Approach to Childhood Dyslipidemia – CPS Podcast

Developed by Katherine Tom and Dr. Peter Wong for PedsCases.com.
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Introduction

Hi Everyone! My name is Katherine Tom, and I am a final year medical student at McMaster University in Hamilton. This PedsCases podcast aims to provide an approach to childhood dyslipidemia, reviewing components of the Canadian Cardiovascular Society and Canadian Pediatric Cardiology Association Clinical Practice Update on "The Detection, Evaluation, and Management of Dyslipidemia in Children and Adolescents." This podcast was created under the supervision of clinical practice update author, Dr. Peter Wong, a community paediatric cardiologist and Associate Professor in the Department of Paediatrics at the University of Toronto.

Atherosclerotic processes begin in childhood and are associated with the development of cardiovascular disease in later life(1,2). Cardiovascular disease progression depends on the presence and severity of risk factors, including childhood dyslipidemia (2,3). Therefore, early detection of childhood dyslipidemia may allow paediatricians to slow atherosclerotic disease by addressing modifiable risk factors and initiating early treatment.

A 2019 Canadian Paediatric Surveillance Program (CPSP) survey suggests that childhood dyslipidemia may be under detected. Of the 759 participating paediatricians, only 3% reported universal lipid screening with more clinicians opting to screen children based on risk factors and family history(4). Even if childhood dyslipidemia was identified, only 7% of paediatricians reported they would start statin therapy themselves.

As such, our learning objectives for this podcast are as follows:

Learning Objectives:

1. Define childhood dyslipidemia
2. Review the etiologies and risk factors for childhood dyslipidemia
3. Describe screening strategies for childhood dyslipidemia
4. Develop an approach to the evaluation of childhood dyslipidemia
5. Discuss management options for childhood dyslipidemia

To help frame our discussion and apply these concepts to clinical practice we will use the following case:

CASE: Ryan is an 8-year-old boy that is followed in your community pediatric clinic for obesity. He presents today with his mom who is concerned about his cardiovascular health. She is worried that his sedentary behaviours and increased weight put him at additional risk for future disease.

Defining Childhood Dyslipidemia

Childhood dyslipidemia refers to disorders of lipoprotein metabolism causing abnormal lipid levels in children(1,5). The authors of the clinical practice update provide suggested thresholds for acceptable, borderline, and abnormal lipid levels based on the 2011 National Heart, Lung, and Blood Institute (NHLBI) Expert Panel cardiovascular health guidelines for children and adolescents(6).

The following values define the abnormal range of lipid levels:

Category	**Abnormal Lipid Levels (mmol/L)**
Total Cholesterol	≥ 5.2
Low-density lipoprotein (LDL) cholesterol	≥ 3.4
Non-high-density lipoprotein (Non-HDL) cholesterol	≥ 3.75
Triglycerides	
0-9 years	≥ 1.1
10-19 years	≥ 1.5
High-density lipoprotein (HDL) cholesterol	< 1.0

Etiology of Childhood Dyslipidemia

When we think of causes of childhood dyslipidemia, we can break it down into genetic or inherited causes, and non-genetic or lifestyle causes.

Genetic Causes

The most common single gene dyslipidemia is heterozygous familial hypercholesterolemia (FH) which is inherited in an autosomal co-dominant pattern (7). Children with FH have elevated LDL-C levels and are at increased risk of premature cardiovascular disease(7). Identifying children with FH is important because early statin initiation has been found to mitigate this risk and promote normal life expectancies(7). Screening for FH is recommended for first-degree relatives of known cases, including children as young as 2 years of age(6,7). Diagnosis of FH can be made through genetic testing or based on clinical data of elevated LDL-C and a positive family history of elevated LDL-C or premature CVD(6).

Other genetic causes of childhood dyslipidemia exist but are less common. Although genetic testing helps identify affected individuals, it is often limited by clinical availability and currently does not affect management (6). Therefore, genetic testing is only recommended to help identify genetic dyslipidemias but otherwise, diagnoses of dyslipidemia can be made with clinical data.

