

Atherosclerosis: A Nutritional Disease of Childhood

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The development of coronary atherosclerosis begins in childhood. A clear relation between diet and cardiovascular disease risk has been demonstrated. Findings from the Bogalusa Heart Study indicate that most children still exceed national recommendations for intake of total and saturated fat. In addition, children's mean total energy intake is greater than energy expenditure, contributing to the high prevalence of obesity beginning in childhood. Even in childhood, obesity often occurs with other risk factors for cardiovascular disease, such as increased blood pressure, adverse changes in serum

lipoproteins, and hyperinsulinemia. This clustering of risk factors has been linked to acceleration of atherosclerotic lesions in the coronary arteries of young individuals. Decreasing the incidence of coronary artery disease in mid and late life necessitates healthy habits in nutrition and lifestyle in early life. Public health measures to favorably alter lifestyle can have a major impact on heart disease prevention and should be pursued vigorously. ©1998 by Excerpta Medica, Inc.

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Although the incidence of coronary artery disease has decreased since the 1960s, cardiovascular disease still accounts for almost half of the deaths in the United States. As part of the globalization of heart disease, coronary artery disease appears to be increasing in countries in which it traditionally has had a low prevalence.¹

In the United States, >70% of the adult population has coronary atherosclerosis. Hypertension affects about 20% of the adult white population and >40% of adult blacks. Epidemiologic studies coupled with pathologic observations and autopsies of children and young adults demonstrate that cardiovascular disease begins in childhood.²⁻⁸ Although the basis for the development of atherosclerotic heart disease is often attributed to genetic factors, heart disease is related to environmental factors as well.⁹ For example, the rate of cardiovascular disease among individuals born in Japan increases following their migration to Honolulu or San Francisco.¹⁰ As immigrants adopt a Westernized culture and lifestyle, diabetes mellitus and obesity also tend to develop in them more often than in their counterparts at home.

The early natural histories of arteriosclerosis, coronary artery atherosclerosis, and essential hypertension were examined in the Bogalusa Heart Study by observing traditional cardiovascular risk factors and lifestyles, including diet, smoking, and other behavioral characteristics.^{11,12} Over the past 25 years, data have been gathered on >16,000 residents whose ages range from birth to 38 years and who live in a semi-rural, biracial (black/white) community. This article will focus on the relation between unhealthy dietary

patterns and increasing obesity in children, the aggregate influence of multiple risk factors on coronary atherosclerosis, and approaches to prevention of coronary artery disease beginning in early life.

DIET AND POTENTIAL IMPACT ON EARLY CARDIOVASCULAR RISK

Dietary intake is a major determinant of cardiovascular risk. Experimental studies in humans and animals show a clear relation between diet and cardiovascular risk. Variations in diets of different cultures correspond with the prevalence of coronary artery disease and its risk factors, according to international and crosscultural studies. In contrast, studies within populations show only a weak association between diet and risk factors, underscoring a genetic basis for interindividual differences within a population exposed to a similar dietary pattern.¹³ Excessive intake of saturated fat and cholesterol with little interindividual contrast probably accounts for this low relation. Despite this weak intrapopulation association, when the relation between diet and coronary lesions was examined by autopsy studies, high dietary intakes of starch and vegetable protein were associated with less atherosclerosis than high intakes of animal protein and fat.¹⁴

Trends in dietary patterns: The Bogalusa Heart Study¹⁵ has been documenting the dietary intakes of children without attempts to change dietary patterns of the inhabitants. Changes in food choices and nutrient intakes reflect natural changes in food consumption patterns in the United States, as influenced by industry, mass communication, and commercial advertising. Total energy intakes of children have remained unchanged, or in some cases decreased, since the study's inception in 1973-1974, and total energy intake per kilogram of body weight has significantly decreased because of a mean increase in body weight. The percentage of energy obtained from protein and carbohydrate has significantly increased. In contrast, the percentage of energy from total fat has decreased

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from 38% to 34%, and the percentage of energy from saturated fat has decreased from 16% to 13%. The decrease in total fat intake reflects a decrease in palmitic, stearic, and oleic fatty acid intakes. The percentage of children whose diet exceeds the recommendations for total fat and saturated fat intake has also decreased over time, but the diet of >75% of children still exceeds recommended dietary guidelines for intake of saturated fat.

