

Adolescent Health Update

A Clinical Guide
for Pediatricians

Vol. 19, No. 3
July 2007

Atherosclerosis Prevention and Cholesterol Management in Adolescents

by Marc S. Jacobson, MD, FAAP

While the consequences of atherosclerosis (ie, myocardial infarct, stroke, and peripheral vascular disease) are delayed until adulthood, the pathophysiologic process of arterial plaque development begins in early childhood and accelerates during adolescence. This issue of *Adolescent Health Update* will explain the pathophysiology of atherosclerosis, consider the role of cholesterol, lipids, and other risk factors, and give guidance on assessment and management of adolescents at risk. Practical tips on lifestyle modification, medical nutritional therapy, and pharmacotherapy will be emphasized.

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THE PROCESS OF ATHEROSCLEROSIS

Atherosclerosis is a pathologic process that develops in the arterial intima-media over a period of many decades. The initial stages of plaque accumulation, infiltration of lipid-laden macrophages and proliferation of smooth muscle cells in the intimal layer at susceptible locations in the arterial tree can be seen in the aorta and coronary arteries of infants. During adolescence, these initial changes progress and ultimately result in altered endothelial architecture and function known as atheromatous plaques. These plaques can cause narrowing of the arterial lumen in 3 ways: (1) by mechanically taking up space as they grow; (2) by causing arterial dysfunction, stiffening, and failure of dilatation mediated via nitrous oxide; and (3) by setting in motion and providing a nidus for a cascade of inflammatory and clotting events leading to thrombus and eventual clinical symptoms. In the relatively small arteries that supply the heart, narrowing due to plaque with associated stiffness and risk for thrombus is the basis for clinical coronary heart disease.

The development of atherosclerotic lesions has been extensively studied in adolescents using autopsy material

Goals and Objectives

Goal: After reading this issue, pediatricians will be better prepared to evaluate, treat, and counsel adolescents about the risk for atherosclerosis and the roles that cholesterol and lipids play in this process.

Objectives: Reading this issue will prepare pediatricians to:

1. Understand the process and etiology of atherosclerosis in children and adolescents
2. Understand the role of elevated cholesterol and hyperlipidemia in the development of atherosclerosis
3. Obtain a comprehensive assessment of an adolescent's risk for atherosclerosis and cardiovascular disease
4. Identify those adolescents at risk for lipid problems and interpret results of lipid profiles.
5. Develop an initial approach to management, including lifestyle changes, medication, and referral

Supported through an educational grant from
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combined with pre- and post-mortem risk factor assessments. Studies over the past 20 years have clearly shown that the commonly described risk factors in adults (elevated low-density lipoprotein [LDL] cholesterol, low high-density lipoprotein [HDL] cholesterol, high triglycerides, hypertension, obesity, diabetes, and smoking) are associated with the prevalence and extent of arterial lesions in adolescents and young adults in a dose-response fashion. Therefore, one can be confident that risk factors easily assessed in office practice will correlate with development

TALKING POINT

How to identify the teen at risk

There has been a heated debate among pediatricians over the past 30 years about whether cholesterol testing for atherosclerosis prevention should be universal (that is, every child or adolescent gets a cholesterol test as part of health maintenance) or selective (that is, only those with positive family history or an associated risk factor like hypertension get tested). It is my opinion that all adolescents should know their cholesterol along with their blood pressure, BMI percentile, and family history of cardiovascular disease. While we have seen a modest lowering of mean cholesterol in adolescents over the past 20 years, the incidence of other risk factors like obesity and diabetes is rising. Also, cholesterol testing is crucial in identifying the 1/500 individuals with heterozygous FH who have a significant risk of myocardial infarct in their 20s and 30s. Furthermore, for males, who are at the highest risk for early heart disease, the adolescent visit may be the last preventive health care visit before their first heart attack, and half of all first heart attacks are fatal. For all of these reasons, I believe that cholesterol testing in adolescence is extremely important. Therefore, I recommend that a random total cholesterol or preferably a fasting lipid profile be part of routine care for all adolescents.