Non-Genetic Causes

There are many non-genetic causes for childhood dyslipidemia, with obesity-related dyslipidemia being the most common (1,6). Other contributors of dyslipidemia include lifestyle factors such as diet and calorie balance, certain medications including corticosteroids, medical conditions including diabetes mellitus, and conditions affecting the liver, thyroid, and kidneys(6).

It is important that non-genetic causes are always considered, even in cases with a clear genetic cause(6). Addressing modifiable risk factors can help minimize or eliminate contributing factors to atherosclerotic processes and dyslipidemia(6).

Screening Strategies of Childhood Dyslipidemia

Rationale for Screening

Screening for dyslipidemia is important as conditions often have no clinical symptoms(6). Early identification of dyslipidemia allows for early initiation of lipid lowering therapy to prevent premature cardiovascular disease, particularly in cases of FH (8).

Screening Strategies

Screening for dyslipidemia involves a simple non-fasting lipid blood test(6). Commonly used screening practices in primary care include selective vs. universal screening practices and cascade or reverse-cascade screening.

Selective vs. Universal Screening

Selective screening involves screening children for dyslipidemia if they have risk factors such as a family history of early cardiovascular disease, obesity or type 2 diabetes(6,9). However, it is estimated that this screening method misses 30-60% of children with dyslipidemia(8).

Universal screening involves screening every child, regardless of baseline risk, with the goal of identifying all individuals with dyslipidemia. This method was recommended by the 2011 NHLBI Expert Panel with screening of all children at 9-11 years of age and again at 17-21 years of age to improve identification of inherited lipid disorders(9).

Cascade & Reverse-Cascade Screening

Cascade screening involves screening all first-degree relatives of known cases of FH, including children(7). Similarly, reverse-cascade screening involves screening parents

of children with known FH to prevent cardiovascular disease development(7). Both methods make use of identified cases to then screen other family members for dyslipidemia.

Given the simple screening process and high prevalence of FH, clinical practice update authors recommend universal lipid screening with either fasting or non-fasting, non-HDL-C or LDL-C for children 2 years and older within the first decade of life(6). Cascade and reverse-cascade screening is recommended for individuals with probable or definite genetic cause dyslipidemia. Selective screening should be considered at any time when a child is thought to be at increased risk given the family history or other risk factors.

Let's go to our case: In Ryan's case, you follow the universal screening recommendation and send him for lipid screening as he is within his first decade of life. Lipid screening is also supported by his history of obesity.

Ryan's non-fasting laboratory results return with an abnormal LDL-C value of 3.5mmol/L. You arrange a follow-up appointment with Ryan and his family to discuss the positive screening result and to discuss further evaluation.

Evaluation of Childhood Dyslipidemia

Children with dyslipidemia should undergo a thorough evaluation, particularly for contributing non-genetic causes.

On history it is important to elicit(6,9):

- Family history of premature cardiovascular disease (angina, myocardial infarction, coronary artery disease, or sudden cardiac death in first degree relatives <55 years of age for men and <65 years of age for women)
- Symptoms of contributing medical conditions including diabetes, liver, renal, or thyroid disease
- Diet and exercise
- Medications

On physical examination, helpful clinical features to evaluate for include(6,7):

- Height, weight, BMI plotted on standard growth charts
- Signs suggestive of underlying medical conditions: pubertal development, goiter, hepatosplenomegaly, acanthosis nigricans
- Clinical features of dyslipidemia: corneal arcus, tendon xanthomas, xanthelasmas

The following are recommended as initial laboratory investigations(6):

- Complete blood count
- Lipid profile

- Thyroid stimulating hormone
- Liver and renal function markers
- Urinalysis
- Fasting glucose and hemoglobin A1C

Back to our case:
History
You review the history with Ryan and his parents. Ryan's family history is significant for early cardiovascular disease. Ryan's father was diagnosed with angina at age 54. His parents describe Ryan as having a poor diet, and sedentary lifestyle.

