

Lipid abnormalities in children: should we be doing more?

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Australia needs to develop its own guidelines based on local data

New guidelines for testing and treating lipid abnormalities in children have recently been published by the American Academy of Pediatrics and the American Heart Association (Box).^{1,2} These recommendations, made partly in response to the high prevalence of obesity in children in the United States, provoke consideration of whether they should also be adopted in Australia. The previous US recommendations,³ which targeted cholesterol testing to children with a family history of premature cardiovascular disease or high cholesterol levels, had focused on a population-based approach to treatment through a fat- and cholesterol-restricted diet. Drug therapy was reserved for children with more persistent and extreme elevations in cholesterol level. In contrast, the recent guidelines recommend that testing be broadened to include *all* overweight or obese children, with the first cholesterol assessment to be done between the ages of 2 and 10 years. The new guidelines further recommend that initiation of drug therapy be considered at a younger age (from 8 years) and with a lower low-density lipoprotein cholesterol (LDL-C) level target for children with multiple cardiovascular risk factors.

Indirect evidence suggests that childhood lipid abnormalities are important in the development of cardiovascular disease in adults. For example, autopsy studies indicate that atherosclerosis begins in the young and that the extent of lesions correlates with traditional cardiovascular risk factors, including lipid levels.⁴ However, advanced atherosclerosis rarely occurs in children and adolescents. Arterial wall thickness in adults, as assessed by carotid artery ultrasonography, is associated with childhood lipid levels, and children with lipid abnormalities display altered arterial structure and function.^{5,6} However, direct evidence for an association between childhood lipid levels and adult cardiovascular outcomes, such as myocardial infarction and stroke, is not available. Why, then, test children and adolescents at all? Would it be equally effective to test young adults?

One important potential rationale for cholesterol testing in children is that lipoprotein levels tend to track from childhood into adult life.^{7,8} Detection of lipid abnormalities in young children could prompt changes in diet and physical activity that would be required through the whole of life. It is important to note, however, that both universal and targeted lipid testing in children result in a high false-positive rate for adult dyslipidaemia.^{8,9} Moreover, the predictive value of childhood lipid levels depends on the threshold values used to define dyslipidaemia. Threshold values derived from populations of US children may not be sensitive to trends in childhood lipid levels and overweight and obesity in Australia.

The prevalence of childhood overweight and obesity is high and increasing in both Australia and the US.^{10,11} Moreover, in both countries, lipid abnormalities are common in overweight and obese children,^{12,13} with low high-density lipoprotein cholesterol (HDL-C) and high triglyceride levels particularly prevalent. Importantly, targeting overweight and obese children for LDL-C testing does not improve the specificity for detecting elevated LDL-C

Summary of recent changes to recommendations in the United States for cholesterol testing and treatment in children^{1,2}

- Stronger recommendations for cholesterol testing in children who have cardiovascular risk factors other than lipid abnormalities — particularly overweight and obesity, but also hypertension, cigarette smoking or diabetes.
- A stronger recommendation on the timing of initial cholesterol testing: between the ages of 2 and 10 years.
- A recommendation to consider commencing drug therapy in children aged over 8 years (rather than 10 years), with a target low-density lipoprotein cholesterol level of <3.3 mmol/L (rather than <4.1 mmol/L). ◆

levels in adults.⁸ Although most overweight and obese children with low HDL-C levels become adults with low HDL-C levels, targeting overweight and obese children for HDL-C testing will not identify the majority of adults with low HDL-C levels.⁸

Overweight and obese children, whether or not they have high triglyceride and low HDL-C levels, require weight management through changes in diet and physical activity levels. But it is uncertain, particularly in the case of young children, whether knowledge of their lipid status will lead to greater motivation to implement such changes. Improved diet and increased physical activity are both safe and effective ways of reducing cardiovascular risk factors in children, and should be promoted across the whole paediatric population.¹⁴⁻¹⁷ Most overweight and obese children could be encouraged to adopt these lifestyle changes without testing their lipid status. Testing for lipid abnormalities could be reserved for older, obese children (>10 years of age) in the context of an overall assessment of their risk for future cardiovascular disease.

Screening based on family history may be hampered by inaccurate or incomplete information and the need for adult family members to have their cholesterol levels measured. However, obtaining an accurate family history, combined with testing of adults to detect those with significant elevation in LDL-C levels, may help identify children with inherited dyslipidaemias (eg, familial hypercholesterolaemia). Such children have the highest risk of premature cardiovascular disease and may benefit most from drug therapy at a young age.

The new US recommendations also raise questions about which children should be considered for drug therapy for lipid abnormalities. A number of randomised clinical trials have demonstrated the short-term safety and efficacy of HMG-CoA reductase inhibitors (statins) in children.¹⁸ Statins are currently the first-line drug treatment for elevated cholesterol levels in children. However, there is a lack of evidence for their long-term safety, and animal studies have shown they may be toxic to the developing fetus.¹⁹ Although there have been no controlled epidemiological studies relating gestational exposure to statins with adverse human preg-

nancy outcomes, case reports of structural anomalies and the biological plausibility of a teratogenic effect mean that statins are contraindicated in pregnancy.²⁰

Thus, a case can be made for reserving statin therapy for older children at high risk of future cardiovascular disease. In girls, it may be appropriate to delay statin therapy until an age when discussions about reproduction and contraception can occur. A strong family history of premature cardiovascular disease or a rapid progression in surrogate measures of atherosclerosis (eg, carotid arterial wall thickness, measured by ultrasound) may lower the age threshold for statin therapy.

In Australia, we should be taking action to address the increasing prevalence of childhood cardiovascular risk factors. However, guidelines from the US may not be appropriate for Australian children, and it is imperative that we formulate new local recommendations based on recent local data. Guidelines for lipid assessment and management in Australia should also propose strategies for reducing cardiovascular risk factors in childhood more generally. This will require discussion and collaboration between clinicians, researchers, and governmental and non-governmental organisations, such as Diabetes Australia, the National Heart Foundation, the Paediatric Cardiac Council of the Cardiac Society of Australia and New Zealand, and the Royal Australasian College of Physicians.

In the interim, a careful assessment of the risk of future cardiovascular disease is required for *all* paediatric patients. This will be based on ascertainment of an accurate family history of premature cardiovascular disease, information on diet and physical activity, anthropometric and blood pressure measurements made at routine paediatric health checks, and the targeted assessment of blood lipid levels in older children with a family history of premature cardiovascular disease or hyperlipidaemia and/or multiple other cardiovascular risk factors, including obesity.

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