Pediatric Lipid Management

An Earlier Approach

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KEYWORDS

• Pediatrics • Lipids • Atherosclerosis • Dyslipidemia

KEY POINTS

- Numerous long-term observational cohort studies show that subclinical atherosclerosis is a progressive disease that arises in childhood and continues through the adulthood.
- Deficiencies in targeted lipid screening to identify high-risk individuals led the 2011 National Heart, Lung and Blood Institute Expert Panel for Pediatric Cardiovascular Disease (CVD) Risk Reduction to recommend universal screening.
- Amid concerns that extended screening may induce inappropriate treatment, pharmacotherapy is restricted to patients with genetic dyslipidemias and multiple high-risk CVD factors.
- This article summarizes the current guidelines, enumerates challenges to the guidelines, and suggests future directions.

INTRODUCTION

Although adult cardiovascular disease (CVD) mortality has been curtailed primarily from improvements in atherosclerotic risk factor treatment, an alarming countervailing trend dominates the present and future of CVD: obesity, obesity-related dyslipidemia, and type 2 diabetes.[1–6] Children offer a prime opportunity to continue CVD risk factor reduction and address emerging trends, especially dyslipidemia.

There are 4 general classes of pediatric dyslipidemias:

- Medication-related dyslipidemia
- Dyslipidemia related to lifestyle factors

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- Genetic dyslipidemia
- Dyslipidemia secondary to a medical condition.

There are 3 chief genetic dyslipidemias (Table 1).

- Familial hypercholesterolemia (FH). FH is an autosomal dominant disorder that interferes with either apolipoprotein B (ApoB) assembly or the receptor-mediated clearance of low-density lipoprotein cholesterol (LDL-C) in roughly 1 in 500 persons with heterozygosity or 1 in a million homozygotes.[7–10] However, homozygotes frequently develop xanthelasmas of the canthi, xanthomas on the extensor surfaces of limb joints, arcus senilis of the eye, and internal consequences, including myocardial infarction and ischemic cardiomyopathy, often in the first 2 decades of life. The heterozygous phenotype predisposes to early atherosclerosis and is more common than, and as treatable as, any disorder within national newborn screening programs.
- Familial combined hyperlipidemia. Familial combined hyperlipidemia is another genetic dyslipidemia with high LDL-C and triglycerides (TGs), but lacks the degree of TG increase necessary to trigger pancreatitis. It confers CVD risks nearly as high as FH and may be as prevalent as 1% of the population.[11,12]
- Familial severe hypertriglyceridemia (HTG). Although 1 in 600 individuals have severe HTG (defined as TG>10 mmol/L or 885 mg/dL),[13] much of this is caused by environment and lifestyle. Genetic or familial HTG has many implicated genes, but the most common is homozygous autosomal recessive loss of function mutations in lipoprotein lipase or apolipoprotein C2 and occurs in 1 in 1×10^5 individuals.[13,14] Hindered degradation of TG leads to significantly increased serum TG.[15,16] At levels of more than 1000 mg/dL, the risk of acutely life-threatening pancreatitis increases. However, risk stratification by TG level is inadequate because many lipid providers follow persons with TG greater than 2000 mg/dL who have never had pancreatitis. Despite this uncertainty, prompt treatment is recommended.[17]

Suggested responses to pediatric dyslipidemias include, but are not limited to, removing a causative agent, lifestyle modification, treating an underlying medical condition, and in severe cases pharmacotherapy. Each of these therapeutic maneuvers is intended to accomplish 2 important goals: preventing acute pancreatitis in individuals with very increased TGs levels and preventing atherosclerotic CVD later in life.

Table 1
Prominent genetic dyslipidemias in children

Dyslipidemia	Abnormal Lipid Fraction	Prevalence Estimate	Predominant Mechanism
Familial hypercholesterolemia	High LDL-C	Heterozygotes, 1 in 500 Homozygotes, 1 in million	Decreased LDL-C clearance
Familial combined hypercholesterolemia	High LDL-C and high triglycerides/ VLDL	1 in 100[11]	Increased ApoB production
Familial severe hypertriglyceridemia	High triglycerides/ VLDL	1 in 100,000[13]	Decreased triglyceride/ VLDL degradation

Abbreviations: ApoB, apolipoprotein B; LDL-C, low-density lipoprotein cholesterol; VLDL, very low-density lipoprotein.