Neurological Development of 5-Year-Old Children Receiving a Low–Saturated Fat, Low-Cholesterol Diet Since Infancy
A Randomized Controlled Trial

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Increased serum cholesterol and low-density lipoprotein cholesterol (LDL-C) concentrations are closely associated with aortic fatty streaks in pediatric autopsies,1,2 suggesting that children with high serum cholesterol values are predisposed to atherosclerosis and coronary heart disease (CHD) later in life. The high prevalence of early vascular changes is well documented in the Pathobiological Determinants of Atherosclerosis in Youth study,3 which found that all 15- to 19-year-old Americans have fatty streaks in the aorta, about half had lesions in the right coronary artery, and that the prevalence of coronary fatty streaks increases to 75% before age 35 years. In the Bogalusa Heart Study,4 50% of children whose serum LDL-C concentration was above the 75th percentile of the study population when first measured still had high values 12 years later.

Context Early childhood introduction of nutritional habits aimed at atherosclerosis prevention is compatible with normal growth, but its effect on neurological development is unknown.

Objective To analyze how parental counseling aimed at keeping children’s diets low in saturated fat and cholesterol influences neurodevelopment during the first 5 years of life.

Design Randomized controlled trial conducted between February 1990 and November 1996.

Setting Outpatient clinic of a university department in Turku, Finland.

Participants A total of 1062 seven-month-old infants and their parents, recruited at well-baby clinics between 1990 and 1992. At age 5 years, 496 children still living in the city of Turku were available to participate in neurodevelopmental testing.

Intervention Participants were randomly assigned to receive individualized counseling aimed at limiting the child’s fat intake to 30% to 35% of daily energy, with a saturated:monounsaturated:polyunsaturated fatty acid ratio of 1:1:1 and a cholesterol intake of less than 200 mg/d (n=540) or usual health education (control group, n=522).

Main Outcome Measures Nutrient intake, serum lipid concentrations, and neurological development at 5 years, among children in the intervention vs control groups.

Results Absolute and relative intakes of fat, saturated fatty acids, and cholesterol among children in the intervention group were markedly less than the respective values of control children. Mean (SD) percentages of daily energy at age 5 years for the intervention vs control groups were as follows: for total fat, 30.6% (4.5%) vs 33.4% (4.4%) (P<.001); and for saturated fat, 11.7% (2.3%) vs 14.5% (2.4%) (P<.001). Mean intakes of cholesterol were 164.2 mg (60.1 mg) and 192.5 mg (71.9 mg) (P<.001) for the intervention and control groups, respectively. Serum cholesterol concentrations were continuously 3% to 5% lower in children in the intervention group than in children in the control group. At age 5 years, mean (SD) serum cholesterol concentration of the intervention group was 4.27 (0.63) mmol/L (165 [24] mg/dL) and of the control group, 4.41 (0.74) mmol/L (170 [29] mg/dL) (P=.04). Neurological development of children in the intervention group was at least as good as that of children in the control group. Relative risks for children in the intervention group to fail tests of speech and language skills, gross motor functioning plus perception, and visual motor skills were 0.95 (90% confidence interval [CI], 0.60-1.49), 0.95 (90% CI, 0.58-1.55), and 0.65 (90% CI, 0.39-1.08), respectively (P=.85, .86, and .16, respectively, vs control children).

Conclusion Our data indicate that repeated child-targeted dietary counseling of parents during the first 5 years of a child’s life lessens age-associated increases in children’s serum cholesterol and is compatible with normal neurological development.

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Furthermore, elevated serum cholesterol values in early adult life are associated with cardiovascular disease risk a quarter of a century later. Coronary heart disease is clearly an end point in a lifelong process.

Modification of dietary fat intake beginning in early childhood might diminish CHD risk in a population, but such interventions have been hampered by concerns about possible long-term effects on growth and development.8,9 While results from the Dietary Intervention Study in Children suggest that a low–saturated fat, low-cholesterol diet decreases serum LDL-C concentration in children with hyperlipemia without effects on growth and psychosocial health, and cohort studies indicate that differences in fat consumption do not affect growth, prospective randomized studies are needed to prove the safety of early interventions.

