Detecting and Managing Hyperlipidemia in children

DR fariba ghasemi
pediatric Endocrinologist and metabolism

1-Why screen for high cholesterol?

2- Who should we screen?

3- How should we screen?

4-what`s abnormal?

5-what do we do with an elevated lipid level?

6-when do pediatricians use medicating?

7-what is the goal of treatment ?

SPECIAL FEATURE

Clinical Review

Update on Screening, Etiology, and Treatment of Dyslipidemia in Children

Vaneeta Bamba

Division of Endocrinology and Diabetes, The Children's Hospital of Philadelphia and The Perelman School of Medicine at the University of Pennsylvania, Philadelphia, Pennsylvania 19104

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Why screen for high cholesterol?

- Cardiovascular disease (CVD) is a primary cause of adult morbidity and mortality; pathological studies have demonstrated that this process begins with aortic fatty streaks in the second decade of life.
- Longitudinal epidemiological studies have demonstrated that dyslipidemia, obesity, and other risk factors in childhood predict adult CVD. Importantly, normalization of childhood risk factors can decrease or even eliminate adult risks

Why screen for high cholesterol?

- These principles form the basis of pediatric cholesterol screening guidelines. In 2011, the National Heart, Lung, and Blood Institute (NHLBI), backed by the American Academy of Pediatrics,issued integrated recommendations for cardiovascular (CV) risk reduction, including guidelines for management of hypertension, obesity, and hyperlipidemia

Why screen for high cholesterol?

- **The primary goal of universal screening is:**

to identify those with familial hypercholesterolemia (FH), a condition without identifiable risk factors except family history. It has been shown that family history is incomplete in young individuals because parents and even grandparents maybe too young to have demonstrated early CVD. One study showed that 1.2% of children with family history vs 1.7% of children without qualified for pharmacotherapy for dyslipidemia

- **The second goal of universal screening is:**

to use non-HDL-C to identify children with components of metabolic syndrome in an effort to highlight and prevent progression of additional components.

- These are two key pediatric populations that benefit from early recognition and management of cholesterol abnormalities.

Contraversial Aspect of screening Recommendation

- There are several practical critiques:
  - First, the guidelines do not adequately define the risk-to-benefit ratio, particularly regarding moderate dyslipidemia .
  - Mild to moderate dyslipidemia may not persist into adulthood, and unnecessary therapy may have adverse effects.
  - Although statin therapy has been proven safe and effective in adults, there is a paucity of long-term pediatric data on statin therapy.
  - Statin trials have primarily included children with known high-risk disease such as FH, and studies have been limited in duration.

Controversial Aspect of screening

- Second, screening may potentially lead to anxiety in patients and families because of multiple blood draws,the lable of a choronic medical condition,the stress of undergoing lifestyle and behavior modification,and possible contributionto eating disorders.
- Lastly, there is consideration of financial costs, which include repeated lipid measurements, additional medical visits, and intervention with counseling, nutrition referrals, and medications

Why screen for high cholesterol?

in The Netherlands demonstrates that newly identified individuals gain 3.3 years of life. For every 100 people treated, 26 myocardial infarcts were prevented, and there was an average lifetime cost of $8700 per year gained .The modifiable outcome of metabolic syndrome is diabetes. One group estimates that lifetime direct costs of type 2 diabetes mellitus (T2DM) in those diagnosed at ages 25–44 years are between $124 000 and $130 000

Therefore, economic considerations are relevant, and we need additional studies to properly project estimates of pediatric universal screening, evaluation, and treatment.