Physical Examination
Aside from BMI-for-age in the 98th percentile, which meets criteria for obesity, his physical examination is unremarkable.

You consider this information to inform your next steps in managing Ryan's positive screen for dyslipidemia.

Management of Childhood Dyslipidemia
It is important to note that the diagnosis of dyslipidemia and decision to start pharmacologic therapy is based on the average of at least 2 fasting lipid profiles completed at least 2 weeks but no more than 3 months apart(6).

If children meet diagnostic criteria for dyslipidemia, then early intervention through diet and lifestyle counselling and/or pharmacologic therapy should be considered.

Diet and Lifestyle Counselling
When discussing a healthy lifestyle for children with dyslipidemia it is helpful to encourage the following(6):

- Healthy diet aligning with Canada's food guide.
- Avoiding intake of trans-fats.
- Limiting intake of highly processed foods, red/processed meats, refined carbohydrates, and salt.
- Physical activity aligning with Canada's 24h Movement Guidelines for children and youth.
- Consultation with a dietitian is recommended to help optimize diet, if available.

Optimizing dietary and lifestyle factors are the first-line treatment for virtually all cases of childhood dyslipidemia and remains important even if lipid-lowering medications are started.

Pharmacologic Therapy

Lipid-lowering medications should be considered after dietary and lifestyle changes are not successful. Clinicians will often refer to lipid specialists for initiation and management of statin therapy.

Statin therapy can be started in children 8-12 years old with persistently elevated LDL-C, which is often due to genetic dyslipidemias(6). Current evidence shows that statins effectively decrease markers of early atherosclerosis(6,7).

A referral to a pediatric lipid specialist can be helpful to facilitate lifestyle or medication management. Referrals may be particularly beneficial for children with significant dyslipidemia (LDL-C ≥4.1mmol/L or triglyceride level ≥5.5mmol/L) or dyslipidemia in a child with multiple risk factors (6).

Follow up: To establish a diagnosis of dyslipidemia for Ryan, you order a full fasting lipid profile with a repeat fasting lipid profile to be done 2 weeks after the first. You also add-on the other initial laboratory investigations for dyslipidemia to this bloodwork.

You consider your next steps if laboratory results identify dyslipidemia. You would consider availability of genetic testing to evaluate for genetic cause and facilitate reverse-cascade screening. At the same time, you would start management by counselling on lifestyle and dietary changes.

If his LDL-C remained persistently elevated despite lifestyle modifications, you may consider a referral to a pediatric lipid specialist for support and possible statin therapy.

Let's review our key learning points for this podcast:

- Atherosclerotic processes begin in childhood with disease progression linked to the presence and severity of risk factors, including dyslipidemia.
- Genetic testing is helpful to identify genetic causes of dyslipidemia and to facilitate cascade/reverse cascade screening, where available
- Universal screening is recommended for children between 2-10 years of age to improve detection of dyslipidemia. Selective and cascade screening is also encouraged.
- Individuals with dyslipidemia should have a comprehensive evaluation including history, physical examination and biochemical investigations, particularly to identify non-genetic contributors to dyslipidemia.
- Diagnoses and decisions regarding management should be based on the average of at least 2 fasting lipid profiles completed at least 2 weeks but no more than 3 months apart.
- First-line management of dyslipidemia is through lifestyle and dietary optimization. Lifestyle interventions remain an important component of treatment, even if lipid-lowering medications are started.

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- Statin therapy can be initiated in children between 8-12 years of age if LDL-C levels remain persistently elevated despite lifestyle modifications.
- Referrals can be made to pediatric lipid specialists for support with lifestyle or pharmacotherapy management, particularly in cases with marked dyslipidemia.

Thank you for listening!

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