These trends in Bogalusa reflect national trends in types of foods consumed.¹⁵ For example, there has been an overall decrease nationally in the consumption of milk, vegetables/soups, breads/grains, and eggs and an increase in total amounts consumed of fruits/fruit juices, carbonated beverages, seafood, poultry, cheese, and beef. The percentage of total fat obtained from consumption of milk, beef, pork, and desserts has decreased, whereas the percent fat from mixed meats (i.e., combination dishes including meat), poultry, and breads and grains has increased. In general, dietary intakes and food consumption patterns of Bogalusa children are similar to those reported in national surveys made between 1987 and 1994.¹⁶ Although such trends are favorable, the current dietary pattern will not prevent progression or achieve regression of coronary atherosclerosis, as seen in recent drug clinical trials.¹⁷

The mean total energy intake of children continues to exceed the Recommended Dietary Allowances (RDA) and is greater than total energy expenditure, leading to an increase in the prevalence of obesity.¹⁸ The macronutrient composition of children's diets is far in excess of the total and saturated fat intake recommended by the American Heart Association. The types of foods consumed by children may differ from adults but the macronutrient composition is similar, reflecting the generally unhealthy diet in the United States.

Impact of school meals on children's diets: Today, >25 million children participate daily in the National School Lunch Program; 66% of children aged 6–10 years eat lunches provided at schools. For some 10-year-old children, approximately 50–60% of their total daily intake of energy, protein, cholesterol, carbohydrate, and sodium comes from school meals.¹⁹ The contribution of school meals to total daily intake of vitamins and minerals ranges from 45% for iron to 77% for calcium. On average, school lunch provides 22% of a child's daily energy intake. Each school lunch derives 39% of its energy from fat and 14% from saturated fatty acid. School lunch is the source of one-third of a child's total sodium intake and only 8% of total sucrose intake. Breakfast, an important meal for growing children, is also consumed in school by a large number of children. Consequently, the school meal program can influence dietary composition in a positive way. Although these observations are given for children, the composition of the adult diet in the United States is similar in excess total and saturated fat, cholesterol, and salt.

OBESITY AND ADULT CORONARY ARTERY DISEASE

Epidemiology of obesity: Excess caloric intake and sedentary behavior contribute to the high prevalence of obesity beginning in childhood in the US population.²⁰ At an individual level, the onset of obesity appears to be related to both a genetic predisposition and an imbalance between energy expenditure and energy intake. Studying obesity in childhood is complex because it entails differentiating changes in obesity from the changes of normal growth and redistribution of body fat. In general, white children have more body fat than do black children, who demonstrate a greater lean body mass.²¹ In adolescence, black girls begin to show a marked increase in obesity that precedes the morbid obesity commonly seen in adult black women.²² In the population 19–32 years old in the United States, 9% of white females and 20% of black females exceed a body mass index of 32.3, a measure of marked obesity. Such obesity parallels the occurrence of adverse changes in other risk factors (Figure 1).

Secular trends of obesity: The number of overweight children and young adults has more than doubled in the past decade. Although no changes in height have been noted over a 20-year span of the Bogalusa Heart Study, a 5-kg increase in average weight has occurred²³ (Figure 2). Secular trends toward increased obesity have been observed in all ages but are most pronounced during and after adolescence, especially among those at the upper ponderal index (weight/height³) percentiles. The temporal increase in weight is approximately 2% for persons in the lower 3 quartiles of body weight but 7–10% among those in the upper quartile. Subscapular skin fold thickness, an indicator of central fat deposition, increases most dramatically after adolescence.²⁴ This trend toward weight gain is occurring among adults in the United States and is associated with worsened cardiovascular risk, including an increase in type 2 diabetes mellitus. The increased prevalence of obesity may explain the current leveling off of what had been a declining trend in the incidence of cardiovascular disease that began in the 1960s.