We showed in the prospective randomized Special Turku Coronary Risk Factor Intervention Project (STRIP) that serum cholesterol concentration increased only slightly in children in the intervention group who were exposed to a low–saturated fat, low-cholesterol diet after age 7 months, whereas a greater increase in cholesterol values was seen in control children during the first 3 years of life. Furthermore, the intervention did not influence growth. In the current phase of the project, we evaluated the effects of a diet low in saturated fat and cholesterol on children’s neurological development at age 5 years.

**METHODS**

**Study Design**

The STRIP project is a randomized trial aimed at decreasing exposure to known environmental atherosclerosis risk factors. As previously described, the nurses at the well-baby clinics in the city of Turku recruited families to the project at the regular 5-month visit of the infants. After obtaining informed consent from the parents, 7-month-old infants were allocated into an intervention group or a control group by random numbers. The families in the intervention and control groups met a pediatrician and a dietitian at 1- to 3-month and 4- to 6-month intervals, respectively; after age 2 years, the visits in both groups were at 6-month intervals. The parents and personnel of community-run or private day care centers recorded the child’s food consumption in a 3-day record at ages 8, 13, and 18 months, and in a 4-day record twice a year thereafter, always including 1 weekend day. The records were analyzed with Micro-Nutrica program (Research and Development Unit of the Social Insurance Institution, Turku, Finland; version 2.5), using the Food and Nutrient Database of the Social Insurance Institution, Turku. Venous blood samples were drawn for serum lipid measurement at ages 7, 13, and 24 months and yearly thereafter. A pediatrician examined the child at each visit.

Infants were recruited to the study between February 1990 and June 1992. All 5-year-old children had been evaluated by November 1996.

The study was approved by the Joint Commission on Ethics of Turku University and Turku University Central Hospital.

**Counseling**

Families in the intervention group received individualized counseling aimed at maintaining the child’s fat intake at 30% to 35% of daily energy, saturated:monounsaturated:polyunsaturated fatty acid (PUFA) ratio of 1:1:1, and cholesterol intake of less than 200 mg/d. In practice, families were advised to continue breastfeeding as long as the mother felt it feasible or to use formula as the milk source until the infant reached age 12 months and skim milk, 0.5 to 0.6 L/d, thereafter. Parents were taught to add 2 or 3 teaspoonsfuls of soft margarine or vegetable oil, mainly low–erucic acid rapeseed oil, to the daily food of the 12- to 24-month-old children to maintain fat intake.

Control families received the health education given to all Finnish families at the well-baby clinics. They were advised to continue breastfeeding or to use formula until the infant reached age 12 months, but cows’ milk containing at least 1.9% fat (1.5% after May 1995) was recommended thereafter. No advice concerning dietary fat was given.

In both groups, at least partial breastfeeding continued for a mean (SD) of 5 (4) months, and solid foods were introduced at age 3 to 5 months. All children were weaned by age 13 months. Because accurate measurement of breast-milk consumption was impossible in a trial this large, the intake analysis at age 8 months comprised data on the formula-fed infants only.

**Serum Lipids**

Before age 5 years, nonfasting blood samples were drawn for measurement of serum cholesterol and high-density lipoprotein cholesterol (HDL-C) concentrations. Therefore, non–HDL-C (total cholesterol minus HDL-C) values were used because serum triglyceride values were not available for calculation of LDL-C values. At age 5 years, fasting blood samples were drawn for the first time, allowing calculation of LDL-C values using the formula of Friedewald et al. Only 1 venipuncture attempt was made and was successful in 87.5% of children. Analyses were done in the laboratory of the Research and Development Unit of the Social Insurance Institution in Turku.

**Analysis of Children’s Neurological Development**

At age 5 years, neurological development of children living in Turku was assessed using a collection of development mental screening tests. Although similar screening tests are used in all communities around Turku, the testing was restricted to the city because the tests were validated there, the well-baby clinic nurses were uniformly trained to use the tests, and performance could be continuously monitored and further assessed by an independent team. The test collection comprised tests of speech and language skills, gross motor functioning and perception, and visual motor skills.
The speech and language test, validated for children speaking Finnish, formed the largest part of the testing. The 7 items studied (sentence formation; speech comprehension; oromotor function; auditory serial memory; sentence repetition and kinesthetic skills; serial naming and articulation; and ability to count from 1 to 5, name colors, and follow instructions) covered both expressive and receptive abilities. Voice, fluency of speech, and hearing were evaluated. Items were assessed as pass, fail, or refuse. A child failed the test if he or she failed or refused to perform in 3 different tasks or if the voice, hearing, or fluency of speech were abnormal.

