MOTHER: Yes, I just got terrible upset, it would be natural I guess.

DOCTOR: What did you think being pregnant and all that?

MOTHER: I just wondered why it had to happen then. Why she couldn't have waited. I know she didn't have anything to do with it but why? Because everybody has to lose their parents but it had to happen right then. I don't know why. I never did know why.

DOCTOR: What did you think?

MOTHER: I don't know, I just think what am I facing and my mother's dead on top of it. Worst part was——

DOCTOR: On top of what?

MOTHER: What?

DOCTOR: You said what you are facing and your mother's dead on top of it.

MOTHER: I am going to the hospital any minute with 4 other little children and there is my mother dead right on top of it.

DOCTOR: What did you think when you saw the baby?

MOTHER: Oh daddy, its just a boy. The first thing I could think of was just, my mother's dead, my mother's dead.

DOCTOR: When he was born this is what you could think of?

MOTHER: That's all I could think of. I wasn't caring that it was a boy. I was just more worried about momma but he said he was so hoping it would be a girl, my husband did, because I had enough disappointment right then, you know, heartache but that was that and that never made me—I never held that against anybody or anything.

At the time of discharge from the hospital, I tell parents that their child has been cured of the disease but one problem remains. I ask whether they believe the child's life was threatened. The answer is frequently yes. If so, I state that the threat has passed and it is now important to treat this child normally as if there has been no threat to his life. They must put this disease in the past and not feel that his life remains threatened. I discuss the possibility of becoming overpermissive and overprotective and state that they must demand the same rules of obedience from the child as they had in the past and they must encourage independence. I tell them that I will watch for disruptive behavior in the child as well as overly permissive child-rearing practices as time goes one. At each follow-up visit, I talk with the parents about this in an effort to prevent problems. I inquire about bedtime, sleeping through the night, feeding, temper tantrums, and general obedience and we discuss their manner of dealing with these activities.

Pediatricians should practice preventive medicine in an effort to avert cases like those cited above. We, as ombudsmen for healthy growth and development in children, must address this problem in a positive way. No attempt was made to do this in the above cases. At the time of hospital discharge, we should discuss the possibility of the development of abnormal child-rearing practices and subsequent behavioral problems in the child. It is important that we help parents foster independence and separation in their children and teach their children how to get along in the world. These, after all, are primary goals of optimal pediatric care.

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The Child Is Father of the Man

Wordsworth was both metaphorically and literally[1] accurate in concluding that "... the child is father of the man."[2] The anatomic,[3-5] biochemical, epidemiologic, nutritional, genetic, and clinical genesis of atherosclerosis is in childhood.[1,6-13] There is also compelling evidence that relates antemortem coronary heart disease risk factors to the development of early atherosclerotic lesions,[5] evidence that should stimulate pediatric primary prevention of atherosclerosis.

By virtue of extensive studies of schoolchildren,[11,14-18] and of national population groups (Second National Health and Nutrition Examination Survey),[19] excellent age-, sex-, and race-specific distributional data are available for major coronary heart disease risk factors including total, high-, and low-density lipoprotein cholesterol (HDL-C, LDL-C), height, weight, Quetelet index, skinfolds, BP, nutrient intake, and cigarette smoking. Major apolipoprotein risk factors for coronary heart disease including low-density apolipoprotein B and apolipoprotein A-I can also easily be identified in childhood,[1] and distributional data are becoming available.

After fitting together the mosaic of biochemical, clinical, epidemiologic, genetic, nutritional, and pathologic coronary heart disease precursor data in children,[1] a compelling picture can be perceived relevant to pediatric primary prevention of atherosclerosis. Recognition of the overall pattern in the multifactorial risk factor[1] mosaic has been vastly improved by recent controlled clinical trial data[20-25] which indicates that reduction of plasma total and LDL-C by diet alone or by diet plus cholestyramine resin is successful in the primary and secondary prevention of coronary heart disease. These convincing demonstrations of efficacy,[20-25] along with other evidence,[1,3-13,16] have provided a foundation for a national effort recommending population-wide plasma cholesterol reduction[26] along with design suggestions for public health and medical approaches for the diagnosis and therapy of dyslipoproteinemia.[27]