Clustering of obesity with other risk factors: Abnormal blood pressure levels are associated with obesity, especially in white persons during and after sexual maturation. Similarly, obesity is related strongly to adverse changes of serum lipids and lipoproteins, and this relation appears to be strongest for white children, especially males.²⁵ Correlations between very-low-density lipoprotein cholesterol level and ponderal index are highly significant, especially for white males, and the correlations become stronger as children mature into young adults²⁵ (Figure 3). A negative association occurs between high-density lipoprotein (HDL) cholesterol level and ponderal index; this negative relation increases with age.

A link between carbohydrate–lipid metabolism and risk factors is also evident in childhood. As in adults, childhood obesity is associated with hyperinsulinemia and a related clustering of risk factors known as syn-

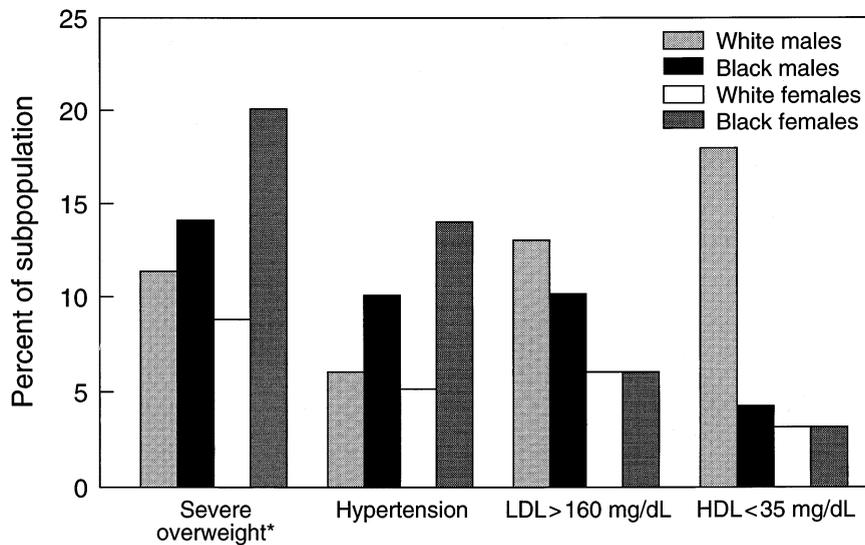


FIGURE 1. Prevalence of adverse risk factors among young adults aged 19–32 years as found in the Bogalusa Heart Study. (*Body mass index >31.1 kg/m² in males and 32.3 kg/m² in females.)

