Dyslipidemia in Obese Children

Julia Steinberger, MD, MS
Professor of Pediatrics
University of Minnesota Amplatz Children’s Hospital
I have no relevant financial relationships with the manufacturers(s) of any commercial products(s) and/or provider of commercial services discussed in this CME activity. I do not intend to discuss an unapproved/investigative use of a commercial product/device in my presentation.
Objectives

- Understand screening and treatment recommendations for pediatric dyslipidemia
- Become familiar with the most recent pediatric lipid screening guidelines (NHLBI, 2011)
- Learn about screening practices in Minnesota
Leading Causes of Death for Males and Females in U.S., 2010

Centers for Disease Control and Prevention
Obesity

- A major increase in the prevalence of obesity has led to a large population of children with dyslipidemia, metabolic syndrome and type 2 diabetes.

- As these risk factors track into adulthood, they may soon burgeon into an epidemic of premature CVD.
Trends in the prevalence of obesity among US children and adolescents by age and survey year


©2013 American Heart Association, Inc. All rights reserved.
Go AS et al. Published online in Circulation Dec. 18, 2013
**Cholesterol levels - coronary heart disease**

In **adults**: reduction of blood cholesterol - reduction in CHD

In **children**: no long term studies, the relationship must be inferred from less direct evidence:

1. Compared with other countries US children and adolescents have higher blood cholesterol and higher intakes of saturated fat, and US adults have higher rates of CHD.

2. Early coronary atherosclerosis begins in childhood and is related to high cholesterol (autopsy)

3. Children with high cholesterol (LDL-C) often come from families with high incidence of adult CHD.

4. The current predominant dyslipidemic pattern in childhood is the combined pattern associated with obesity. Moderate-to-severe elevation in TG, normal-to-mild elevation in LDL cholesterol, and a reduced HDL.
The Effects of Multiple Risk Factors on the Extent of Atherosclerosis in the Aorta and Coronary Arteries in Children and Young Adults

Intimal - Surface Involvement (%)

P=0.01

P=0.01

P=0.003

Aorta

Coronary Arteries

Fatty Streaks

Coronary Arteries

Fibrous Plaques

Screening Recommendations

NCEP 1991: Selectively screen children and adolescents with:
- Family history of premature CVD or at least one parent with high cholesterol (≥240 mg/dL), or
- High risk for CHD (due to smoking, HTN, high fat diet, overweight) (may be tested at the discretion of their physician)
- No age indicated

AAP 2008: Same as NCEP:
- Testing for high risk children is now “recommended” and includes diabetes mellitus. First screening is recommended (for high risk children) between ages 2 and 10

NHLBI 2011: Universal screening:
- Timing based on age
Screening Recommendations, NHLBI

- Birth – 2y: No lipid screening

- 2- 8y: No routine lipid screening, unless risk factors present

- 9-11y: Universal screening

- 12-16y: No routine screening, unless new knowledge of risk factors present

- 17-21y: Universal screening, if not previously done
### Plasma Lipid, Lipoprotein, and Apolipoprotein Concentrations for Children and Adolescents

NCEP 1991, NHLBI 2011*

<table>
<thead>
<tr>
<th>Category</th>
<th>Low</th>
<th>Acceptable</th>
<th>Borderline-High</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC</td>
<td>&lt;170</td>
<td>170-199</td>
<td>≥200</td>
<td></td>
</tr>
<tr>
<td>LDL Chol</td>
<td>&lt;110</td>
<td>110-129</td>
<td>≥130</td>
<td></td>
</tr>
<tr>
<td>Non-HDL Chol</td>
<td>&lt;120</td>
<td>120-144</td>
<td>≥145</td>
<td></td>
</tr>
<tr>
<td>Apolipoprotein B</td>
<td>&lt;90</td>
<td>90-109</td>
<td>≥110</td>
<td></td>
</tr>
<tr>
<td>Triglycerides</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-9y</td>
<td>&lt;75</td>
<td>75-99</td>
<td>≥100</td>
<td></td>
</tr>
<tr>
<td>10-19y</td>
<td>&lt;90</td>
<td>90-129</td>
<td>≥130</td>
<td></td>
</tr>
<tr>
<td>HDL Chol</td>
<td>&lt;40</td>
<td>&gt;45</td>
<td>40-45</td>
<td></td>
</tr>
<tr>
<td>Apolipoprotein A-1</td>
<td>&lt;115</td>
<td>&gt;120</td>
<td>115-120</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Phenotypes</th>
<th>Mode of Inheritance</th>
<th>Frequency in Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exogenous hypertriglyceridemia</td>
<td>I</td>
<td>Auto Recessive</td>
<td>Very Rare</td>
</tr>
<tr>
<td>Familial hypercholesterolemia</td>
<td>IIA, IIB</td>
<td>Auto Dominant</td>
<td>0.5% (1 in 500)</td>
</tr>
<tr>
<td>Familial hypertriglyceridemia</td>
<td>IV, V</td>
<td>Auto Dominant</td>
<td>0.2-0.3%</td>
</tr>
<tr>
<td>Familial combined hyperlipidemia</td>
<td>IIA, IIB, IV, V</td>
<td>Auto Dominant</td>
<td>0.03-0.5%</td>
</tr>
<tr>
<td>Polygenic hypercholesterolemia</td>
<td>IIA, IIB</td>
<td>Polygenic</td>
<td>?</td>
</tr>
<tr>
<td>Broad B disease (dysbetalipoproteinemia)</td>
<td>III, IV</td>
<td>Auto Dominant</td>
<td>Rare</td>
</tr>
</tbody>
</table>
A Changed Focus