– MSJ

Teens with metabolic syndrome are almost always overweight or obese, while adolescents with FH are no more likely to be obese than the general population.

of atherosclerotic plaque, and therefore of cardiovascular disease risk in the patient. Newer *in vivo* imaging studies have shown that early vascular stiffening and intimal thickening can be measured in adolescents at risk, and improvements in observed risk factors such as elevated LDL cholesterol and body mass index (BMI) can be correlated with improved vascular reactivity. These techniques may soon be used in preventive cardiology clinics to evaluate individual patients; they may also be employed in clinical trials for management of hyperlipidemia and other risk factors.

HYPERLIPIDEMIA

Heredity has an important role to play in vulnerability to atherosclerosis because lipid metabolism is affected by many genetically determined traits. The best-characterized form of genetic transmission of risk related to hyperlipidemia is familial hypercholesterolemia, although there are a number of additional diagnoses as described below.

Familial hypercholesterolemia (FH) is the phenotype resulting from a loss of function mutation in alleles that produce hepatic cell surface LDL receptors. This lessened receptor activity, whether due to decreased number or function, reduces clearance of LDL particles from the blood. This results in severely elevated LDL levels and subsequent accelerated atherosclerosis and early coronary artery disease. FH can be homozygous (which is rare) or heterozygous (which is common, occurring in 1:500 individuals in the United States). FH is inherited in an autosomal-dominant fashion. Individuals with heterozygous familial hypercholesterolemia have a 20% risk of myocardial infarction in their 20s, increasing to 75% by their 50s. Therefore it is critical to identify and treat FH in adolescents.

Familial combined hyperlipidemia is characterized by mild elevation in

total and LDL cholesterol, moderate to severe elevation in triglycerides, and reduced HDL cholesterol. In childhood and adolescence, this pattern is usually expressed in the presence of obesity. While significantly increasing cardiovascular risk at later ages, familial combined hyperlipidemia is not associated with the same high risk of very early disease as is seen in patients with FH.

Mixed environmental-genetic hyperlipidemia is the name given to a pattern of mild lipid abnormalities in individuals with a genetic sensitivity that is exacerbated by a diet high in saturated fat and cholesterol. No single gene is responsible, but genes encoding for the apolipoprotein E (APOE) isoforms are known to impart variable sensitivity to diet.

Metabolic syndrome. Unlike the genetically linked types of hyperlipidemia described above, metabolic syndrome is a cluster of risk factors of unknown etiology that impart an elevated risk of cardiovascular disease. First described in the 1980s as syndrome X, metabolic syndrome is now an area of great interest in cardiovascular disease and diabetes prevention. With the rise in incidence of obesity in adolescents, metabolic syndrome could become the most frequent cause of lipid abnormalities seen in pediatric practice. The lipid profile pattern associated with the metabolic syndrome includes normal to mildly increased total and LDL cholesterol levels, moderate to severe increase in triglycerides, and reduced HDL cholesterol.

Online resources

From the National Cholesterol Education Program

Interactive patient education on therapeutic lifestyle change (TLC)
http://nhlbisupport.com/chd1/tlc_lifestyles.htm

Information for health care professionals on cholesterol management
www.nhlbi.nih.gov/guidelines/cholesterol

In adults, metabolic syndrome is currently diagnosed in individuals with 3 or more of the following: (1) high triglycerides, (2) low HDL cholesterol, (3) hypertension, (4) central adiposity, and (5) elevated glucose. In pediatrics, the syndrome is less well defined. At least 5 criteria have been proposed; some are more stringent than others. Consensus on exactly what constitutes pediatric metabolic syndrome has not been reached as of this writing, but all definitions share the commonality of obesity, dyslipidemia, insulin resistance, and hypertension.

EVALUATION

National Cholesterol Education Program (NCEP) guidelines for classification of lipid risk in children and adolescents have been in place since 1992; **Table 1** is based upon these criteria. There is vigorous debate about whether the NCEP guidelines should be updated to include universal screening using blood tests and guidelines for triglycerides and HDL cholesterol, and age-based percentiles instead of single cut-off values. New guidelines are currently under development at the National Heart, Lung and Blood Institute (NHLBI) and

should be published by 2008.

The recent rise in the incidence of obesity has resulted in more pediatric patients presenting with lipid abnormalities, but these are generally of the metabolic syndrome pattern. Patients with metabolic syndrome have not been shown to have the very high 10-year risk of myocardial infarction that is characteristic in adolescents with FH. (**Table 2**) In addition, teens with metabolic syndrome are almost always overweight or obese, while adolescents with FH are no more likely to be obese than the general population.

