Screening 1140 Fifth Graders For Hypercholesterolemia: Family History Inadequate To Predict Results

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***Abstract*: Cholesterol screening was performed on 1140 fifth-grade students in Scottsdale, AZ, as part of a school-affiliated, health-education program. The goals were to determine whether family history of heart disease or high cholesterol can predict which children have high cholesterol levels and to examine the feasibility of screening large numbers of elementary school students. Among the children studied, the mean cholesterol level was 168.3 mg/dL (4.35 mmol/L), and 13 percent had cholesterol levels above 200 mg/dL (5.20 mmol/L). Fifty-four percent had a family member with high cholesterol or a heart attack before age 60 years, but 36 percent of the students with cholesterol levels greater than 200 mg/dL (5.20 mmol/L) had a negative family history. Family history was neither sensitive nor specific as a predictor of elevated cholesterol levels (sensitivity 0.64, specificity 0.47, and positive predictive value 0.16 for predicting cholesterol levels greater than 200 mg/dL [5.20 mmol/L]). Large numbers of children were screened safely and efficiently with good student and parental cooperation. Results of this study do not support the current recommendations to screen children for hypercholesterolemia based upon their family histories. (J Am Board Fam Pract 1990; 3:259-63.)**

The view that treating hypercholesterolemia in childhood will reduce the risk of developing coronary artery disease is extrapolated from studies reporting the benefit of treating high cholesterol in middle-aged men.[1-3] The idea is supported by clear evidence that atherosclerosis starts in childhood[4,5] and that untreated children with high cholesterol levels continue to have high levels.[6,7] Children whose parents or grandparents have hyperlipidemia or develop heart disease at an early age are more likely to have elevated cholesterol levels.[8,9] These studies have led to debate over which children should have cholesterol levels measured.

The American Academy of Pediatrics currently recommends cholesterol screening on all children aged 2 years or greater who have a family history of high cholesterol or early heart disease.[10] The National Institutes of Health similarly recommends screening only children considered "high risk" because of family history.[2] Data are limited on the effectiveness of the current recommendations for screening for hypercholesterolemia in children. Two recent studies have raised concern that many children with elevated cholesterol levels could be missed by testing based on family history alone.[11,12]

The present study describes a cholesterol screening and education program involving 1140 fifth-grade students in Scottsdale, AZ. It examines whether family history of heart disease or high cholesterol can adequately predict which children will have high cholesterol levels. The study also looks at the feasibility of screening large numbers of elementary school children in school-affiliated programs.

Methods

Cholesterol testing was performed on 1140 fifth-grade students in Scottsdale, AZ, during a 1-week period in March 1989. The students were participating in a health-education program sponsored by a Scottsdale Memorial Hospital volunteer organization. All 16 public elementary schools and 4 private elementary schools in the Scottsdale area participated.

Before the screening event, parents received a permission form and a family-health-history questionnaire. The survey instrument described the study and asked about history of heart attack, stroke, angina, high cholesterol, smoking, and high blood pressure in the child's parents and grandparents. Age of first occur-

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rence for heart attack, stroke, or angina was also queried.

The fifth-grade students from each school spent 1 day in a city park rotating among educational stations focusing on topics such as smoking, exercise, fire safety, swimming safety, and nutrition. The nutrition segment included a fingerstick total cholesterol measurement on children who had parental permission.

Nonfasting capillary blood samples were collected from the child's middle or ring finger using an Autoclix™ (spring-driven lancet). Total cholesterol levels were measured by wet-chemistry method using three Abbott Vision™ analyzers. These analyzers were calibrated daily, and a protocol regarding sample collection and cholesterol determination was carefully followed by all screening personnel.

The Vision™ analyzer utilizes single-use cartridges that contain a heparinized capillary tube, a reagent, and a two-dimensional centrifugation system. Plasma is separated during centrifugation and measured and diverted to the reaction chamber. The Vision™ analyzer meets accuracy and precision guidelines established by the National Cholesterol Education Program when operated according to the manufacturer's recommendations.[13]

The children were sent home with their cholesterol results and the National Heart, Lung and Blood Institute's "Facts about Blood Cholesterol" handout, which contains supplementary diet information and recommended cholesterol levels for children. The following recommended levels were taken from Strong and Dennison[14]: Low risk, below 170 mg/dL (4.40 mmol/L); moderate risk, 170 to 185 mg/dL (4.40 to 4.75 mmol/L); and high risk, greater than 185 mg/dL (4.75 mmol/L). Although follow-up data were not obtained, students with levels greater than 170 mg/dL (4.40 mmol/L) were asked to consult their physician.

Sensitivity, specificity, positive predictive value, and odds ratios were calculated by standard methodology from 2 × 2 table analysis. The 95 percent confidence intervals for the odds ratios were calculated by the following equation: $\exp\{\ln OR +/- 1.96(1/a+1/b+1/c+1/d)^{1/2}\}$.