Review Article

Pediatric Dyslipidemia: Recommendations for Clinical Management

Don P. Wilson, MD, Catherine McNeal, MD, PhD, and Piers Blackett, MB, ChB

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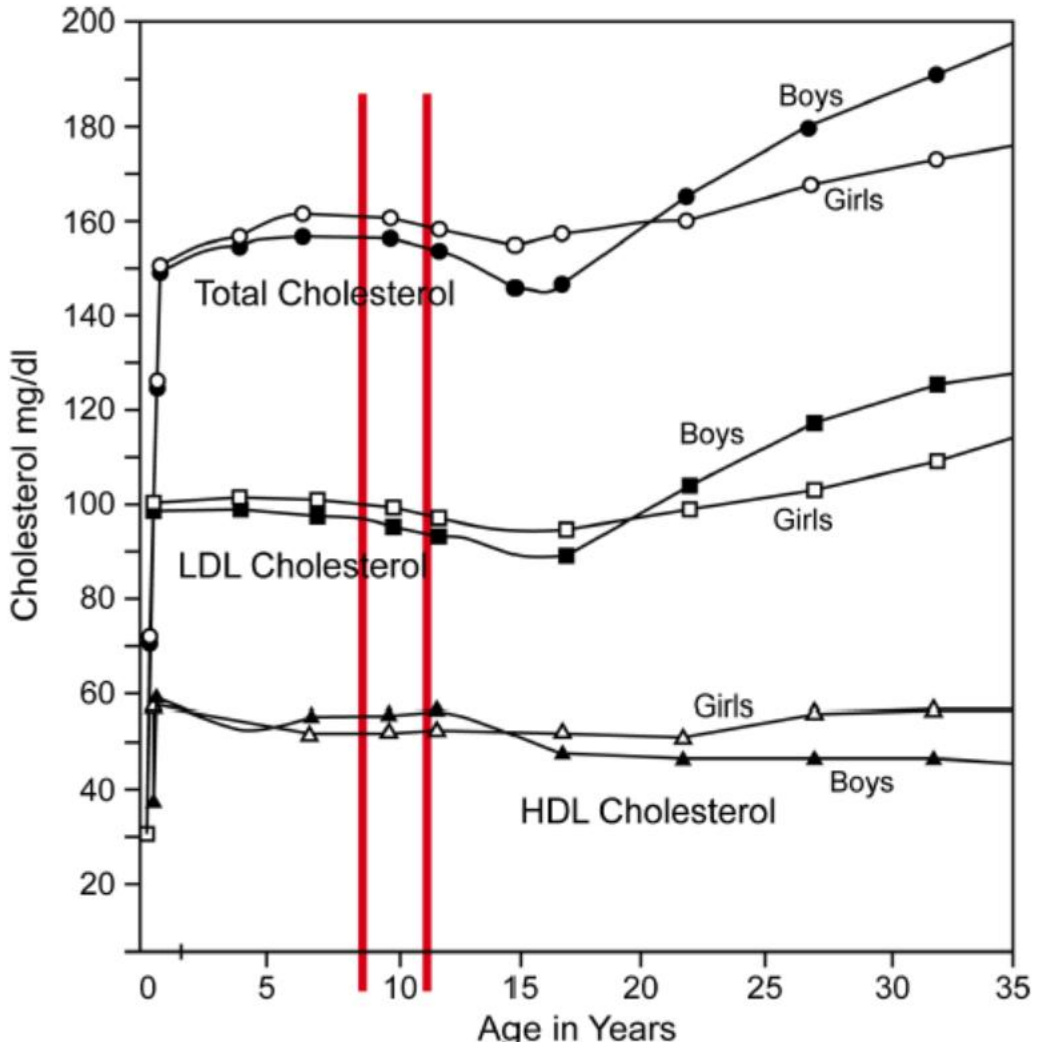
Who should we screen?



Who should we screen?

Two categories of screening have been identified.

- The first:
  - targeted screening, is recommended in any child older than 2 years in whom one or both parents are known to have hypercholesterolemia or are receiving lipid-lowering medications,
  - who have a family history of premature CVD (men younger than 55 years old, women younger than age 65)
  - whose family history is unknown (eg, adopted children),
  - who have a moderate to high risk for premature CVD
- The second category, universal screening, is recommended for:
  - all children 9 to 11 years old, regardless of general health or the presence/absence of CVD risk factors.
  - Screening should be repeated between 17 and 21 years of age.

Who should we screen?

Criteria	Moderate risk	High risk
BMI	≥95th–96th percentile	≥97th percentile
Hypertension	HBP without treatment	HBP with treatment
Cigarette smoking	—	Current smoker
HDL-C	<40 mg/dL	—
Predisposing medical conditions	Kawasaki disease with regressed coronary aneurysms	Kawasaki disease with current coronary aneurysms
	Chronic inflammatory diseases[a]	Types 1 and 2 diabetes mellitus
	HIV infection	Postorthotopic heart transplant
	Nephrotic syndrome	Chronic renal discharge/end-stage renal disease/postrenal transplant

- Screening recommendations

- **Birth-2 years**
  - No lipid screening
- **Ages 2-8 years**
  - Screen high-risk children (family history, diabetes, hypertension, or obesity)
- **Ages 9-11 years**
  - Universal screening
- **Ages 12-16 years**
  - No routine screening
- **Ages 17-21 years**
  - Universal screening should be repeated once

How should we screen?