Diagnosis of a lipid abnormality involves the patient's past medical history, family history, physical examination, and a few simple laboratory studies, including the fasting lipid profile. Other risk factors for early cardiovascular diseases (eg, obesity, hypertension, smoking, diabetes) need to be identified and managed appropriately. If hypercholesterolemia is found, order thyroid, liver, and kidney function tests to rule out the relatively rare secondary causes of high cholesterol or triglycerides.

Foremost among the secondary causes is hypothyroidism, which can

TABLE 1

1992 NCEP Classification of lipid risk for children and adolescents

	At Risk	Borderline	Within Guidelines
Total Cholesterol mg/dl	>200	170-200	<170
LDL Cholesterol mg/dl	>160	130-160	<130

Source: National Cholesterol Education Program, a division of the National Institutes of Health, National Heart, Lung, and Blood Institute (www.nhlbi.nih.gov/guidelines/cholesterol/dskref.htm) (New guidelines are currently under development.)

TABLE 2

Clinical characteristics and treatment options of high-risk adolescents with hyperlipidemia

	Familial Combined Hyperlipidemia	Metabolic Syndrome	FH Heterozygote*	FH Homozygote†
Total cholesterol (mg/dl)	200-250	200-250	250-350	600-700
Triglycerides (mg/dl)	175-350	>150	100-150	100-150
LDL cholesterol (mg/dl)	150-200	130-200	160-250	600-650
HDL cholesterol (mg/dl)	25-35	<35	45-55	45-55
Xanthomata	Rare	None	Common in parents and seen in 10% of teens*	Common
Adolescent's 10-year risk of myocardial infarction	unknown but probably <1%	unknown but probably <1%	high 15% to 20%*	very high 90%†
Treatment used if TLC fails	Extended-release niacin, omega-3s, fibrates	Extended-release niacin, omega-3s, fibrates	Statin with or without ezetimibe, extended-release niacin, or bile acid sequestrant	Biweekly apheresis

*Kwiterovich

†Sprecher et al

be associated with a number of clinical signs (eg, delayed puberty and growth retardation, cold intolerance, constipation, slowed mental development, weight gain, bradycardia, and edema), but is most often asymptomatic. Therefore, thyroid stimulating hormone should be measured routinely in newly discovered hyperlipidemia, particularly if family history is negative for cardiovascular disease. Any liver inflammation can affect lipids, which is why aspartate aminotransferase (AST — previously SGOT) and alanine aminotransferase (ALT — previously SGPT) tests should be routinely ordered as well.

Nephrotic syndrome is accompanied by significant elevations of total and LDL cholesterol, so a random urinary protein assay is also indicated. Type 2 diabetes mellitus and other forms of insulin resistance (eg, polycystic ovary syndrome, metabolic syndrome) are associated with hypertriglyceridemia and low HDL cholesterol.

The other conditions commonly associated with lipid abnormalities are not likely to be missed on history and physical and thus do not warrant routine lab screening. These include connective tissue disorders (eg, systemic lupus erythematosus, juvenile idiopathic arthritis), anorexia nervosa, and drug toxicity from oral corticosteroids, isotretinoin, or antiretrovirals.

Identifying Adolescents at Risk: Case Scenarios

Evidence of a lipid problem that emerges during an unrelated evaluation presents an important opportunity to intervene early in the disease process. These case studies illustrate typical scenarios and suggest appropriate interventions.

Case 1

Lipid issues are identified in an otherwise healthy adolescent male when a chemistry panel ordered as part of an acute illness workup reveals a cholesterol level of 215 mg/dl. Liver and kidney function tests are normal and the acute illness resolves. What should be done regarding his cholesterol?

If there is no family history of early myocardial infarct, stroke, or peripheral vascular disease, give basic lifestyle advice about proper diet and exercise habits and smoking prevention counseling. Repeat his cholesterol in 3 to 6 months. If family history is positive, proceed as in Case 2 below.

Case 2

As part of his routine physical, a 15-year-old boy with no significant past medical history is found to have a parent with significant atherosclerotic cardiovascular disease (myocardial infarct, stroke, or peripheral vascular disease before the age of 55 in males or age 60 in females). His total cholesterol is 240 mg/dl. What is your approach?