Results

Of roughly 1600 fifth-grade students in the Scottsdale area, 1201 returned parental permission and family-history forms before the screening event. During the screening week, 34 students were absent or refused testing, and 27 blood samples were hemolyzed or inadequate. The remaining 1140 students had cholesterol levels measured and were entered into the study.

Sample collection proceeded smoothly during the week. Children were brought into the screening room one class at a time, and there appeared to be some peer pressure to have blood drawn without complaint. One child had a vasovagal episode after the fingerstick but suffered no injury. Three children felt faint and were asked to lie down for a few minutes to recover.

The population tested was middle class to upper-middle class and predominantly white. Cholesterol levels ranged from 91 mg/dL (2.35 mmol/L) to 297 mg/dL (7.70 mmol/L); the mean was 168.3 mg/dL (4.35 mmol/L); standard deviation, 29.6 mg/dL (0.75 mmol/L); and median 165 mg/dL (4.25 mmol/L) (Table 1). The mean cholesterol level for 580 boys was 169.1 mg/dL (4.37 mmol/L) compared with 167 mg/dL (4.33 mmol/L) for 560 girls. The mean cholesterol in this age range in seven North American Lipid Research Clinics was approximately 160 mg/dL (4.15 mmol/L).[15]

Twenty-five percent of all Scottsdale students tested had cholesterol levels greater than 185 mg/dL (4.75 mmol/L), considered high for children, and 13 percent had levels greater than 200 mg/dL (5.20 mmol/L). Only 5 percent of children would be expected to have cholesterol levels greater than 200 mg/dL (5.20 mmol/L) according to the National Institutes of Health.[2] However, the percentage of white children with cholesterol levels greater than 200 mg/dL (5.20 mmol/L) in

Table 1. Cholesterol Levels of Scottsdale Fifth-Grade Students.

Cholesterol Level mg/dL (mmol/L)	Boys n (%)	Girls n (%)	All Children n (%)
<170 (<4.40)	320 (55)	316 (56)	636 (56)
170–185 (4.40–4.75)	104 (18)	113 (20)	217 (19)
186–199 (4.80–5.15)	74 (13)	62 (11)	136 (12)
200–219 (5.20–5.65)	49 (8)	37 (7)	86 (8)
220–239 (5.70–6.15)	26 (4)	18 (3)	44 (4)
≥240 (≥6.20)	7 (1)	14 (3)	21 (2)
Total	580	560	1140

Table 2. Prevalence of Positive Family History in Fifth-Grade Students.

Family Member	High Cholesterol (%)	Hypertension (%)	Vascular Disease* (%)	More than One Factor (%)
Mother	5.5	4.3	1.6	10.0
Father	8.8	9.5	2.3	17.4
Parent	13.8	13.2	3.6	25.3
Parent or grandparent	40.3	63.6	57.2	76.4

*Heart attack, stroke, or angina less than age 60 years.

other studies was 6 percent in Cincinnati, Ohio; 9 percent in Bogalusa, Louisiana; 13 percent in Brusselton, Australia; and 24 percent in Muscatine, Iowa.[16]

The percentages of Scottsdale fifth graders with positive family histories of high cholesterol, hypertension, or vascular disease are presented in Table 2. A history of vascular disease in a parent was very uncommon (3.6 percent). Similar numbers of parents had either high cholesterol (13.8 percent) or hypertension (13.2 percent). Positive histories in grandparents were much more common, and three quarters of all children had at least one positive history factor in either a parent or grandparent.

Family history factors were analyzed individually as possible predictors of elevated total cholesterol levels in the children (Table 3). The strongest predictor was a history of high cholesterol in the parents or grandparents (odds ratio = 1.8). However, this factor still lacked sensitivity as a screening tool. Parental history of heart attack or vascular disease was a poor predictor of hypercholesterolemia in the offspring, and very few of the parents had such a history.

Most current screening recommendations are based on a family history of high cholesterol or early heart attack. In the present study, 620 of the children (54 percent) had a history of high cholesterol or heart attack before age 60 years in a parent or grandparent (Table 4). Children with this history were at slightly increased risk for having an elevated total cholesterol level (odds ratio = 1.6, Table 3). However, using this history as a screening criterion to detect hypercholesterolemia, the sensitivity for identifying children with levels greater than 200 mg/dL (5.20 mmol/L) was only 0.64; the specificity was 0.47, and the positive predictive value was 0.16 (Table 3). The group with a negative family history included 40 percent of all levels greater than 185 mg/dL (4.75 mmol/L) and 36 percent of levels greater than 200 mg/dL (5.20 mmol/L).

When history of stroke, angina, or hypertension was included with history of heart attack before age 60 years or high cholesterol, 76 percent of the students had positive family histories. Using this broader family history as a guide to screening, the sensitivity for identifying children

Table 3. Family History as Predictor of Total Cholesterol ≥200 mg/dL (5.20 mmol/L) in Fifth-Grade Students.