Demonstrations of the coronary heart disease-reducing efficacy of cholesterol lowering in adults[20-26] are seminal to pediatric primary coronary heart disease prevention.[1,10,26] Certitude about the efficacy of pediatric coronary heart disease prevention[1,10,26] is necessarily derived from extrapolations from controlled clinical trials in middle-aged, high-risk, hypercholesterolemic men,[20-26] because there are not and probably never will be long-term (four to six decades) controlled trials to demonstrate that lowering plasma total and LDL-C in children will significantly reduce their likelihood of having coronary heart disease in adulthood.

A second major factor central to the degree of enthusiasm[1,10] for pediatric primary prevention of atherosclerosis can be found in the major secular trends toward declining coronary heart disease mortality in many westernized industrialized countries (including the United States) in the last two decades.[28] This decrease in coronary heart disease mortality has been accompanied by reductions in dietary saturated fat and cholesterol intake and by an increase in polyunsaturated fat consumption.[29] In the same time span, serum cholesterol levels have declined approximately 15 mg/dL.[30] These secular trends were neither legislated, mandated, nor designed, and it is not possible to directly attribute recent decrements in cardiovascular mortality[28] to reductions in population serum cholesterol levels or to confidently attribute the reductions in serum cholesterol levels to changes in diet.[29] However, the congruence of these three changes is intriguing[27] and speculatively suggests that they may be causally related.

Within the frame of reference of secular trends toward coronary heart disease reduction,[28-30] the pediatric genesis of atherosclerosis,[1,3-11] and the relationships of clinically measurable risk factor levels to early atherosclerotic changes,[5] it may be useful to review and broaden guidelines[26] for the diagnosis and management of hypercholesterolemia in children.

PUBLIC HEALTH, POPULATION-WIDE HYGIENIC MEASURES

Irrespective of the scope of pediatric lipid and lipoprotein cholesterol sampling (high risk *v* all schoolchildren), it is important to amplify population-wide hygenic trends (Table).[27-30] These include reduction of dietary saturated fat and cholesterol and increased polyunsaturated fat,[1,10,26] broad-scale diagnosis and control of hypertension,[27] discouragement of and reduction in cigarette smoking, targeting ideal body weight, and encouraging increased habitual physical activity (Table).

FAMILY HISTORY-TRIGGERED SAMPLING

In addition to public health approaches,[1,7,10,26,27] measurement of lipid and lipoprotein cholesterol risk factors in children and their families requires well-defined sampling schemes (Table). The recent Consensus Conference suggested that children at high risk should be identified primarily by carefully obtained family histories rather than routine screening.[26] One approach toward family history-triggered (high-risk) sampling is shown in the Table. Measurements should be made of plasma total cholesterol, triglyceride, and HDL-C, with calculation of LDL-C, to focus on children with high LDL-C, and on those with bottom decile HDL-C.[7-10] After initial identification of hypercholesterolemia and/or other dyslipoproteinemias, at least two samplings should be repeated for diagnostic confirmation. It is very important to then discriminate between dyslipoproteinemia secondary to diseases, drugs, and diets, and primary and/or familial dyslipoproteinemia.[1,6,7-10,12]

INCLUSIVE PEDIATRIC SAMPLING

A second approach involves measurement of lipids and lipoprotein cholesterols in all schoolchildren, preferably before sexual maturation with its reductions in HDL-C and increments in LDL-C. Because most children are seen at least once a year by a physician or a clinic, perhaps even more regularly than adults,[26] such sampling should also be relatively cost effective. Inclusive sampling must be accompanied by accurate laboratory methodology, by improved capillary blood-sampling techniques and micromethodology, and by informed and consistent follow-up. Careful cost to benefit ratio stud-

TABLE. Pediatric Diagnosis and Therapy of Hypercholesterolemia*

Measure plasma total cholesterol (TC), triglyceride (TG), HDL-C, LDL-C

Family History-Triggered (High Risk)

1. All children with parental history (≤60 yr of age) of premature myocardial infarction, angina, cerebrovascular accident, or peripheral vascular disease.
2. All children with parental dyslipoproteinemia: (top quartile) LDL-C, TG, and/or bottom decile HDL-C.
3. All children with parental history of essential hypertension, gout/hyperuricemia, diabetes.