- NCEP guidelines: focused on identification of children with elevated LDL cholesterol

- NHLBI guidelines: focus on a combined pattern associated with obesity
  - moderate-to-severe elevation in TG
  - normal-to-mild elevation in LDL
  - reduced HDL
Highlights of NHLBI Guidelines

- Age-specific recommendations for screening and assessment
  - Universal lipid screening

- Non-HDL cholesterol used as a predictor of atherosclerosis
  - Can be non-fasting

- Measurement of lipoprotein subclasses and their sizes not clinically useful in children
## Atherosclerosis: Dyslipidemia

<table>
<thead>
<tr>
<th>Treatments</th>
<th>Effects/Actions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diet</td>
<td>Low saturated fat, low cholesterol (decrease LDL)</td>
</tr>
<tr>
<td>Exercise</td>
<td>Increase HDL</td>
</tr>
<tr>
<td>Resins</td>
<td>Decrease TC and LDL</td>
</tr>
<tr>
<td>HMG CoA reductase inhibitors</td>
<td>Decrease TC and LDL, increase HDL</td>
</tr>
<tr>
<td>Fibric acid</td>
<td>Decrease TG</td>
</tr>
<tr>
<td>Cholesterol absorption inhibitors</td>
<td>Decrease LDL</td>
</tr>
</tbody>
</table>
Evidence – Based Recommendations for Dietary Management (CHILD-1)

- Diet rich in fruits, vegetables, whole grains, and low fat/fat-free milk and milk products and lower in sugar

- Encourage dietary fiber from foods: age + 5 g/day

- 25-30% calories from fat, 8-10% from saturated fat, up to 20% mono and poly unsaturated fat; <300 mg/day of cholesterol, avoid trans fat

- Limit/avoid sugar-sweetened beverages

- Limit natural juices to 4 fl oz per day
Evidence – Based Recommendations for Dietary Management (CHILD-2-LDL)

Elevated LDL Cholesterol:

• Refer to a registered dietitian

• 25-30% calories from fat, <7% from saturated fat, 10% from mono unsaturated fat; <200 mg/day cholesterol, avoid trans fat
  • Plant stanol/sterol esters up to 2g/day
  • Psyllium: 6g/day for ages 2-12, 12g/day for >12y
  • 1 hour/day of moderate to vigorous PA, and <2hours/day screen time
Elevated TG or non-HDL cholesterol:

- Refer to registered dietitian

- 25-30% calories from fat, <7% from saturated fat, 10% from mono unsaturated fat; <200 mg/d cholesterol, avoid trans fat

- Decrease sugar intake
  - Replace simple with complex carbohydrate
  - No sugar-sweetened beverages

- Increase dietary fish intake to increase ω-3 fatty acids
1. Decisions regarding need for medication should be based on the average of 2 fasting lipid profiles, obtained at least 2 weeks but no more than 3 months apart.

2. Children with an average LDL Chol $\geq 250$ mg/dL or average TG level of $\geq 500$mg/dL should be referred directly to lipid specialist.

3. For children meeting criteria for starting lipid-lowering drug therapy, a statin is recommended as first-line treatment.

4. The goal of LDL-lowering therapy in childhood is LDL cholesterol $\leq 130$ mg/dL
Implementation of Pediatric Lipid Screening Guidelines among Primary Pediatric Providers

Damon B. Dixon, MD¹, Lyn M. Steffen, Ph.D², Annabel Kornblum, MPH¹, Julia Steinberger MD, MS¹

¹Department of Pediatrics, Division of Cardiology
²School of Public Health, Division of Epidemiology & Community Health
Background

- Traditionally cholesterol screening in children was limited to those with parental history of high cholesterol and premature CV disease (series of pediatric lipid guidelines published from 1992 to 2008)

- However recent studies have shown that use of family history alone would miss 30-60% of children with dyslipidemia
Background

- Most recently (Nov. 2011) NHLBI/AHA Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents (also endorsed by NLA) recommend universal screening for ages 9-11
Objective

We hypothesized that awareness and implementation of pediatric lipid screening guidelines among primary pediatric providers is inconsistent and incomplete.