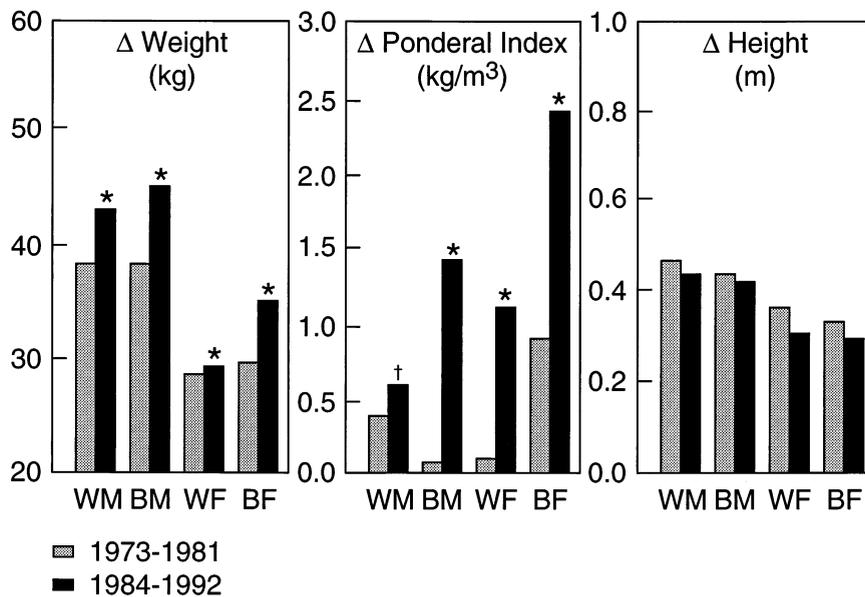


FIGURE 2. Changes in anthropometric measurements of children aged 7–9 years over two 8-year periods, 1973–1981 and 1984–1992, in the Bogalusa Heart Study. Secular trends show significant increases in body weight and ponderal index (weight/height³) without significant change in height. (BM = black males: n = 98 in 1973–1981, n = 52 in 1984–1992; BF = black females: n = 119 in 1973–1981, n = 62 in 1984–1992; WF = white females: n = 91 in 1973–1981, n = 73 in 1984–1992; WM = white males: n = 109 in 1973–1981, n = 48 in 1984–1992; * p < 0.0001; † p < 0.05.)

drome X.²⁶ Central body fatness has a greater impact than total body fat on this metabolic cluster of risk factors in children as well as in adults. The syndrome X of hyperinsulinemia, dyslipidemia, high blood pressure, and obesity can be identified clearly in childhood, but the excessively high concentration of triglycerides and the development of mixed hyperlipoproteinemia do not become evident until the third decade of life.

Occurrence of multiple risk factors in children: Epidemiologic studies, such as Framingham, have established that multiple risk factors are synergistic or additive in predicting morbidity and mortality from cardiovascular events. Findings from the Bogalusa Heart Study indicate that this clustering of risk factors begins in childhood, increases with age and obesity, and predicts adult levels of cardiovascular risk factors (Figure 4).²⁷

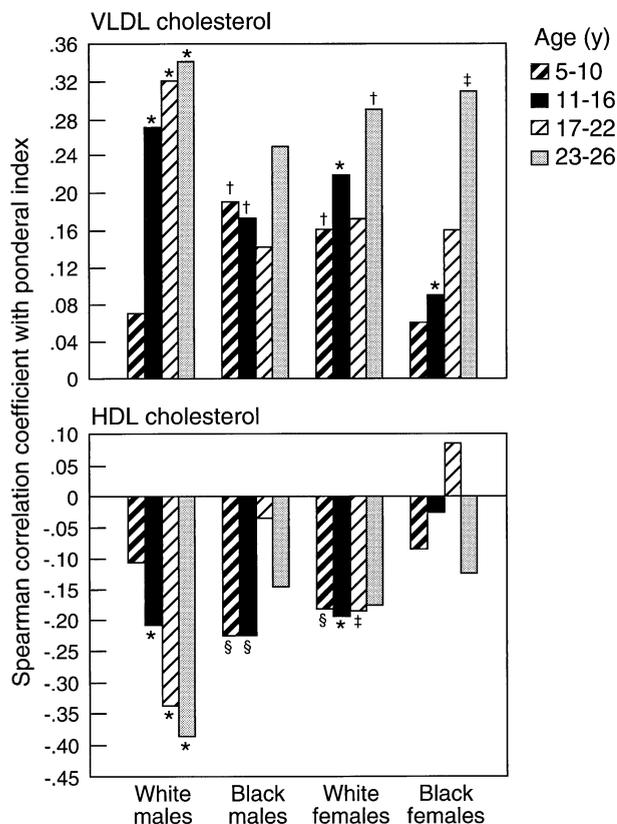


FIGURE 3. Relation of very-low-density lipoprotein (VLDL) and high-density lipoprotein (HDL) cholesterol with ponderal index (weight/height³) by age groups, race, and sex in the Bogalusa Heart Study. (* p < 0.0001; † p < 0.01; ‡ p < 0.05; § p < 0.001.)

