Lipid concentrations in children and adolescents: it is not all about obesity\textsuperscript{1,2}

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It has been known for some time that there is an association between adiposity and lipid and lipoprotein concentrations in both adults and children (1). Data from the Muscatine Study have shown that the strongest predictors of adult lipid and lipoprotein concentrations are the corresponding concentrations during childhood and increasing BMI, a surrogate measure for adiposity (2). The presence of obesity is one factor that has been recommended as a trigger for screening for lipid and lipoprotein abnormalities in children. Obesity is also one of the risk factors that may indicate a more aggressive approach to treatment of lipid abnormalities, including the use of pharmacologic treatment (3). However, it is a common experience in the clinical setting for parents or pediatricians to be surprised that a child with a normal BMI is found to have abnormal concentrations of lipids and lipoproteins, particularly of LDL cholesterol. This calls for a closer examination of the relation of adiposity to the specific components of the lipid profile and discussion of how obesity might be best used in clinical decision making about abnormal lipid concentrations.

It is important to recognize that adiposity is most strongly related to increased triglycerides and low HDL cholesterol. This is true in both children and adults. There is some relation between adiposity and LDL cholesterol, but it is substantially weaker. The presence of high triglycerides and low HDL cholesterol has been called atherogenic dyslipidemia and is frequently found in association with the metabolic syndrome, including increased central adiposity, increased insulin resistance, and elevated blood pressure (4). This combination of abnormalities has been found to be associated with increased risk of cardiovascular disease (CVD) in adults (5). These relations are also seen in children, and the clustering of risk factors as seen in the metabolic syndrome has been associated with increased burden of atherosclerosis in autopsy studies (6).

Historically, the focus of lipid screening in the pediatric age group has been to identify elevated LDL cholesterol as is seen in genetic disorders such as familial hypercholesterolemia, which results from genetic defects in the LDL receptor. This is because familial hypercholesterolemia in both its homozygous and heterozygous forms is associated with accelerated atherosclerosis. The heterozygous form of familial hypercholesterolemia is relatively common and occurs in 1 of 500 live births (7). Because genetic forms of hypercholesterolemia do not implicate a pathophysiology associated with alterations in energy balance or fuel partitioning, they typically are not associated with obesity.

So why would the presence of obesity be a useful trigger for lipid screening in the pediatric age range? First, it is known that the presence of other risk factors for CVD, along with lipid and lipoprotein abnormalities, creates a higher risk situation for the development of atherosclerosis (6). In the setting of obesity and elevated LDL cholesterol due to a genetic form of hypercholesterolemia, reducing the degree of adiposity may have only a limited effect on the concentration of LDL cholesterol but may have a substantial effect on the overall risk of CVD. However, even if the obesity is improved, if the LDL cholesterol remains quite high because of the genetic disorder that results in hypercholesterolemia, the patient may still need pharmacologic treatment to lower his or her LDL cholesterol. The second reason is that increased adiposity is associated with atherogenic dyslipidemia and the metabolic syndrome. Lipid screening may identify this lipid pattern. There is no specific treatment of metabolic syndrome, and when this constellation of risk factors is present, lifestyle intervention to reduce the level of obesity is key. It is important to note that one does not need to accomplish ideal body weight or amount of adiposity to achieve improvement in the lipid profile. Even a 5–10% improvement can result in substantial and clinically important changes (8). In the setting of metabolic syndrome and atherogenic dyslipidemia alone, LDL cholesterol may be slightly to moderately elevated, but aggressive treatment with pharmacologic agents is almost never required in pediatric patients.

In this issue of the Journal, Lamb et al (9) present important data from NHANES 1999–2004 that support these clinical concepts. The use of dual-energy X-ray absorptiometry to evaluate body adiposity more directly confirms previous results that used BMI, the measure that is most frequently and easily applied in the clinical setting. In this large population-based sample, they reaffirmed the relation between adiposity and elevated triglycerides and low HDL cholesterol among youth in the United States. They report a much weaker relation between adiposity and LDL cholesterol, with the prevalence of high LDL cholesterol differing by adiposity status only in non-Hispanic blacks. In addition, a much smaller proportion of the variance of LDL cholesterol

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First published online August 3, 2011; doi: 10.3945/ajcn.111.022483.
was explained by the percentage body fat in multiple regression analysis compared with total cholesterol, HDL cholesterol, and triglycerides.

The majority of youth with high adiposity do not have lipid abnormalities. The majority of youth with elevated LDL cholesterol as the result of genetic forms of hypercholesterolemia are not obese. Thus, thin or normal-weight children can still have increased CVD risk, and guidelines for screening offspring of parents with CVD or a history of dyslipidemia remain appropriate. We must use a more nuanced approach to the relation between adiposity and lipid concentrations in the clinical setting.

The author has served as a consultant for Merck, Schering-Plough.

REFERENCES