This patient's family history is positive for cardiovascular disease and hypercholesterolemia. He should have a fasting lipid profile. If his LDL cholesterol is >160 mg/dl averaged over

FIGURE 1

Flow sheet for management of atherosclerosis risk

This chart indicates benchmarks to be monitored for patients beginning a cholesterol-management program.

Timeline	Target value
Height/pct	
Weight/pct	
BMI/pct	<85th
Blood pressure systolic/diastolic	<90th percentile
Tanner stage	
Total cholesterol	170 mg/dl
Triglyceride	<150 mg/dl
LDL cholesterol	<130 mg/dl
HDL cholesterol	>40 mg/dl
Glucose	<100 mg/dl
Insulin	<17 μ U/mL
Creatinine kinase*	
ALT [†]	
AST [†]	
Thyroid screen	
Smoking prevention	
Pregnancy prevention	
Dietary compliance/dietitian visits	
Food Supplements	
Medication	
Dosage	

* Worrisome level of CK: 10 times above the upper limit of normal (McCordle, et al)

† Worrisome level of ALT or AST: 3 times upper limit of normal (McCordle, et al)

Pediatricians who use this table to create a record-keeping page in the patient chart will want to enter initial data, then update at follow up to chart progress. On TLC, follow up is indicated every 3 to 6 months until lipid profile targets are met, then yearly. For patients on medication, follow package insert guidelines for medical monitoring and lipid profile frequency.

TABLE 3

Basic elements of a therapeutic lifestyle changes (TLC) diet

- Less than 7% of the day's total calories from **saturated fat**
- No more than 25% to 35% of the day's total calories from **fat**
- Less than 200 mg of dietary **cholesterol** per day
- Less than 2,400 mg of dietary **sodium** per day
- Just enough **calories** to achieve or maintain a healthy weight and reduce your blood cholesterol level. (Ask your doctor or registered dietitian what is a reasonable calorie level for you.)

These criteria are those recommended for adults by the National Cholesterol Education Program (NCEP) of the National Institutes of Health. TLC is a 3-pronged cholesterol management approach that incorporates diet, physical activity, and weight management.

2 measurements, he has presumptive heterozygous familial hypercholesterolemia (FH). His target LDL cholesterol is <130 mg/dl and he should be managed with therapeutic lifestyle changes (TLC) as discussed below. If TLC fails to bring his LDL within target range within 1 to 2 years, he is a candidate for cholesterol-lowering medication.

Case 3

A 15-year-old female complains of fever, malaise, joint pain, and an evanescent facial eruption. Her workup for a rheumatologic condition reveals an abnormal lipid profile (total cholesterol 220 mg/dl, triglycerides 275 mg/dl, LDL cholesterol 135mg/dl, and HDL 35 mg /dl). She has no family history of early cardiovascular disease. How should this patient be managed in terms of her lipids?

This patient's dyslipidemia is likely to have a secondary cause. Consider disorders affecting the thyroid, liver, kidney, or the immune system. Serum measures of thyroid stimulating hormone, hepatic enzymes (ALT, AST), albumin, globulin, antinuclear antibody, and erythrocyte sedimentation rate or C-reactive protein will cover the important secondary causes of hyperlipidemia and help rule in or out significant abnormalities affecting the lipid profile. Manage the patient's underlying disease first. Counseling to improve her diet (see **Table 4**) is the first-line treatment of her dyslipidemia.

MANAGEMENT

Once an adolescent is found to have hyperlipidemia with or without other risk factors, management consists of prioritizing the risk factors and intervening in a step-wise fashion. Diet needs to be explored with a prospective diet diary, a food frequency questionnaire, or questions in the clinical interview about usual intake. Focus on sources of saturated fat and simple sugars, then ask which food choices could be most easily modified. Record what changes your patients agree to make so that you can query and assess progress in terms of weight change or lipid targets each time you see them.

Exercise is valuable in maintaining or

improving BMI and can be assessed by investigating the teen's usual after-school and weekend activities. It is important to assess sedentary activity as well by recording the number of hours of television watched daily. Let the adolescent come up with things he or she would like to change. Suggest walking to school, friends' houses, or activities. Additional useful suggestions are gym membership, home exercise equipment, active video games, and organized or spontaneous individual or team sports.

