P=0.12 \) in girls). M2 was the first sign of puberty in most girls, and there was no difference between the study groups in the proportion of girls who progressed to P2 before M2 (\( P=0.09 \)). Age at menarche did not differ between intervention and control girls (\( P=0.52 \)). The 25th percentile, median, and 75th percentile ages at menarche were 12.1, 13.0, and 13.6 years in the intervention girls and 12.0, 12.8, and 13.6 years in the control girls.

Serum Cholesterol, Lipoprotein, and Apolipoprotein Concentrations
The dietary intervention significantly influenced serum lipid and lipoprotein values throughout childhood (Figure 2). The difference between intervention and control children persisted in serum cholesterol through 14 years of age in boys...
but the difference in girls was nonsignificant ($P=0.12$). There was a gender group interaction ($P=0.043$) in serum cholesterol; ie, the intervention influenced sexes differently. Boys had lower serum cholesterol and LDL cholesterol values than girls throughout childhood ($P<0.001$). Differences between groups were not seen in HDL cholesterol values. Boys had higher ratios of HDL to total cholesterol than girls ($P<0.001$). The effects of inter-
vention and gender on ApoB values resembled those on LDL cholesterol, whereas changes in ApoA-1 resembled those in HDL values (data not shown). The ratio of ApoA-I to ApoB was higher in boys than in girls until adolescence ($P<0.001$ between sexes; $P<0.001, \text{Sex}=0.37$). Serum triglyceride values were lower in boys than girls, but intervention had an effect on serum triglyceride values only in boys. Adjustment for

<table>
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TABLE 1. Continued

Sex: $P=0.15$ at 14 years of age, but there was no group difference ($P=0.12$). Serum triglyceride values were lower in boys than girls, but intervention had an effect on serum triglyceride values only in boys. Adjustment for
energy intake, saturated fatty acid intake (as E%), height (SD), and BMI did not alter these results; the intervention effect remained significant on serum LDL concentration and HDL ratio in both genders and on serum cholesterol and triglyceride concentrations in boys, whereas it was not significant on HDL concentrations.

The peak of the mean serum cholesterol level was reached at 7 to 9 years of age. At 14 years of age, serum cholesterol concentrations had decreased to values observed at 7 months of age.

Serum Lipoprotein and Apolipoprotein Concentrations According to Pubertal Stage

The serum total, LDL, and HDL cholesterol values decreased as puberty progressed, especially in boys (Table 3). Prepubertal boys had higher ratios of HDL to cholesterol (0.30 to 0.31) than girls (0.28 to 0.29), but at late puberty, this ratio clearly was lower in boys (≈0.25) than girls (≈0.28). Pubertal changes in ApoA-I resembled those in HDL cholesterol, whereas ApoB changes resembled changes in LDL cholesterol (data not shown).

Discussion

We previously showed that saturated fat intakes and serum cholesterol values were lower in children receiving fat-oriented dietary counseling than in control children up to age 7 years. Furthermore, insulin sensitivity was better in the

<table>
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<th>Boys</th>
<th>By 10 Years, %</th>
<th>By 11 Years, %</th>
<th>By 12 Years, %</th>
<th>By 13 Years, %</th>
<th>By 14 Years, %</th>
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<td>67</td>
<td>95</td>
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<td>100</td>
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<tr>
<td>Control</td>
<td>15</td>
<td>57</td>
<td>92</td>
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Girls

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<th>Girls</th>
<th>By 10 Years, %</th>
<th>By 11 Years, %</th>
<th>By 12 Years, %</th>
<th>By 13 Years, %</th>
<th>By 14 Years, %</th>
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<td>Intervention</td>
<td>35</td>
<td>57</td>
<td>88</td>
<td>98</td>
<td>100</td>
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<tr>
<td>Control</td>
<td>39</td>
<td>66</td>
<td>89</td>
<td>99</td>
<td>100</td>
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</table>