Routine—All Schoolchildren: Preferably before sexual maturation with its attendant dynamic lipoprotein cholesterol changes.

Intervention

1. "Moderate hypercholesterolemia" (75th–90th percentile): TC, 170–190 mg/dL; LDL-C, 110–125 mg/dL. Diet therapy, reevaluate twice per year or more. Target TC and LDL-C reduction to <170 and <110 mg/dL, respectively.
2. "Severe hypercholesterolemia" (≥90th percentile): TC > 190 and LDL-C > 125 mg/dL. Intensive diet, serial reevaluation. Target TC and LDL-C reduction to <170 and <110 mg/dL, respectively.
3. Children heterozygous for familial hypercholesterolemia. If, despite best diet intervention, LDL-C remains ≥90th percentile (125 mg/dL), add bile acid-binding resins, targeting ≥25% reduction of LDL-C from baseline.

Population-Wide Hygienic Approach

1. Reduce total fat intake to 30% of calories, lower staturated fat intake to <10% of calories, increase polyunsaturated fat (to ≤10% of calories), reduce cholesterol intake to <250–300 mg/d.[26] Target reduction of mean total plasma cholesterol from approximate current mean of 160 to 140 mg/dL.[7]
2. Diagnose and control hypertension.
3. Discourage initiation of and reduce cigarette smoking.
4. Target "ideal" body weight, encourage increased habitual physical activity.

* After initial identification of dyslipoproteinemia, repeat sampling at least twice for confirmation; discriminate between dyslipoproteinemia secondary to diseases, drugs, and diets, and primary and/or familial dyslipoproteinemia. Abbreviations used are: LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TC, total cholesterol; TG, triglyceride.

ies comparing family history triggered-high risk sampling and inclusive sampling are needed.

STEPWISE CHOLESTEROL-LOWERING INTERVENTION

Because diet- and drug-mediated reductions in total and LDL-C are efficacious in reducing coronary heart disease in adults,[20–25] stepwise intervention strategies based upon definitions of moderate, severe, and severe familial hypercholesterolemia should also be carefully considered for children.[1,7,9,10,26] Although most hypercholesterolemic children do not have monogenic familial hypercholesterolemia,[7–10] approximately 1 in 200 to 1 in 500 American children are heterozygous for familial hypercholesterolemia. They have a major gene for elevated LDL-C and a propensity toward sharply increased risk for premature coronary heart disease in adulthood.[6–10] Diet and bile acid-binding resins are effective in reducing total and LDL-C in children heterozygous for familial hypercholesterolemia (Table) and appear to be safe.[1,6–10,31] In our recent long-term (6 years) studies in 73 children heterozygous for familial hypercholesterolemia,[10,31] mean reductions in plasma total cholesterol (9.6% and 12.5% on diet and diet plus cholestyramine, respectively) were greater than those (4.9% and 8.5%) on diet alone and diet plus cholestyramine resin achieved during 7.4 years by hypercholesterolemic men in the Lipid Research Clinics Coronary Primary Prevention Trial.[20–22] Rigorous diet and bile acid-binding resin cholesterol-lowering regimens did not affect normal growth and development in the 73 children heterozygous for familial hypercholesterolemia[10,31] and lowered their total plasma cholesterol levels within ranges shown to have efficacy in reducing coronary heart disease events in hypercholesterolemic men.[20–22]

Pediatricians have historically been in the forefront of preventive medicine. The pediatric diagnosis and therapy of dyslipoproteinemia offers a unique opportunity to initiate and maintain safe and effective intervention to retard, regress, or prevent the development of the mature atherosclerotic plaque.[1,3–5,10,32] We have entered into a new era in which data-based[20–27] hopes for prevention of coronary heart disease have been raised and reinforced. Diagnosis and therapy of major coronary heart disease risk factors in childhood represent (even if following the narrow, high-risk strategy) a major

responsibility for physicians, nutritionists, and behaviorists but, at the same time, has extraordinary potential for the primary prevention of atherosclerosis. Not only was Wordsworth metaphorically visionary in this regard, ". . .the child is father of the man,"[2] but so was Milton,[33] ". . .the childhood shows the man, as morning shows the day."