Therapeutic Lifestyle Changes (TLC)

TLC is a system of initial nonpharmacological interventions that should be initiated and maintained whether or not medication is needed. **Table 3**, based upon the recommendations of the NHLBI, describes the basic diet and exercise elements of TLC, and **Table 4** provides counseling cues.

When introducing TLC, recommend beginning a physical activity for a few minutes most days. New American Acad-

TABLE 4

Counseling adolescents to achieve TLC

1. Keep your recommendations simple. Focus on 1 to 3 small changes per visit.
2. Avoid drastic statements. Rather than ruling out pizza or french fries, help the adolescent figure out how to limit frequency or portion size of problem foods
3. Begin with the adolescent's current lifestyle and make gradual changes. Find out what he or she would like to work on first, even if it may not be the most important concern in your view. For example, find out whether he or she will agree to walk to or from school some days each week.
4. Many boys welcome an opportunity to train with weights. Let them use light weights with a high number of repetitions after some instruction. In order to reduce risk of injury, younger adolescents should not use heavier weights.
5. Talk about spending less time watching television and at the computer.
6. Stress smoking prevention or cessation.
7. Determine what role the family should play. Many adolescents need family involvement to change their eating and exercise habits. If the teen resents a parental role, however, focus on what is eaten outside the home. For adolescents who are not yet ready to make menu choices that differ from those of their friends, focus on what is consumed at home.
8. Ask the adolescent and family to identify the perceived barriers to change, then talk about how to overcome those barriers.
9. Suggest that the family consult a registered dietitian.
10. Educate the teen about reducing dietary saturated fat, emphasizing its role as the most potent LDL-lowering strategy. Teach the adolescent to read labels for saturated fat content. Start with snacks, recommending choices with less than 2 gm saturated fat per serving and no more than 10 gms of sugar per 1 serving, or focus on dairy intake, lowering the saturated fat by choosing the lowest acceptable alternative.
11. Explain to teens with hypertriglyceridemia that reducing simple carbohydrates in the diet is an effective treatment. Simple carbohydrates common in adolescent diets are (a) alcoholic and sugar-sweetened beverages (soda, juice, sports drinks, and sweetened teas); (b) snack foods (sweets, chips, fries); and (c) white foods (white bread, white rice, white potatoes, white pasta). Focus a little on each category at each visit, trying to elicit which foods are most prevalent in the diet and which can be most easily replaced with a healthier version. Suggest substitutions, such as whole-grain bread with at least 2 gm fiber per serving.

emy of Pediatrics guidelines on physical activity for children and adolescents recommend limiting sedentary activity/screen time to less than 2 hours per day and promoting 1 hour of physical activity per day on most days of the week.

Within 6 weeks to 3 months of the initial intervention, a repeat evaluation and counseling session needs to be scheduled to record progress and make adjustments to the intervention. Repeat these at 3- to 5-month intervals until the lipid goals are met. In a patient with heterozygous FH, if after 1 to 2 years the LDL-cholesterol goal of <130mg/dl has not been met, consideration of pharmacotherapy is indicated. (Tables 5, 6)

Managing Clinical Challenges: Three Case Studies

The three case studies below illustrate some of the clinical challenges that occur in the care of these patients. Table 2 will help classify the patient's lipid

abnormality and suggest treatment. It may be helpful to adopt an office form to monitor patient progress. **Figure 1**, which provides target values, can be used as a model; a downloadable version is posted with this issue on the AAP Members Only Channel, www.aap.org.

Case 1

An 18-year-old female comes to the office for a checkup. Her past medical history is unremarkable except for the fact she is sexually active and on low-dose oral contraceptives. Her family history includes a father with hypercholesterolemia on medication and a paternal grandfather who died of a myocardial infarction at age 50. Her lipid profile is total cholesterol 255 mg/dl, triglycerides 125 mg/dl, LDL cholesterol 190 mg/dl, and HDL cholesterol 40 mg/dl. Once TLC is given a sufficient chance to work (1-2 years) and her lipids are unchanged, what is the next step?

Answer: This patient meets the family history and LDL cholesterol criteria for heterozygous familial hypercholesterolemia. She should have pharmacotherapy with a low dose of statin. Before prescribing, her clinician should make her aware of the low risk of muscle and liver side effects and the risks to the developing fetus. The need for continued TLC, including smoking prevention, should be emphasized. Her lipids, creatinine phosphokinase (CK), ALT, and AST should be followed at recommended intervals of 6 weeks, 3 months, 6 months, and then yearly. The contraindications of statins during pregnancy should be stressed and appropriate follow up ensured.