P=0.19 for boys, P=0.12 for girls (Cochran-Mantel-Haenszel method for general association).
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<td>125</td>
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<td>108</td>
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<td>66</td>
<td>7</td>
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<tr>
<td>Control</td>
<td>121</td>
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<td>131</td>
<td>103</td>
<td>123</td>
<td>56</td>
<td>77</td>
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<td>Serum cholesterol, mmol/L</td>
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<td>Pub &lt;0.001, Sex &lt;0.001, Group &lt;0.007, Sex×Pub &lt;0.001</td>
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<td>Intervention</td>
<td>4.44 (0.60)</td>
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<td>4.43 (0.63)</td>
<td>4.05 (0.57)</td>
<td>4.25 (0.58)</td>
<td>3.78 (0.60)</td>
<td>4.17 (0.65)</td>
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<td>Control</td>
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<td>4.71 (0.77)</td>
<td>4.48 (0.75)</td>
<td>4.54 (0.74)</td>
<td>4.34 (0.71)</td>
<td>4.36 (0.75)</td>
<td>3.95 (0.72)</td>
<td>4.17 (0.79)</td>
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<td>4.18 (0.80)</td>
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<td>LDL cholesterol, mmol/L</td>
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<tr>
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<td>2.88 (0.54)</td>
<td>2.62 (0.50)</td>
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<td>2.64 (0.53)</td>
<td>2.36 (0.52)</td>
<td>2.56 (0.56)</td>
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<tr>
<td>Control</td>
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<td>2.81 (0.66)</td>
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<tr>
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<td>1.32 (0.22)</td>
<td>1.34 (0.27)</td>
<td>1.25 (0.22)</td>
<td>1.20 (0.25)</td>
<td>1.21 (0.20)</td>
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<td>1.23 (0.21)</td>
<td>0.95 (0.22)</td>
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<td>1.29 (0.25)</td>
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<td>1.23 (0.24)</td>
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<td>HDL ratio</td>
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<td>0.31 (0.06)</td>
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<tr>
<td>Intervention</td>
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<td>0.76 (0.71 to 0.81)</td>
<td>0.68 (0.63 to 0.73)</td>
<td>0.84 (0.78 to 0.90)</td>
<td>0.70 (0.65 to 0.76)</td>
<td>0.85 (0.79 to 0.91)</td>
<td>0.73 (0.66 to 0.79)</td>
<td>0.77 (0.69 to 0.85)</td>
<td>1.00 (0.63 to 1.53)</td>
<td>0.89 (0.72 to 1.09)</td>
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<tr>
<td>Control</td>
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<td>0.76 (0.76 to 0.82)</td>
<td>0.83 (0.78 to 0.89)</td>
<td>0.82 (0.75 to 0.90)</td>
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<td>0.80 (0.73 to 0.98)</td>
<td>0.91 (0.46 to 1.81)</td>
<td>0.80 (0.66 to 0.98)</td>
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Pub indicates puberty. Values were averaged within the time period in children who remained in certain pubertal stage for >1 year.

*Geometric mean (95% CI), analysis with log transformation.
intervention children at 9 years of age, and the prevalence of overweight was slightly reduced at 10 years of age. We have shown here that saturated fat intake remains markedly lower in the intervention children than in control children through the first 14 years of life; lower serum cholesterol values among intervention children also were maintained throughout these years. The beneficial influences of the dietary counseling do not fade away during the years when the children start consuming more of their nutrients away from home and enter puberty. Furthermore, the lower saturated fat intake in the intervention children was not associated with altered physical growth between 7 months and 14 years of age.

Cholesterol values differed more between the intervention and control boys than girls. This gender difference cannot be explained by different adherence to the nutrition counseling because the saturated fat intake was significantly lower in both intervention boys and girls compared with control boys and girls, and adjustment for saturated fat intake did not alter this finding. The absolute serum cholesterol difference between the intervention and control boys was \( \approx 0.2 \) mmol/L, ie, \( \approx 5\% \). A larger decrease in serum cholesterol values in boys also may explain why the endothelial function improved in intervention compared with control boys but not in girls. Moreover, LDL cholesterol response to sitostanol margarine use also was greater in boys than girls. The reasons for the different serum lipid responses to the STRIP diet between genders remain unidentified, but divergent hormonal status, body composition, and physical exercise habits may all contribute to this outcome. Indeed, we previously showed that teenaged boys are physically more active than girls.