IMPACT OF MULTIPLE RISK FACTORS ON CORONARY ARTERY DISEASE

Anatomic studies of coronary artery disease and risk factors: Coronary arteriography has contributed considerably to our understanding of the relation between the severity of coronary artery disease and clinical risk factors, but these studies are more limited than actual anatomic studies.²⁸ Furthermore, coronary arteriogra-

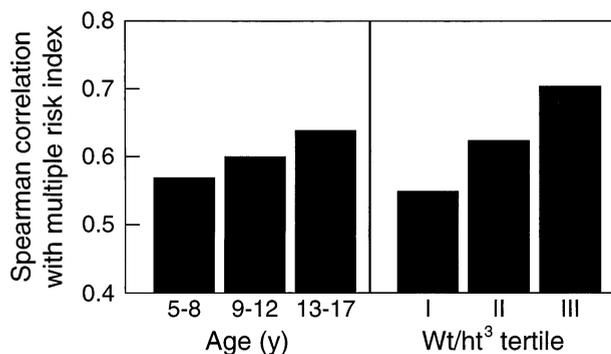


FIGURE 4. Correlation of a multiple risk index in children and young adults by age and obesity status over 8 years in the Bogalusa Heart Study (n = 1,176; p = 0.0001). The multiple risk index denotes age, race, and sex-specific rank sum of systolic blood pressure, insulin, and total-to-HDL cholesterol ratio. (Reprinted with permission from *Arch Intern Med*.²⁷)

phy is not practical in an asymptomatic young population. An important question is whether multiple risk factors influence substantial coronary atherosclerosis in youth.

Autopsy studies: Autopsy studies show an impressive relation between cardiovascular/renal lesions and clinical cardiovascular risk factors. Autopsies have been conducted in the Bogalusa Heart Study on accident victims, aged 3–38 years, who had prior cardiovascular risk factor examinations.^{6,8} Earlier observations have demonstrated a strong association of specific antemortem risk factor variables with aortic and coronary atherosclerotic lesions. These observations have been extended by findings from a larger post-mortem multicenter study, Pathobiologic Determinants of Atherosclerosis in Youth (PDAY).⁷

The extent of atherosclerotic lesions, especially in coronary vessels, correlates positively and significantly with body mass index, systolic blood pressure, serum triglyceride level, total cholesterol level, low-density lipoprotein (LDL) cholesterol level, and the total/HDL cholesterol ratio.⁸ Table I shows the correlation between the extent of aortic lesions and coronary artery lesions and antemortem multiple risk factor indices. The correlation between the extent of fatty streaks or raised collagen-capped fibrous plaques and individual risk factors differs for the aorta, with similar correlations for the coronary vessels. The amount of collagenous, raised plaques as a percentage of the total surface is greater in coronary vessels than in the aorta. Of the 4 race–sex groups, white males show relatively higher correlations between the extent of coronary lesions and body mass index and other risk factors. Because diet influences obesity, lipoprotein concentrations, and blood pressure, nutrition is implicated as a major environmental factor that underlies the high incidence of atherosclerosis in industrialized cultures.

The relation of clustering of risk factors to the extent of atherosclerosis indicates that multiple risk factors tend to cause acceleration of atherosclerotic lesions, especially the progressive type of disease in coronary vessels (Figure 5). This relation appears to be curvilinear, indicating a synergistic effect of multiple risk factors. This observation adds credence to the concept that risk factors are multiplicative or additive, leading to end-stage morbidity and mortality from coronary artery disease, as shown in the Framingham Study.²⁹

The extent of lesions in the coronary arteries, especially the lumen-encroaching fibrous plaques, increases with age and with cardiovascular risk factors in these young individuals. Cigarette smoking produces a further increase in the severity of coronary atherosclerosis, as observed in both the PDAY³⁰ and Bogalusa autopsies. At this period of life, the disease remains asymptomatic but presages future morbid events and mortality from coronary artery disease. The cluster of metabolic risk factors related to syndrome X or insulin-resistance syndrome seems to have a major effect that underlies progressive atherosclerotic disease.

