

## Should Family Physicians Routinely Screen for Hypercholesterolemia in Children?

For a summary of the NHLBI guidelines on cardiovascular risk reduction in children, see Practice Guidelines on page 776.

### Yes: The Evidence Supports Universal Screening

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Atherosclerotic cardiovascular disease events are the culmination of a process that has clearly been shown to begin in childhood, with accumulation of abnormal lipids in the vascular intima.<sup>1</sup> Autopsy studies demonstrate significant correlations between elevated levels of total cholesterol, low-density lipoprotein (LDL) cholesterol, and non-high-density lipoprotein (HDL) cholesterol and the extent of atherosclerosis in children, adolescents, and young adults.<sup>2,3</sup> For example, one study of 15- to 34-year-olds who died accidentally found that non-HDL cholesterol was the major correlate of coronary atherosclerosis, with a 30 mg per dL increase in non-HDL cholesterol equivalent to two years of vascular aging.<sup>3</sup> Equally important, absence of risk factors is associated with absence of advanced atherosclerotic lesions at autopsy, and very rare clinical events in natural history studies following individuals from childhood into middle age.<sup>2-5</sup>

In addition, childhood lipid levels correlate with lipid levels several decades later, although this correlation is much stronger with severe elevations and repeated elevated values.<sup>2,3</sup> National Heart, Lung, and Blood Institute (NHLBI) guidelines recommend using non-fasting non-HDL cholesterol measurements for screening, which makes testing more economical, practical, and acceptable to children and families. There is no evidence of harm from a child being



This is one in a series of pro/con editorials discussing controversial issues in family medicine.

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labeled as a result of abnormal lipid screening.<sup>6-8</sup> Previous guidelines recommend selective screening in children based on a positive family history of early cardiovascular disease or dyslipidemia,<sup>9</sup> but evidence shows that this will miss 30 to 50 percent of children with severe hypercholesterolemia.<sup>2,3,10</sup>

Cholesterol-lowering therapy has been shown to improve clinical outcomes in asymptomatic adults, with a meta-analysis demonstrating a 20 percent relative risk reduction of major vascular events for each 39 mg per dL (1 mmol per L) reduction in LDL cholesterol level.<sup>11</sup> In children with familial hypercholesterolemia and extreme cholesterol elevation from birth, clinical cardiovascular events begin in the teen years, with death often before 30 years of age.<sup>2,3</sup> Treatment with periodic apheresis and statins has delayed development of cardiovascular events and prolonged survival in these patients.<sup>12</sup> Familial hypercholesterolemia occurs in one out of 500 persons, with severe elevations in LDL cholesterol from infancy. Untreated, 50 percent of males with the disease have a clinical cardiovascular event by 50 years of age, and 5 percent of these events occur before 30 years of age. For these patients, statin therapy in adulthood has led to a significant increase in average age at first event.<sup>13</sup>

In children, a diet low in fat and saturated fat is safe and is modestly effective in lowering LDL cholesterol levels.<sup>2,3</sup> Eight randomized controlled trials showed that in patients eight to 18 years of age with

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elevated LDL cholesterol levels despite diet modification, statin therapy effectively reduced levels without adverse effects for up to 4.5 years.<sup>2,3</sup> The LDL cholesterol level for eligibility was at least 190 mg per dL (5 mmol per L), or at least 160 mg per dL (4 mmol per L) with at least two additional risk factors, with an LDL cholesterol goal of less than 130 mg per dL (3 mmol per L), the 95th percentile through adolescence; these are the same criteria used in the NHLBI guidelines. In adolescents with familial hypercholesterolemia, statin treatment has been shown to slow the progression of atherosclerosis.<sup>2,3</sup>

One concern with universal lipid screening in children is that medications would be indicated in many healthy children, especially those who are obese. Because the dyslipidemia of obesity is characterized by elevated triglyceride levels and reduced HDL cholesterol levels, with little increase in total or LDL cholesterol levels, large numbers of healthy children should not need medication.<sup>2,3</sup> According to National Health and Nutrition Examination Survey data from 1999 to 2006, less than 1 percent of the screened adolescents would be candidates for medication.<sup>14</sup>

Evidence is lacking on the long-term safety and effectiveness of cholesterol-lowering therapy in childhood, and on the cost of case finding. There are no randomized controlled trials of event reduction after screening in childhood because of ethical problems in withholding effective care in those with identified high-risk hypercholesterolemia, as well as the time, costs, and attrition involved. Findings from other kinds of studies can amplify the evidence, and these studies are a priority for further research.<sup>15</sup>

The evidence is clear: severe cholesterol elevation starting in early childhood is associated with cardiovascular disease, and therapy to lower LDL cholesterol is safe and effective in risk reduction. Because selective screening is ineffective, universal screening before puberty is the only way to identify children with extreme cholesterol abnormalities who will benefit most from treatment. Finally, childhood is an important time to optimize cardiovascular health because it is when health behaviors develop, risk factors manifest, and risk reduction will have the greatest impact.

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