Gross motor functioning and perception were tested using parts of the Test of Motor Impairment,22 the Miller Assessment for Preschoolers,23 and the Southern California Sensory Integration Tests.24 A total of 6 items (jumping on 1 foot, cross steps, throwing and catching a ball, block designs, finger localization, and imitation of postures) were assessed with the terms pass, fail, or refuse. A child failed the test if he or she failed or refused to perform in 1 of the tasks.

Parts of the Bender Gestalt Test (forms A1, A2, 3, 6.1, and 6.2)25 and the Goodenough Draw-a-Man Test26 were used in testing visual motor skills and eye-hand coordination. A child failed the test if he or she made 3 errors in copying the forms of the Bender Gestalt Test. In addition, a child failed if he or she made 2 errors in copying the forms and had 2 of the following characteristics: failed the speech and language skills tests or the gross motor functioning and perception tests; was unable to draw a man as expected for children at age 5 years; or behaved in a clearly abnormal manner during the testing, such as evidencing lack of concentration, restlessness, poor motivation, and contact difficulties. In the data analysis, the tests of the visual motor skills were combined with behavioral characteristics because these 2 parts of the test together efficiently determine whether a child is avoiding a task by demonstrating abnormal behavior.

The nurses who performed the testing were blinded to whether the child belonged to the intervention or control group.

**Representativeness of the Study Children**

Recruitment was performed at well-baby clinics, visited regularly by more than 98% of Finnish families, representing equally all socioeconomic classes. All 1880 eligible families received information about the long-term trial; 1054 families with 1062 children (56.5% of the eligible children at that age) decided to participate (FIGURE 1). At age 5 years, 764 children (72% of the original study cohort) were still participating in the trial. Of the children, 522 lived within the city boundaries of Turku and 496 (95% of Turku residents; 65% of the available 5-year cohort) were included in the neurodevelopmental analysis.

Reasons for nonparticipation in the trial or later discontinuation were evaluated. After recruitment, a random sample of 442 families who did not participate in the study was contacted and asked for the reasons for nonparticipation via a mailed questionnaire. The most common reasons were situational (difficulties in arranging visits to the Cardiorespiratory Research Unit) or attitudinal (eg, no changes wanted in child’s diet and lifestyle). The socioeconomic (parent education and family size) and health belief characteristics (attitudes toward food and dietary counseling and locus of control) of the participating and a randomly selected group of 417 nonparticipating families were also analyzed. No major differences in the measured parameters were found between the 2 groups. Finally, reasons for discontinuing trial participation were evaluated. The most common reason was moving to a remote location. Other reasons were frequent contacts with other physicians because of the child’s recurrent infections, the child being afraid of blood draws, lack of time, or the family’s unwillingness to keep food diaries.

We also compared the mean heights, weights, and serum cholesterol concentrations of the children who remained in the study at age 5 years with the same measurements for the entire initial study cohort when all the children were aged 7 months. All values studied were similar in the 2 groups. Children who were still participating in the trial at age 5 years but who had moved out of Turku (n=242) or whose parents refused permission to use developmental data (15 intervention and 11 control families) did not differ from the children who were tested. Proportions of children in the intervention and control groups and of boys and girls did not differ between those continuing and discontinuing participation, and the longitudinal data on serum lipid concentrations in these 2 groups showed no difference over time. The 26 children whose parents refused permis-
Because the aim of the study was to show that children in the intervention group performed at least as well as the control children in the testing of children's neurological development (i.e., were not inferior to the control children [noninferiority]), relative risk (RR) of failing (intervention vs control) was used as a measure for group differences. The interpretation of RR is RR=1, probabilities of failure are equal; RR<1, probability of failure in the intervention group is less than in the control group; and RR>1, probability of failure in the intervention group is greater than in the control group. Adjusted RRs of failing the developmental screening tests were estimated using the Mantel-Haenszel method and stratified by sex because of the markedly better outcome of girls in the testing.