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Screening for Anemia and Erythrocyte Disorders in Children

The American Academy of Pediatrics currently recommends that children should be screened for anemia during infancy, in early childhood, in late childhood, and again some time during adolescence. In this issue of *Pediatrics*, Young and co-workers[1] report their comparison of two different commonly used tests to screen for anemia. Specifically, they compared the sensitivity of the microhematocrit using capillary blood *v* electronically determined cell counts (ie, Coulter count) using venous blood. The authors conclude that the capillary blood microhematocrit test is an acceptable office screening test for anemia and very few children with low venous hemoglobin concentrations escape detection using this procedure.

The conclusions of Young and co-workers reported here seem quite reasonable. This report, however, does not address the issue that the electronic complete blood cell count also may provide useful information regarding RBC disorders not necessarily associated with anemia. For example, children heterozygous for β-thalassemia (ie, β-thalassemia trait) or α-thalassemia (ie, α-thalassemia trait) are not necessarily "anemic," although they manifest RBC microcytosis and an elevated RBC count relative to the hemoglobin concentration.[2] Because these children, as well as some of their family members, potentially could transmit a gene for a serious medical disorder, one might question whether children at risk for thalassemia trait (ie, those of Mediterranean ancestry, blacks, and orientals) should have a "screening" electronic cell count some time during childhood. In the case of both of these heterozygous disorders, the likelihood of carrying a thalassemic gene may be as high as 15% to 20% in certain ethnic groups.

Another example of an RBC abnormality that may not be associated with anemia is seen in children with hemoglobin E (hemoglobin E trait, homozygous hemoglobin E).[3,4] This hemoglobin variant, the third most common in the world, occurs primarily in Southeast Asia where its incidence in certain regions may be as high as 25%.[4] Until recently, hemoglobin E rarely was encountered in the United States. Now, however, with the immigration of large numbers of Southeast Asians, hemoglobin E abnormalities have become common in many pediatric clinics. By itself, hemoglobin E (heterozygous or homozygous) usually is of no major clinical significance, although the combination of hemoglobin E with β-thalassemia trait leads to a severe form of thalassemia. Just as for thalassemia trait, however, characteristic features of heterozygous or homozygous hemoglobin E are microcytic RBC and an elevated erythrocyte count for a given hemoglobin level.[3–5] The presence of hemoglobin E thus might first be suspected by the values observed on an electronic complete blood cell determination.

Screening for anemia is an essential component in the clinical evaluation of healthy children. In addition, however, we as pediatricians have the responsibility to identify genetic abnormalities that might be passed on to future generations. In the case of hereditary genetic RBC disorders, the large majority of nonanemic individuals with abnormal genes can be identified by simple, relatively inexpensive tests. Thus, the important questions are who to screen, how to screen, and when to screen.

Who to Screen? High-risk children include those of Mediterranean ancestry, Asians, and blacks.

How to Screen? A simple electronic complete blood cell count that includes a mean corpuscular volume determination will detect microcytosis and erythrocytosis, thereby identifying those children who might have thalassemia trait or hemoglobin E. (In the absence of iron deficiency, the specific RBC abnormality can be identified by hemoglobin electrophoresis and quantitative determinations of hemoglobin A_2 and fetal hemoglobin.)

When to Screen? This is a more controversial issue, although most physicians believe screening should be done when a child reaches maturity. Information provided at this time obviously will be useful to the child as a potential parent. In my opinion, however, screening also should be considered in early childhood (1 to 2 years of age) because familial RBC defects often are detected first in nonanemic healthy children. Thus, the identification of potential genetic abnormalities in young children may be critical if both parents carry an abnormal gene and, most importantly, if they anticipate having more children.

The views presented here are not meant to minimize the clinical utility of the microhematocrit in screening children for anemia. Rather, these comments are made to emphasize that electronic complete blood cell determinations provide a significant amount of information above and beyond whether a child is anemic. For this reason, I believe that

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