- Either a fasting or non-fasting lipid panel can be used for screening. If the individual is fasting, a standard lipid panel can be used (TC, triglycerides, HDL-C, LDL-C). If the individual is not fasting, a non-HDL-C (TC-HDL-C) is recommended for the initial screening test because it is not affected by food or beverages, which often raise triglyceride or triglyceride dependent values such as a calculated LDL-C. Significant elevations in triglycerides (eg, > 400 mg/dL) preclude calculation of the LDL-C using the Friedewald equation (TC-triglyceride/5 + HDL-C), commonly used by most commercial laboratories.
- Ingestion of food or beverages has a minimal effect on directly measured LDL-C and the calculated non-HDL-C. If the non-HDL-C is > 145 mg/dL, two fasting lipid profiles should be obtained and the results averaged before determining the most appropriate intervention.

How should we screen?

- Children should be on their regular diet for 4-6 weeks before lipid testing
- TG and lipid profile measurement should follow an overnight fast of least 8 hours, preferably 12-14 hours.
- Recent severe illness (hospitalization within the last 4-6wk) is a contraindication to lipid testing
- LPs are negative acute phase reactants and their concentrations decline within 24 hr of severe acute stress.
- Standing TC levels are 8-12% higher than recumbent value

2015

Pediatric Lipid Screening Guidelines: Information for Patients and Families

Erin R. Pichiotino, MPH
UVM College of Medicine

What's abnormal?

	Goal	Borderline	High+ (Low for HDL)
Total Cholesterol	<170 (0-19yrs) <190 (20-24yrs)	170-199 (0-19yrs) 190-224 (20-24yrs)	≥200 (0-19yrs) ≥225 (20-24yrs)
LDL-C	<110 (0-19yrs) <120 (20-24yrs)	110-129 (0-19yrs) 120-159 (20-24yrs)	≥130 (0-19yrs) ≥160 (0-24yrs)
Non-HDL-C	<120 (0-19yrs) <150 (20-24yrs)	120-144 (0-19yrs) 150-189 (0-24yrs)	≥145 (0-19yrs) ≥190 (20-24yrs)
HDL-C	>45 (0-19yrs) >45 (20-24yrs)	40-45 (0-19yrs) 40-44 (20-24yrs)	<40 (0-19yrs) <40 (20-24yrs)
Trigs	<75 (0-9yrs) <90 (10-19yrs) <115 (20-24yrs)	75-99 (0-9yr) 90-129 (10-19yrs) 115-149 (20-24yrs)	≥100 (0-9yr) ≥130 (10-19yr) ≥150 (20-24yrs)

what do we do with an elevated lipid level?

Non-pharmacologic therapy

a. Diet

- Cardiovascular Health Integrated Lifestyle Diet
- CHILD 1
  - First stage in dietary change for children with identified dyslipidemia, overweight and obesity, risk factor clustering, and high risk medical conditions
  - Recommended diet for children with a positive family history of early CV disease, dyslipidemia, obesity, primary, hypertension, diabetes, or children exposed to smoking
  - Breast feeding recommended until age 6 months
  - Limit drinks to 100% fruit juice for age 6-12 months
  - 2% fat-free milk age 12-14 months
  - Avoid trans fat
  - 25% to 30% of calories from fat
  - ≤7% of calories from saturated fat

- CHILD 2-LDL
  - For elevated LDL-C
  - 25-30% calories from fat
  - ≤7% of calories from saturated fat
  - ~10% from monounsaturated fat
  - <200 mg/day of cholesterol
  - Avoid trans-fat as much as possible
  - Plant sterol esters and/or plant stanol esters up 2 g/day can be used after age 2
  - Water-soluble fiber psyllium can be added to diet as an enriched cereal
  - 1 hour/day of moderate-to-vigorous activity
  - <2 hours/day of sedentary screen time

- CHILD 2-LDL
  - For elevated LDL-C
  - 25-30% calories from fat
  - ≤7% of calories from saturated fat
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  - Water-soluble fiber psyllium can be added to diet as an enriched cereal
  - 1 hour/day of moderate-to-vigorous activity
  - <2 hours/day of sedentary screen time

- CHILD 2-TG
  - For elevated triglycerides
  - 25-30% of calories from fat
  - ≤7% of calories from saturated fat
  - ~10% from monounsaturated fat
  - < 200mg/day of cholesterol
  - Decrease sugar intake
    - Replace simple with complex carbohydrates
    - No sugar sweetened beverages
    - Increase dietary fish to increase omega-three fatty acids

b. Weight management

- Increase fiber
- Increased physical activity- moderate to vigorous physical activity for one hour each day
- Limit screen time (television, computer, video games) <2 hours a day

when do pediatricians use medicatin?