The statistical test for the null hypothesis of inferiority vs the alternative hypothesis of noninferiority is the 1-sided test at 3% level for the hypothesis: H_0: RR>RR_0 and H_1: RR<RR_0, where RR_0 is the stated noninferiority limit. The 1-sided test procedure at the 5% level is equal to calculating a 90% 2-sided CI. Noninferiority was accepted when the upper limit of a 90% CI was less than the stated noninferiority limit RR_0. The noninferiority limit for RR_0 was set at 1.5 because the proportion of failures in the 3 major areas studied in a normal population is approximately 10% so that an increase of 5% is considered insignificant. We have not noninferiority and noninferiority of borderline significance and presented 90% CIs where appropriate. Differences were considered significant at P<.05. Analysis was done with SAS, version 6.12. The sample size of 496 children had 60% power to show noninferiority at the 5% level when the true population proportions of failures are 10% in both target populations.

**RESULTS**

**Dietary intake**

At age 8 months, when only data of formula-fed infants were included, children in intervention and control groups had similar intakes of energy, energy nutrients; and saturated, monounsaturated, and PUFAs (Table 1). Daily energy intake of children in the intervention group was continuously somewhat lower than that of the control children thereafter.

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**Table 1.** Daily Energy and Energy Nutrient Intakes of the Children in the Intervention and Control Groups at Different Ages*

<table>
<thead>
<tr>
<th>Variable</th>
<th>8 Months†</th>
<th>P Value (95% CI)‡</th>
<th>13 Months</th>
<th>P Value (95% CI)‡</th>
<th>24 Months</th>
<th>P Value (95% CI)‡</th>
</tr>
</thead>
<tbody>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Children, No.</td>
<td>117</td>
<td>103</td>
<td>250</td>
<td>236</td>
<td>239</td>
<td>233</td>
</tr>
<tr>
<td>Energy, kcal</td>
<td>806 (125)</td>
<td>803 (171)</td>
<td>961 (175)</td>
<td>977 (170)</td>
<td>1118</td>
<td>1150</td>
</tr>
<tr>
<td>Total fat, % of energy</td>
<td>28.9 (4.6)</td>
<td>28.4 (4.3)</td>
<td>25.5 (5.9)</td>
<td>27.6 (4.9)</td>
<td>29.7</td>
<td>32.8</td>
</tr>
<tr>
<td>Saturated fat, % of energy</td>
<td>12.7 (2.4)</td>
<td>12.3 (2.4)</td>
<td>8.7 (3.0)</td>
<td>12.1 (3.1)</td>
<td>10.9</td>
<td>14.4</td>
</tr>
<tr>
<td>Monounsaturated fat, % of energy</td>
<td>8.6 (1.8)</td>
<td>8.6 (1.7)</td>
<td>8.9 (2.6)</td>
<td>8.6 (1.9)</td>
<td>10.4</td>
<td>10.8</td>
</tr>
<tr>
<td>Polyunsaturated fat, % of energy</td>
<td>4.1 (1.0)</td>
<td>4.8 (0.8)</td>
<td>4.9 (2.1)</td>
<td>3.7 (1.3)</td>
<td>5.3</td>
<td>4.5</td>
</tr>
<tr>
<td>Cholesterol, mg</td>
<td>69 (25.0)</td>
<td>70.6 (30.1)</td>
<td>85.1 (37.8)</td>
<td>106.5 (46.1)</td>
<td>128.9</td>
<td>158.7</td>
</tr>
<tr>
<td>Linoleic acid, % of energy</td>
<td>4.1 (0.3)</td>
<td>4.0 (0.8)</td>
<td>3.8 (1.8)</td>
<td>3.0 (1.2)</td>
<td>4.2</td>
<td>3.7</td>
</tr>
<tr>
<td>Linoleic acid, % of energy</td>
<td>0.52 (0.16)</td>
<td>0.53 (0.11)</td>
<td>0.75 (0.45)</td>
<td>0.48 (0.17)</td>
<td>0.69</td>
<td>0.52</td>
</tr>
</tbody>
</table>

