

Dyslipidemia and obesity

History:

A 13-year-old girl is seen for a routine clinic follow-up visit. She has been previously healthy, but her growth curve shows increasing body mass index (BMI) percentiles throughout her childhood. At her present visit, her BMI is 34.7, above the 99th percentile. She participates in physical education at school 1 day per week but does not participate in any organized sports. She rarely eats breakfast. She had menarche last year.

Both parents are obese. There is no known family history of early cardiovascular disease. The mother is taking a medication for hypertension. She is unaware whether any family members have hypercholesterolemia.

Physical examination:

Height 164 cm (65th percentile), weight 98 kg (>95th percentile), BMI 36.4 (>99th percentile), blood pressure 136/76. No enlargement of the thyroid gland. Acanthosis nigricans on the posterior neck. Significant abdominal obesity.

Laboratory studies:

Lipid profile: Total cholesterol: 185 mg/dL

- Triglycerides: 169 mg/dL
- HDL cholesterol: 34 mg/dL
- LDL cholesterol: 122 mg/dL

Glucose: 92 mg/dL

ALT/AST: Normal

TSH: Normal

Questions:

1. Which of the following is the most likely cause of her dyslipidemia?

- a. Heterozygous familial hypercholesterolemia.
- b. Familial hypertriglyceridemia.
- c. Familial lipoprotein lipase deficiency.
- d. Dyslipidemia secondary to exogenous obesity.

Answer: d. Dyslipidemia secondary to exogenous obesity.

Discussion: For children between 2 and 19 years of age, obesity is defined as a BMI ≥ 95 th percentile for children of the same age and sex. Nineteen percent of children 6 to 19 years of age have a BMI >95 th percentile (based on 1963–1994 norms). The increasing prevalence of obesity in childhood is associated with increasing rates of pediatric hypertension, dyslipidemia and type 2 diabetes. Obesity in childhood is associated with increased evidence of atherosclerosis at autopsy and of subclinical measures of atherosclerosis on vascular imaging. Studies estimate that 80 percent of overweight adolescents become obese adults. Thus, the effect of the current pediatric obesity epidemic on future cardiovascular disease and type 2 diabetes is a major public health concern.

The typical dyslipidemic pattern seen in obesity is a mixed pattern of moderate to severe elevation in triglyceride level, normal to mild elevation in LDL level and a low HDL cholesterol level, the pattern seen in this case. Heterozygous familial hypercholesterolemia is a genetic disorder associated with markedly elevated LDL and total cholesterol levels; thus, option (a) is not correct. Familial hypertriglyceridemia is an autosomal dominant disorder that results in moderate to markedly elevated triglyceride levels and low to normal LDL and HDL cholesterol; therefore, option (b) is not correct. Lipoprotein lipase deficiency is a rare genetic disorder resulting in increased triglyceride levels. In the heterozygous state, patients have triglyceride levels ranging from 200 to 750 mg/dL. In the homozygous state, triglyceride levels can reach 10,000 mg/dL or higher.

2. What is the most appropriate initial treatment for her dyslipidemia?

- a. Initiate statin therapy.
- b. Recommend therapeutic lifestyle modifications focused on diet and physical activity.
- c. Initiate omega-3 fatty acid 2000 mg daily.
- d. Recheck fasting lipid panel in 12 months.

Answer: b. Recommend therapeutic lifestyle modifications focused on diet and physical activity.

Discussion: Age-specific treatment recommendations for children with abnormal lipid panels were included in the 2011 Summary Report of the Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents. The first step recommended in the management of children with dyslipidemias is a focused intervention on diet and physical activity. The Cardiovascular Health Integrated Lifestyle Diet (CHILD-1) is recommended for all children who are overweight or obese and have dyslipidemia, hypertension and other high-risk medical conditions.

This patient's triglyceride level is in the high range for children 10 to 19 years of age. The HDL level is in the low range. The LDL and total cholesterol levels are in the borderline- high range, but not in a range in which medical therapy would be indicated. If the patient's cholesterol pattern has not changed after a 3-month trial of the CHILD-1 diet, then a lipid parameter-specific diet is recommended. In this setting of triglyceride elevation and obesity, the CHILD-2-TG diet is the recommended diet. This diet is characterized by: 1) limit 25–30 percent of calories from fat, ≤ 7 percent from saturated fat, <200 mg/day of cholesterol and avoidance of trans fats, 2) decrease sugar intake by replacing simple with complex carbohydrate and no sugar-sweetened beverages and 3) increase dietary fish to increase omega-3 fatty acids.

3. Which of the following statements is most accurate regarding elevated triglyceride levels in children?

- a. Severely elevated triglyceride levels can cause pancreatitis.
- b. Fibric acid derivatives are recommended for triglyceride levels >150 mg/dL.
- c. Omega-3 fish oil can cause elevation of glucose levels.
- d. Omega-3 fish oil is FDA approved for the indication of hypertriglyceridemia in children.

Answer: a. Severely elevated triglyceride levels can cause pancreatitis.

Discussion: Patients are at risk for pancreatitis when triglyceride levels exceed 500 mg/dL. Several studies in adults have found hypertriglyceridemia to be an independent risk factor for coronary artery disease.

In adults, use of omega-3 fish oil has been shown to lower the triglyceride level by 30– 40 percent. The medical evidence is more limited in children. According to the expert panel, in children with a high fasting triglyceride level, the CHILD-2-TG diet should be implemented under the guidance of a registered dietician. If the fasting triglyceride level is ≥ 200 –499 mg/dL after 6 months of lifestyle management, omega-3 fish oil supplementation can be considered, although it is only FDA approved for this indication in adults. Adverse effects of omega-3 fish oil include occasional gastrointestinal complaints, fishy smelling breath or burp and increased bleeding time, but adverse effects on glucose levels have not been reported.

Key points:

1. The prevalence of pediatric obesity has risen dramatically over the past 30 years, and there has been a concomitant increase in the prevalence of pediatric dyslipidemia.
2. Obesity is strongly correlated with atherosclerosis and future risk of cardiovascular disease. The typical dyslipidemic pattern seen in obesity is a mixed pattern of moderate to severe elevation in triglyceride level, normal to mild elevations in LDL and total cholesterol level and a low HDL cholesterol level.
2. The first step recommended in managing lipid abnormalities in children (other than an LDL cholesterol level of ≥ 250 mg/dL or triglyceride level of > 500 mg/dL) is a focused intervention regarding diet and physical activity.

References/suggested reading:

1. Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents: Summary Report. *Pediatrics*. 2011 Dec; 128 Suppl 5:S213–56.
2. Freemark, M. Pathogenesis and Management of Dyslipidemia in Obese Children. *Pediatric Obesity*; 2010, 175–199.
3. Halfon N, Verhoef PA, Kuo AA. Childhood Antecedents to Adult Cardiovascular Disease. *Pediatrics in Review*. 2012 Feb;33(2):51–61.
4. Manlhiot C, et al. Spectrum and Management of Hypertriglyceridemia Among Children in Clinical Practice. *Pediatrics*. 2009 Feb;123(2):458–65.