TABLE I Spearman Correlation Coefficients Between Extent of Aortic and Coronary Artery Lesions and Multiple Risk Factor Indices

	White Males (n = 41)	Black Males (n = 23)	White Females (n = 19)	Black Females (n = 10)	Total (N = 93)
Systolic BP, BMI, and LDL-cholesterol combination					
Fatty streak, aorta	0.61*	0.67 [†]	0.43	0.52	0.57 [‡]
Fibrous plaque, aorta	0.18	0.60 [§]	0.07	0.68	0.23
Fatty streak, coronary	0.63*	0.45	0.61 [§]	0.90	0.54 [‡]
Fibrous plaque, coronary	0.56 [†]	0.59 [§]	0.09	0.35	0.44*
Systolic BP, BMI, and triglycerides combination					
Fatty streak, aorta	0.53 [†]	0.35	0.53	0.61	0.41*
Fibrous plaque, aorta	0.26	0.40	0.09	0.68	0.27 [§]
Fatty streak, coronary	0.76 [†]	0.37	0.51	0.99 [‡]	0.58 [‡]
Fibrous plaque, coronary	0.66*	0.58 [†]	0.17	0.35	0.51 [‡]
Systolic BP, BMI, triglycerides, and total/HDL-cholesterol combination					
Fatty streak, aorta	0.61*	0.56 [§]	0.47	0.93 [†]	0.53 [‡]
Fibrous plaque, aorta	0.26	0.56 [§]	0.09	0.51	0.26 [§]
Fatty streak, coronary	0.67 [†]	0.53 [§]	0.50	0.99 [‡]	0.54 [‡]
Fibrous plaque, coronary	0.65*	0.63 [†]	0.16	0.35	0.49 [‡]

Calculated as sum of the study-, age-, race-, and sex-specific z-scores of risk factor variable combinations shown in the table. Sample size varies based on variables used.

BP = blood pressure; BMI = body mass index; HDL = high-density lipoprotein; LDL = low-density lipoprotein.

*p < 0.001.

[†]p < 0.01.

[‡]p < 0.0001.

[§]p < 0.05.

The evidence linking cardiovascular risk factors to early atherosclerosis is impressive and supports examination of risk factors early in life. Furthermore, it shows the need to adopt healthy lifestyles to prevent obesity. Encouraging a prudent diet and increasing physical activity will help control weight and may retard the initiation and progression of early atherosclerosis.

PREVENTIVE CARDIOLOGY

Background: Cardiovascular disease, atherosclerotic coronary artery disease, hypertension, and diabetes mellitus are major public health problems. Two epidemiologic approaches for prevention of heart disease are possible: the high-risk clinical model and the public health or general population approach. Currently, cardiologists focus primarily on high-risk individuals who have already demonstrated clinical coronary artery disease. Reduction of LDL cholesterol levels has been effective in decreasing morbidity and mortality in many clinical trials. Use of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors ("statins") has been shown to be effective in preventing future coronary events, even in asymptomatic individuals with levels of LDL cholesterol near the average of the US population. A rigidly modified diet also favorably alters the progression of coronary atherosclerosis. Ornish et al³¹ have demonstrated accomplishments with rigid dietary modification and stress management similar to those with lipid-lowering drugs.

Family health promotion for high-risk individuals: Cardiologists have an opportunity to broaden their role in preventive cardiology by involving the spouse, family members, and offspring of cardiac patients in

an intervention program.³² The shared household exposure and familial nature of heart disease necessitate extending prevention beyond current practices of including only cardiac patients. General guidelines for screening children and families at high risk are shown in Table II.