*CI indicates confidence interval. Data are presented as mean (SD) unless otherwise indicated. To convert kcal to KJ, multiply by 4.184.
† Only infants who received formula instead of breast milk as their sole milk source were included (for details see “Methods” section).
‡ Test for comparison of intakes between the 2 groups of children; 95% CI of the difference between the mean values for children in the intervention and control groups.
The absolute and relative intakes of fat, saturated fatty acids, and cholesterol at 13 months and later were consistently lower in the intervention group than in the control group (Table 1). Fat provided a surprisingly small proportion of energy in the diet of children in the intervention as well as of the control group at ages 8 and 13 months, but the proportion increased rapidly with age so that at age 5 years the mean fat (saturated fat) intake of children in the intervention group was 30.6% (11.7%) of energy and that of children in the control group 33.4% (14.5%) of energy. After age 8 months, children in the intervention group had constantly higher intake of PUFAs than children in the control group (Figure 2). Similarly, the slopes of the regression models for serum non–HDL-C values of the intervention and control children differed during the follow-up (P = .01).

Serum HDL-C values were, in general, slightly lower in the intervention group than in the control group. The intervention and control groups showed a difference in linear trends (P = .03). The regression lines differed during the first 3 years of life but not at later ages. Linear trends of the HDL-C to total cholesterol ratios of the intervention and control groups were similar for the entire study period (P = .95 and .82 for difference in the intercepts and slopes, respectively).

At age 5 years, mean (SD) serum cholesterol concentrations of the intervention group were 4.27 (0.63) mmol/L (165 [24] mg/dL) and of the control group, 4.41 (0.74) mmol/L (170 [29] mg/dL) (95% CI, −0.27 to −0.01 mmol/L [−10.4 to −0.4 mg/dL]; P = .04). The mean (SD) serum LDL-C concentration of the intervention group was lower than that of the control group (2.75 [0.57] mmol/L [106 [22] mg/dL] vs. 2.88 [0.64] mmol/L; [111 [25] mg/dL]; 95% CI, −0.24 to −0.02 mmol/L [−9 to −1 mg/dL]; P = .03) (95% CI is for difference between the mean values for children in the intervention and control groups). The intervention group had 4.5% lower mean LDL-C values than the control group. The mean serum triglyceride value of the intervention group was slightly higher (0.68 [0.22] mmol/L [60 [19] mg/dL]) than that of the control group (0.64 [0.21] mmol/L [57 [19] mg/dL]; P = .04).

### Neurological and Neuropsychological Development

The proportion of children who failed the individual tests ranged from 0.4% to 35.9%, but when the results were combined to cover the 3 major areas

<table>
<thead>
<tr>
<th>Group</th>
<th>36 Months</th>
<th>48 Months</th>
<th>60 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intervention</td>
<td>Control</td>
<td>P Value (95% CI)‡</td>
</tr>
<tr>
<td>234</td>
<td>227</td>
<td>.005</td>
<td>236</td>
</tr>
<tr>
<td>1208</td>
<td>1246</td>
<td>.07</td>
<td>1292</td>
</tr>
<tr>
<td>30.5</td>
<td>33.5</td>
<td>&lt;.001</td>
<td>30.8</td>
</tr>
<tr>
<td>(4.8)</td>
<td>(4.6)</td>
<td>(−3.8 to −2.1)</td>
<td>(4.8)</td>
</tr>
<tr>
<td>11.8</td>
<td>14.8</td>
<td>&lt;.001</td>
<td>12.0</td>
</tr>
<tr>
<td>(2.6)</td>
<td>(2.6)</td>
<td>(−3.5 to −2.5)</td>
<td>(2.6)</td>
</tr>
<tr>
<td>10.3</td>
<td>10.8</td>
<td>.005</td>
<td>10.5</td>
</tr>
<tr>
<td>(2.0)</td>
<td>(1.9)</td>
<td>(−0.9 to −0.2)</td>
<td>(2.0)</td>
</tr>
<tr>
<td>5.3</td>
<td>4.7</td>
<td>&lt;.001</td>
<td>5.2</td>
</tr>
<tr>
<td>(1.3)</td>
<td>(1.1)</td>
<td>(0.3 to 0.8)</td>
<td>(1.2)</td>
</tr>
<tr>
<td>143.0</td>
<td>171.1</td>
<td>&lt;.001</td>
<td>148.6</td>
</tr>
<tr>
<td>(52.2)</td>
<td>(63.3)</td>
<td>(−38.8 to −17.6)</td>
<td>(55.9)</td>
</tr>
<tr>
<td>3.8</td>
<td>3.5</td>
<td>.006</td>
<td>3.8</td>
</tr>
<tr>
<td>(1.1)</td>
<td>(0.9)</td>
<td>(0.1 to 0.4)</td>
<td>(1.1)</td>
</tr>
<tr>
<td>0.65</td>
<td>0.55</td>
<td>&lt;.001</td>
<td>0.66</td>
</tr>
<tr>
<td>(0.27)</td>
<td>(0.18)</td>
<td>(0.06 to 0.15)</td>
<td>(0.25)</td>
</tr>
</tbody>
</table>
studied, the percentages of failures in the 3 major areas were quite uniform (FIGURE 3).