- If lifestyle changes over 6–12 months are inadequate to achieve target LDL-C levels, medication may be indicated in children above the age of 10 years

when do pediatricians use medicatin?

Elevation in LDL-C
- LDL-C ≥190 mg/dL
  - Lifestyle changes × 6 mo (may be abbreviated)
  - Consider statin therapy after age >10 y or after Tanner 2 in boys, post menarche in girls
- LDL-C ≥130–189 mg/dL with no family history or risk factors/Conditions
  - Lifestyle changes
  - Reassess every 6–12 mo
- LDL-C ≥160–189 mg/dL with family history or 1 high-level risk factor/condition or ≥2 moderate-level risk factors/ conditions
  - Lifestyle changes × 6–12 mo
  - Consider statin therapy after age >10 y or after Tanner 2 in boys, post menarche in girls
- LDL-C ≥130–159 mg/dL with clinical CVD or 2 high-level risk factors/conditions or (1 high-level risk factor/condition and 2 moderate-level risk factors/conditions)
  - Lifestyle changes × 6–12 mo
  - Consider statin therapy after age >10 y or after Tanner 2 in boys, postmenarche in girls

when do pediatricians use medicatin?

Elevation in TGs
- TGs ≥500 mg/dL
  - Lifestyle changes[a]
  - Counsel on risk of pancreatitis
  - Referral to lipid specialist
  - Fish oil, fibrate/other medication
- TG >200–499 mg/dL
  - Lifestyle changes[a] 6–12 mo
  - Consider omega-3 fish oil therapy
  - Consider referral to lipid specialist, especially if LDL-C target achieved
- TG ≥100–200 mg/dL (<10 y) or ≥130–200 mg/dL (>10 y)
  - Lifestyle changes[a] 6–12 mo
  - Increase dietary fish content
  - Fasting lipid panel every 6 mo
- TG <100 mg/dL (<10 y) or <130 mg/dL (>10 y)
  - Continue lifestyle changes[a]
  - Fasting lipid panel annually

when do pediatricians use medicatin?

- In youth, statins should be started at the lowest dose with baseline measurements of alanine aminotransferase, aspartate aminotransferase, and creatinine kinase performed.
- These levels plus a fasting lipid profile should be repeated 4 and 8 weeks after initiation of therapy, and then every 3–6 months
  - If liver enzymes are above three times the upper limit of normal
  - if creatinine kinase is above 10 times the upper limit of normal,
  - if the patient reports any adverse effects,

medication should be stopped to determine whether there is improvement. Importantly, statins may be teratogenic, so females should be counseled and prescribed contraceptive therapy when indicated.

when do pediatricians use medicatin?

- Treatment of hypertriglyceridemia is primarily driven toward lifestyle changes Historically the influence of hypertriglyceridemia on atherosclerotic lesions has been less clear. Only recently has there been evidence that TG elevations may predispose to atherosclerosis and CVD independent of metabolic risks
- For severe hypertriglyceridemia, pharmacological therapy is limited and treatment should be guided by a lipid specialist. Although omega-3 fatty acids in the form of docosahexaenoic acid and eicosapentaenoic acid at 2–4 g daily have been shown in adults to lower TG by 20–30%, prescription forms of mega-3 fatty acids are not currently FDA-approved for children.

when do pediatricians use medicatin?

Fibrates and niacin lower TG levels via modulations of LPL and thus may be largely ineffective in those with defective LPL activity. Orlistat, a pancreatic lipase inhibitor, was combined with a very low-fat diet in two siblings with compound heterozygous mutations in LPL. Three years of treatment led to a reduction of fasting TG below 600 mg/dL, and recurrent pancreatitis had all but resolved.

Novel treatment for inherited defects of LPL via gene therapy has been approved in Europe. Alipogene tiparvovec contains a gain-of-function LPL variant, and short term trials show improved postprandial chylomicron metabolism and metabolic parameters

what is the goal of treatment ?

- Target LDL-C is typically below 130 mg/dL, but it is ideally under 100 mg/dL in high-risk populations such as FH patients.
- If target levels are not achieved within 3 months, the dose can be incrementally increased to maximum dose. Occasionally, a second agent such as a bile acid sequestrant maybe useful . Multiple drug therapy should be guided by a lipid specialist.

Thank You for Your Attention