The effect of nutrition counseling on serum cholesterol concentrations in STRIP children was within the range achieved in previous studies in healthy children, whereas the decreases in serum LDL cholesterol values have been greater in hypercholesterolemic children. The results of STRIP intervention are unique because the lower serum cholesterol values were maintained from 1 to at least 14 years of age.

Serum cholesterol and HDL cholesterol concentrations were lower in the pubertal than prepubertal children, resembling serum lipid and lipoprotein changes induced by puberty reported earlier. The decreases in our study were of the same magnitude as in the DISC study, in which serum LDL cholesterol values decreased \( \approx 0.6 \) mmol/L in boys and \( \approx 0.3 \) mmol/L in girls when their Tanner stage increased from 1 to 4++. Androgens may regulate HDL cholesterol concentrations in boys during puberty. We found that HDL cholesterol concentration clearly decreased more in boys than in girls during puberty. Prepubertal boys had higher HDL cholesterol than prepubertal girls, whereas the situation was the opposite at late puberty.

It has been hypothesized that early nutrition, possibly energy, protein, or fat intake, might influence pubertal development. Given that cholesterol is the precursor of sex steroids and that dietary fat intake is one of the major determinants of pubertal development in girls, the slightly higher fat and saturated fat intake by the control girls could hasten their pubertal development, whereas the tempo of pubertal changes in the intervention girls might be slower. In the DISC study, a significant decrease in several serum sex hormones, ie, \( \approx 30\% \) lower serum estradiol and estrone concentrations, was observed in adolescent girls receiving counseling that suggested lower saturated fat and cholesterol intake compared with girls consuming an unrestricted diet.

We did not find any differences in the pubertal development in either gender between the 2 study groups. The current mean age of breast budding in Western countries (excluding the United States) is about 11 years, and the mean age of the beginning of testicular growth is \( \approx 11.5 \) years. Approximately half of the STRIP children had reached these stages by 11 years of age. The STRIP study boys progressed to puberty quite early; \( \approx 60\% \) of the boys were in Tanner stage 2 at 11 years of age. We used testicular length \( >20 \) mm as the indicator of entry into puberty, whereas in other studies testicular length of 25 mm (\( \approx 1 \) inch) has commonly been used. This may increase the proportion of boys considered pubertal in the present study. Median age at menarche in STRIP girls was 12.8 to 13.0 years, and it did not differ between the study groups. This age resembles the menarcheal age observed in Western countries lately and is a few months earlier than reported in Finland 3 decades ago.

**Conclusions**

A low-saturated-fat, low-cholesterol–oriented nutrition intervention had a favorable effect on saturated fat intake and serum total and LDL cholesterol concentrations throughout the first 14 years of life. The lipid-lowering effect was maintained through prepuberty and puberty, when children consume exceedingly more of their dietary intakes away from home. Puberty induced major changes in serum cholesterol and HDL cholesterol values, and the decrease in total cholesterol was clearly greater in boys than girls. Growth and pubertal development remained similar between the intervention and control children. Thus, our present data do not support the fear that saturated fat restriction influences either growth or pubertal timing or tempo in healthy children.

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**Disclosures**

None.

**References**

Atherosclerosis develops as a result of a lifelong process that often leads to coronary heart disease in middle age or later. Therefore, extensive dietary recommendations to reduce saturated fat intake have been delivered to the general community to manage this epidemic. However, there have been fears that low intake of saturated fat and cholesterol might influence growth and development of young children. In the Special Turku Coronary Risk Factors Intervention Project (STRIP), a low-saturated-fat diet was introduced to healthy infants in the intervention group before their 1-year birthday, whereas control children received no specific counseling concerning dietary fats. The aim was to improve the dietary fat quality.

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