The intervention group managed at least as well as the control group in the tests of speech and language skills, gross motor functioning and perception, and visual motor development (TABLE 2) (RRs of children in the intervention group to fail were 1 in every major area studied). The noninferiority of children in the intervention group vs those in the control group was shown in the tests of speech and language skills and visual motor skills (upper 90% confidence limits, 1.49 and 1.08, respectively), and the noninferiority of borderline significance was shown in the testing of gross motor functioning and perception (upper 90% confidence limit, 1.55). Only 4 children (1.6%) in the intervention group and 5 control children (2.1%) refused to participate in all of the main tests.

COMMENT

This study shows that in a randomized, controlled trial in which a low-saturated-fat, low-cholesterol diet was recommended by individualized dietary counseling, intake of saturated fatty acids was markedly reduced, age-related increase in serum cholesterol concentrations was diminished, and the neurological development of children in the intervention group was at least as good as that of children in the control group, with no specific areas of developmental dysfunction.

Despite current recommendations that intake of fat by adults and children older than 2 years should be less than 30% of energy, that of saturated fatty acids less than 10% of energy, and that of cholesterol less than 300 mg/d,31-33 the ability to hold intakes to such low levels during childhood has been questioned.8 Furthermore, the safety of fat-modified diets in young children has raised much concern, including fears of disturbing normal growth and neurological development.9 Growth has been affected in a few children who received extremely restricted, energy-deficient, unsupervised diets,6,11 but this contrasts with the findings of this study and of others where the diet provides adequate amounts of...
energy and essential nutrients. All such studies show that relative intake of fat and growth are not associated.\textsuperscript{11,12,13,16}

The fears of neurological dysfunction in children exposed early to fat-modified diets are based on the rapid development of the central nervous system during the first years of life. Because 75\% of brain growth is completed by age 3 years,\textsuperscript{34} the ability of the brain to recover from early nutritional deficiencies is limited. Severe malnutrition in the first year of life, even if corrected later, is associated with intelligence deficiencies at ages 11 to 18 years.\textsuperscript{35} Endogenous synthesis of cholesterol in humans fulfills the requirements of membrane synthesis and hormone production, and no dietary cholesterol is actually needed. The only essential components in dietary fats are 2 PUFAs, the linoleic and α-linolenic acids, that are the precursors of n-3 and n-6 long-chain PUFAs present prominently in neural membranes in the central nervous system and that are important for cognitive development and visual function.\textsuperscript{36} Premature, and also possibly young term infants, may require long-chain PUFAs during the first few months of life. If the diet provides an adequate supply of calories, vitamins, essential fatty acids, and other nutrients, there are no theoretical reasons why modification of dietary fat quality might be detrimental to a child’s development. Children receiving the intervention in our study consumed more PUFAs than control children, including essential linoleic and linolenic acids.

Normal growth of the children in this STRIP study\textsuperscript{15,16} and in other studies where children have been consuming diets similar to that recommended here show that moderately decreased fat intake has little impact on growth.\textsuperscript{10-12} However, neurological development of children has previously been evaluated in only 1 long-term intervention study,\textsuperscript{6} in which 51 three-year-old children who had received a low-saturated fat, low-cholesterol diet from birth failed in a screening test as rarely as their 420 controls. Unfortunately, no details of the test results are given, and

the true composition of the diet used by the children was not analyzed. In the Dietary Intervention Study in Children,\textsuperscript{10} which recruited 663 eight- to ten-year-old children with hyperlipidemia, a psychological assessment revealed no differences between adolescents in the intervention and control groups except that adolescents in the intervention group had less depression at the end of the 3-year follow-up than the control adolescents.