We have developed a Family Health Promotion model, using a multidisciplinary team, to motivate and train high-risk individuals and their families to improve lifestyles.^{32,33} Paraprofessionals consisting of dietitians, counselors, and exercise specialists provide support to cardiologists in working with patients and their families. The program provides 10–12 weekly sessions that cover such topics as cessation of cigarette smoking, dietary alterations, increasing physical activity, and stress reduction. Cardiologists monitor risk factor changes and guide the work of the paraprofessionals.

Rationale for public health prevention of heart disease: Findings from the Bogalusa Heart Study provide the evidence to begin heart disease prevention in the general population, especially for young individuals. These findings can be summarized as follows: *First*, in the first and second decades of life, unfavorable lifestyles prevail in the United States and contribute to the pattern of key major risk factors found in the population of children and young adults: (a) 80% of children exceed the amounts of dietary total fat, saturated fat, cholesterol, and sodium recommended in the American Heart Association's Step I diet; children and adults are increasingly becoming obese because of inactivity and excessive caloric intake; and (b) habitual cigarette smoking, tobacco use, and alcohol consumption are reported in one-third of adolescents and

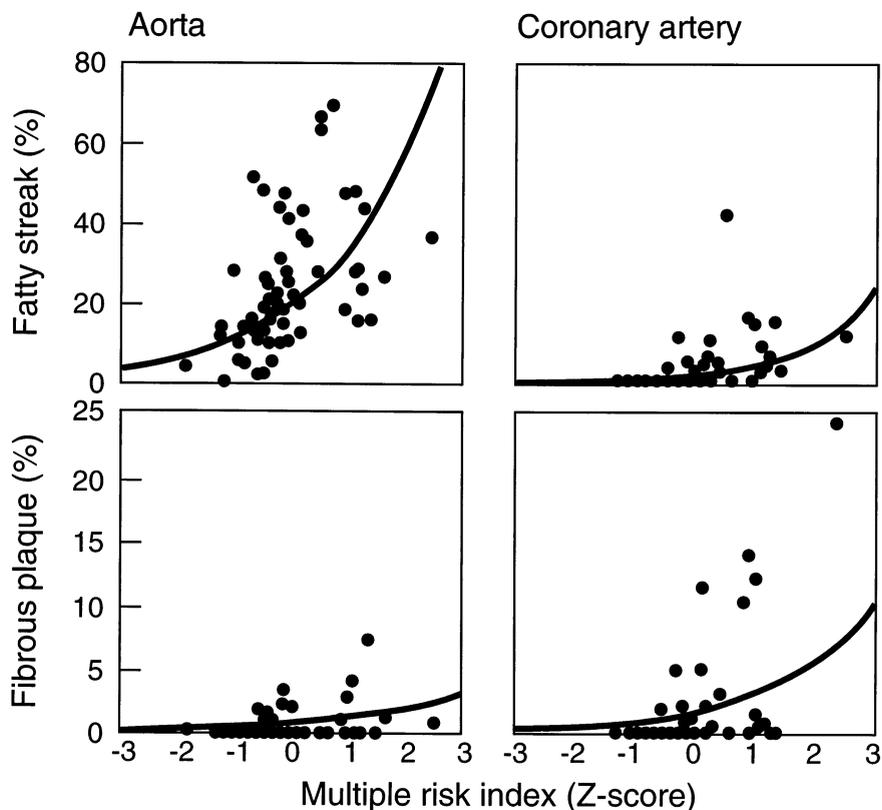


FIGURE 5. Relation of the extent of atherosclerosis to a multiple risk index, comprising body mass index ($\text{weight}/\text{height}^2$), systolic blood pressure, and low-density lipoprotein (LDL) cholesterol level in children and young adults. The multiple risk index represents age, race, and sex-specific rank sum of risk variables. Note the acceleration of lesions with multiple risk factors, especially fibrous plaques in coronary arteries. (Reprinted with permission from *Ann N Y Acad Sci*.³⁸)

young adults. These unhealthy lifestyles begin in young children. *Second*, in the general population, which is already at high risk, risk factors evolve unfavorably from youth into adulthood and translate into high morbidity and mortality at middle age. *Third*, young persons with risk factor profiles at the upper levels of the distribution, which would be considered within a normal range by adult standards, are at particular risk. This is confirmed by autopsy findings showing that coronary atherosclerosis correlates with existing clinical risk factors at a young age.