Therefore we sought to:

• Evaluate the awareness and implementation of published pediatric lipid guidelines among primary pediatric providers.
• Understand the barriers for implementing pediatric lipid screening in current medical practice.
Methods

- Surveyed Primary Pediatric Providers
  - Pediatricians (MD/DO)
  - Family Medicine, General Practitioners (MD/DO)
  - Advance Practitioners (NP/PA)

- Minnesota State Board Physician License List:
  - Minneapolis/St. Paul Metro Area, Rochester, MN

- Approved by University of Minnesota IRB (exempt)
Methods

- **21-item Cross Sectional Electronic Survey**
  - Multiple-Choice Format
    - 3 questions on demographics
    - 18 questions on lipid screening practices
  - Data collection period: 3 months

- **E-mail:**
  - Description of Study and Consent (Voluntary)
  - Access to web-linked survey (Survey Monkey®)
  - Reminder E-mail sent to initial non-responders after 1 month
1488 Total E-mails Sent to Providers

- 86 Unsuccessful E-mails
- 1402 Successful E-mails

547 Responses (39%)
Demographics of Respondents

**Medical Specialty**
- Physician Assistant: 2%
- Other: 3%
- Sub-Specialist: 5%
- Nurse Practitioner: 6%
- General Practitioner: 37%
- Pediatrician: 37%
- Family Medicine: 11%

**Clinical Setting**
- Indian Health Service: 0.4%
- Military: 2%
- Other: 3%
- University/Academic: 28%
- Public Health Service: 16%
- Community Clinic: 21%
- Private Practice: 30%
Time Since Medical Training

- >20 years: 34%
- 0-5 years: 15%
- 6-10 years: 18%
- 11-15 years: 13%
- 15-20 years: 20%
Do you screen for lipid disorders in children?

- **Selectively-patient risk**
- **Do not screen**
- **Selectively-family history**
- **Universal screening**

[Bar chart showing percentage responses]
Do you think screening and treating a child for elevated lipid levels will reduce future cardiovascular risk?

Yes

No

Indifferent
Do you think that cholesterol lowering medications should be used in children?

- Yes
- No
- Indifferent

[Bar chart showing percentages]
Are you familiar with normal/abnormal lipid values in children?

Yes

No
Are you aware of any lipid guidelines in pediatrics?

Yes

No
Which of the following guidelines do you use in your practice?

- None
- 2012-ADA
- 2011-NLA
- 2011-NHLBI
- 2008-AAP
- 2007-USPSTF
- 2001-ATP III
- 1992-NCEP
Are you comfortable in managing a child with lipid disorders?

- Yes
- No
Which of the following do you see as a barrier in screening children for lipid disorders?

- No barriers
- Not a significant problem
- Family opposition
- Poor reimbursement
- Uncomfortable addressing
- Unfamiliar knowledge
- Other

0% 20% 40% 60% 80% 100%
Which of the following approaches do you implement in children with abnormal lipid levels?

- Repeat in future
- Referral to specialist
- Lifestyle changes (diet/PA)
- Repeat with advanced lipid biomarkers
- Other
Which of the following dietary guidelines do you use in your practice?

- None
- Reduced cholesterol
- Reduced total fat
- Low carbohydrate
- CHILD-1 diet AHA 1 & 2
- Mediterranean Diet
- None
- Other
Have you ever prescribed cholesterol lowering medications in children with abnormal lipid levels?

Yes

No
If you have prescribed cholesterol lowering medications, which of the following was your first choice?

- Bile Acid Sequestrants
- Fibric Acid Derivatives
- Statin-HMG CoA Reductase Inhibitors
- Cholesterol Absorption Inhibitors
- Omega-3 Fatty Acids
- Nicotinic Acid
- Other
Provider Perceptions/Practices

- 74% believe screening/treating abnormal lipids is beneficial
- 83% uncomfortable managing lipid disorders
- 50% screen selectively (child/parent CV risk)
- 15% universal screening
- 35% do not screen at all
Perceived Barriers to Screening

- 67% not familiar with normal/abnormal lipid levels in children
- 43% uncomfortable addressing topic of lipid disorders
- 31% unfamiliar with screening guidelines
Provider Practices

- 61% counsel for lifestyle changes
- 37% recommend low cholesterol diet
- Only 23% refer to lipid specialist
- 57% opposed to use of lipid lowering medications
Conclusions

1. Insufficient awareness and implementation of published pediatric lipid guidelines among primary pediatric providers

2. Despite recognition that treating lipid disorders may reduce future CV risk:
   - only 2/3 perform screening
   - majority are uncomfortable addressing lipid issues
   - minority refer to specialist
   - minority recommend drug therapy
Limitations

- Categorical analysis (multiple choice)
- Localized sampling bias (geographic area)
- Survey follows short interval from release of recent guidelines
Significance

• Need to further educate primary pediatric providers regarding dyslipidemia in children

• Provide more accessible information for primary care providers on screening and management of lipid disorders in children
THANK YOU
Changes from baseline (colored bar) to 28 weeks (white bar) in flow-mediated dilation (FMD) in the placebo and simvastatin groups of children with familial hypercholesterolemia (FH). *P<0.0001 vs baseline; †P<0.05 for change in placebo vs change in simvastatin groups. Reproduced from de Jongh et al. with permission from the American College of Cardiology Foundation. Copyright 2002 American College of Cardiology Foundation.
Mean carotid intima-media thickness (IMT) changes from baseline for the different carotid arterial wall segments in the pravastatin and placebo groups of children with familial hypercholesterolemia. Reproduced from Wiegman et al. with permission from the American Medical Association. Copyright 2004 American Medical Association.