Minor neurodevelopmental deficits are difficult to recognize during the first few years of life, but at age 5 years appropriate analysis is possible, and the test results correlate well with later academic skills and neurological performance.\textsuperscript{37} Children in STRIP were examined by experienced, specially trained nurses, and, combined with pediatrician’s examination, the results of the testing should be reliable. However, it is still possible that families of children with developmental difficulties may be overrepresented among those families who have discontinued participation in the trial or refused permission to use the developmental data. Because the number of the dropouts and the socioeconomic status of the families were similar in the intervention and control groups, such bias in the outcome is unlikely.

Although the test collection used in our study covers the most important aspects of a child’s development, several details in performance that might be detectable using more extensive neuropsychological testing may remain unrecognized. However, in a trial this large, a more detailed testing of the children was impossible because of the limited resources available. Because the RR of failure of children in the intervention group was less than 1.0 in all 3 major areas studied, the appearance of serious adverse effects of such dietary intervention later in life is unlikely.

Whether the original sample of children represents the Finnish population is a difficult question to answer, although comparison of the nonparticipating and participating families revealed no significant differences. Recruiting a more representative cohort in such a long-term intervention study would be difficult. The proportion of families remaining in the study for more than 4 years is reasonable. Furthermore, the socioeconomic characteristics and health beliefs of the families in the 5-year cohort and in the original study cohort were quite similar, suggesting that the 496 children included in the final analysis probably represent the original study cohort reasonably well.

The strongest long-term effect of dietary fat modification in children on serum cholesterol concentration shows that the value remained 6\% lower among

<table>
<thead>
<tr>
<th>Test</th>
<th>Total, No.</th>
<th>Pass, No.</th>
<th>Fail, No. (%)</th>
<th>$P$</th>
<th>RR of Failure (90% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Speech and language skills</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Intervention</td>
<td>255</td>
<td>231</td>
<td>24 (9.4)</td>
<td>.85</td>
<td>0.95 (0.60-1.49)†</td>
</tr>
<tr>
<td>Control</td>
<td>239</td>
<td>216</td>
<td>23 (9.6)</td>
<td></td>
<td>1.0</td>
</tr>
<tr>
<td>Gross motor functioning and perception</td>
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<tr>
<td>Intervention</td>
<td>254</td>
<td>233</td>
<td>21 (8.3)</td>
<td>.86</td>
<td>0.95 (0.58-1.55)§</td>
</tr>
<tr>
<td>Control</td>
<td>239</td>
<td>219</td>
<td>20 (8.4)</td>
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<td>1.0</td>
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<tr>
<td>Visual motor skills</td>
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<tr>
<td>Intervention</td>
<td>255</td>
<td>239</td>
<td>16 (6.3)</td>
<td>.16</td>
<td>0.65 (0.39-1.08)‡</td>
</tr>
<tr>
<td>Control</td>
<td>239</td>
<td>217</td>
<td>22 (9.2)</td>
<td></td>
<td>1.0</td>
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*RR indicates relative risk; CI, confidence interval. Control and intervention groups consisted of 240 and 256 children, respectively. Nine children did not participate in all individual tests (4 in intervention group and 5 in control group). $P$ value for difference between failures of children in the intervention and control groups. \textsuperscript{†}An upper 90\% confidence limit suggests noninferiority of borderline significance of children in the intervention group compared with control children. §An upper 90\% confidence limit suggests noninferiority of borderline significance of children in the intervention group compared with control children.
3-year-old children in the intervention group than among control children if a low-saturated-fat, low-cholesterol diet is consumed from birth. In another study, a school-based intervention, the net mean change in serum cholesterol concentration ranged from 2.9% to 5.1% during the 5-year follow-up, whereas in the studies concerning hypercholesterolemic children, the decreases in serum LDL-C values were even greater. In emic children, the decreases in serum studies concerning hypercholesterolemia in children, the decreases in serum LDL-C values of children receiving the intervention in this trial were slightly lower during the first 2.5 years of follow-up, the ratio of HDL-C to total cholesterol for the intervention and control groups was similar for the entire study period. Assuming that the earlier the age at which serum cholesterol values are decreased, the greater the decrease in incidence of CHD later in life, a 3% to 5% permanent reduction in serum cholesterol concentration starting in early childhood may considerably influence the incidence of CHD in adulthood without adverse effects on neurological development.

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