In terms of a public health approach, no direct evidence can be provided to show that alteration in early life can actually prevent heart disease decades later. Documentation of this type of information requires 30–40 years of research on a large population base and is almost impossible to obtain. Recommended components of public health intervention such as (1) reductions of total dietary fat, saturated fat, cholesterol, and sodium; (2) control of obesity; (3) increased physical activity; and (4) elimination of tobacco use are safe. Dietary excesses, obesity, and cigarette smoking are clearly major risks for the future development of cardiovascular morbidity. With this background, health education for school children is

one approach to reach large numbers of young individuals destined to be at risk for cardiovascular events as adults.

School education programs: Cardiovascular health education and changing the environment of schools constitute an appropriate public health approach that can have a major impact on the prevention of heart disease.^{34,35} We have developed a program for elementary school children (K–6), the Health Ahead/Heart Smart Program, which addresses the entire school environment.^{35,36} It includes traditional classroom training and health promotion by altering school nutrition, improving exercise programs, and encouraging teachers and parents, as role models, to adopt healthy lifestyles. Social problems also influence health and the adoption of unhealthy lifestyles: cigarette smoking, drugs, alcohol, dropping out of school, teenage pregnancy, and even violent behavior pose obstacles to achieving prudent nutrition and exercise programs. The Health Ahead/Heart Smart Program focuses on self-esteem and decision-making, encourages children to assume responsibility for their own health, and addresses these social problems as well.

The major question remaining is this: How can primary care physicians and cardiologists address prevention while still meeting the demands of crisis med-

TABLE II Recommendation for Examination of Children for Cardiovascular Risk: General Guidelines

- Family history
 - Premature heart disease, i.e., myocardial infarction in males <55 yr and females <65 yr
 - Hypertension
 - Hyperlipidemia: high LDL-cholesterol level
 - Low HDL-cholesterol level
 - Diabetes mellitus
 - Cerebrovascular accident
- Routine examination by physician
 - Blood pressure, height, weight, skinfolds, waist measurement
 - Venipuncture for determination of levels of cholesterol, triglycerides, and lipoproteins; as a minimum, serum total cholesterol and HDL-cholesterol levels
- Evaluation of
 - Type A-B behavior
 - Cigarette smoking
 - Exercise

HDL = high-density lipoprotein; LDL = low-density lipoprotein.

icine?³⁷ To answer that question, we must also address these issues: (1) Do cardiologists and primary care physicians accept the premise that primary prevention is beneficial? (2) Is it the responsibility of cardiologists only to practice secondary preventive cardiology? (3) What can cardiologists do related to prevention? (4) What prevention programs are practical? (5) Should primary prevention of heart disease be the role of cardiologists, internists, family practitioners, or pediatricians? (6) How will primary care physicians incorporate other healthcare professionals (nutritionists, counselors, exercise specialists, etc.) into preventive cardiology? The recommendation to train cardiologists in prevention is a start.

SUMMARY

Cardiovascular risk factors begin in childhood and are associated with accelerated coronary atherosclerosis, a truly silent disease. Unhealthy lifestyles and behaviors also begin in childhood and include excessive intake of calories, saturated fat, and cholesterol; inactivity; obesity; and cigarette smoking. The appearance of these behaviors in youth indicates the need for preventive programs, not only for individuals identified at high risk, but also for children and young adults in general. Most underlying risk factors are modifiable. Improved nutrition, increased physical activity, weight control, and elimination of tobacco use remain essential goals of preventive cardiology. Cardiologists and primary care physicians can play a vital role in this regard.

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