Factor	Sensitivity	Specificity	Positive Predictive Value	Odds Ratio*
Parents				
High cholesterol	0.19	0.87	0.18	1.5 (1.0–2.4)
Hypertension	0.14	0.87	0.14	1.1 (0.7–1.8)
Heart attack	0.01	0.98	0.13	0.7 (0.2–3.0)
Vascular disease†	0.03	0.96	0.12	0.9 (0.4–2.4)
Parents or grandparents				
High cholesterol	0.53	0.62	0.17	1.8 (1.3–2.6)
Hypertension	0.66	0.37	0.14	1.1 (0.8–1.6)
Heart attack	0.36	0.72	0.16	1.4 (1.0–2.0)
High cholesterol or heart attack	0.64	0.47	0.16	1.6 (1.1–2.2)
High cholesterol, hypertension, or vascular disease†	0.77	0.24	0.13	1.1 (0.7–1.6)

*Numbers in parentheses are 95th percentile confidence intervals.
†Heart attack, stroke, or angina less than age 60 years.

Table 4. Cholesterol Level in Fifth-Grade Students by Family History of Heart Attack before Age 60 Years or High Cholesterol in Parent or Grandparent.

Cholesterol Level mg/dL (mmol/L)	Positive Family History n (%)	Negative Family History n(%)	All Children n
<170 (<4.40)	335 (53)	301 (47)	636
170–185 (4.40–4.75)	112 (52)	105 (48)	217
186–199 (4.80–5.15)	77 (57)	59 (43)	136
≥200 (5.20)	96 (64)	55 (36)	151
Total	620 (54)	520 (46)	1140

with cholesterol levels greater than 200 mg/dL (5.20 mmol/L) increased to 0.77, but the specificity was only 0.24 with a positive predictive value of just 0.13 (Table 3). Thus, despite testing 76 percent of the children, 23 percent of those with cholesterol levels greater than 200 mg/dL (5.20 mmol/L) would not be detected.

Overall, feedback from parents, children, and the media regarding the program was positive. The only negative comments came from two parents, who said their children with high cholesterol levels had been teased by classmates or had been unduly anxious about the results.

Discussion

Consensus has steadily grown that the prevention of atherosclerosis should begin in childhood.[17] Current recommendations suggest screening for hypercholesterolemia only children identified as "high risk" by positive family history rather than recommending routine screening of all children.

Following these recommendations, the number of children screened will vary widely depending on what factors are considered in the family history. Using a history of high cholesterol or heart attack before age 60 years in either parents or grandparents, more than half the children in this study population would have been screened. However, under such limited criteria, more than one-third of those with cholesterol levels greater than 200 mg/dL (5.20 mmol/L) would not have been tested.

Using a broader definition of positive family history that included a history of stroke, angina, or hypertension, more than three-quarters of children in this study would have been screened. Even so, nearly one-fourth of those with levels greater than 200 mg/dL (5.20 mmol/L) would not have been detected.

In any case, family history was neither sensitive nor specific as a predictor of which children have elevated cholesterol levels. Thus, data in the present study do not support current screening recommendations.

Thorough identification of children with elevated cholesterol levels would clearly require screening of all children. Whether the cost of universal screening is justified by the benefits of early diagnosis remains controversial.

It will be very difficult to prove that identification and treatment of hypercholesterolemia in children will reduce development of atherosclerotic disease. On the other hand, many indirect benefits of screening children became apparent during the current study. The screening program was an important educational event for both the children and their families. It was an excellent time to instruct families about healthy dietary habits and the notion that modifying fat intake may have several healthy ramifications. Many parents and siblings of children with elevated cholesterol levels were identified as having hypercholesterolemia. Considering these indirect benefits, there may be better justification for universal cholesterol screening in childhood than for some traditional tests such as urinalysis and hematocrit.

Cholesterol screening should not begin in infancy because of concerns that a fat-restricted diet in the early years of life may prevent optimum brain development. Initial screening at age 4 or 5 years would be reasonable, with further testing during adolescence. Providing appropriate information at the time of testing about the meaning of the results is crucial to prevent undue anxiety.

Children found to have high random total cholesterol levels should have fasting lipid profiles performed to confirm the initial cholesterol measurement and to quantitate high-density lipoprotein (HDL) and low-density lipoprotein (LDL) levels. Ten to 15 percent of children with hypercholesterolemia have elevated protective HDL levels and thus are not at increased risk of developing heart disease.[14,18] Further research to determine whether family history can identify

this subset of children with elevated HDL levels would be informative.

Parents whose children participated in this study were receptive to the idea of cholesterol screening, and the fifth graders themselves were very cooperative. Thus, large numbers of children were screened safely and efficiently. The current study shows that large-scale screening programs are feasible as school-related activities.

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