Case 2

A 16-year-old girl, somewhat overweight (BMI percentile 90), with polycystic ovary syndrome but a normal fasting insulin level comes into your office. Her mother is on a statin medication. Fasting profile: total cholesterol 166 mg/dl, triglycerides 203 mg/dl, LDL cholesterol 98 mg/dl, HDL cholesterol 27 mg/dl. Her diet includes chicken, fish, pasta, rice, cereal, and skim milk. How would you approach this nutritionally in light of the elevated triglycerides, and which medication(s) might be considered?

Answer: This is a case of familial combined hyperlipidemia in an adolescent with polycystic ovary syndrome. Simple carbohydrates (white rice, bread, pasta, potatoes, sweets, sugar-sweetened beverages and alcohol) are known to raise triglycerides, which in turn lower HDL cholesterol. These foods and beverages are also associated with insulin resistance, a feature of polycystic ovary syndrome and metabolic syndrome. We know that even a small weight loss can normalize the lipid profile in this setting. For these reasons, dietary recommendations should begin with limitations on simple carbohydrate consumption, both in terms of portion size and frequency, and an increase in lean protein and complex carbohydrates like vegetables and whole grains. Counseling should stress the importance of making lifestyle changes that increase overall physical activity level. Lipid-

TABLE 5

Important considerations and counseling points before initiating pharmacotherapy

Either

1. The patient should have an LDL cholesterol >190 mg/dl plus the presence of xanthomas or xanthelasma (these skin lesions indicate familial hypercholesterolemia).

Or

2. The history should reflect all 4 of the following:

- a) Patient over 10 years of age. A sexual maturity rating (Tanner stage) greater than 2 in males. Menarche in females. LDL cholesterol >190 mg/dl without other risk factors or 160 mg/dl if risk factors like hypertension, smoking or obesity are present.
- b) Careful monitoring of TLC for 6 months to 2 years by a registered dietician experienced in working with adolescents and lipid abnormalities.
- c) Failure to achieve significant LDL cholesterol lowering (15% or greater) with TLC.
- d) Positive family history for early cardiovascular disease in an expanded first-degree pedigree.

In addition

3. The patient and family should be clear about the low risk of muscle and liver side effects.

4. The patient and family should understand risks to the developing fetus, as well as the need for continued TLC, including smoking prevention.

5. There should be a commitment to come in at 6 weeks, 3 months, 6 months, and then yearly so that lipids, CK, ALT, and AST can be monitored.

Source: McCrindle et al

lowering medications for this type of dyslipidemia are the fibric acids and extended-release niacin. (These drugs are not FDA-approved for use below age 18; referral to a lipid specialist, endocrinologist, or cardiologist is the next step if medication is needed.) Statins are not indicated because the LDL cholesterol is not elevated.

Case 3

This patient is a 17-year-old girl whose fasting lipid profile is: total cholesterol 152 mg/dl, triglycerides 175 mg/dl, LDL cholesterol 101 mg/dl, HDL 22 mg/dl. She has a positive family history of hypercholesterolemia and early myocardial infarction. The patient is sexually active and wants to begin oral contraceptives. She is thin, menstruating regularly, normotensive, and nonsmoking. Would you suggest using a statin, and if so, at what dose?

Answer: Her lipid pattern is that of familial combined hyperlipidemia. Total and LDL cholesterol are within normal limits making statins a poor choice of medication, but her combination of high triglycerides and low HDL

cholesterol put her at risk for premature cardiovascular disease. Statins are also contraindicated in pregnancy, so must be used with caution in sexually active adolescent females. Patients with an HDL this low are at risk for early coronary disease. HDL levels may rise slightly in response to routine exercise and this should be recommended. If TLC fails to improve her lipids, the best choice of medication would be extended-release niacin or a fibric acid derivative as in case 2. Lipids should be monitored 6 weeks after initiation of oral contraceptives and then twice yearly once stable.

A Word About “Natural” Means to Lower Cholesterol

The first line of treatment for hyperlipidemia is TLC (see Table 3). Studies consistently report LDL cholesterol lowering of 10% to 15% with this alone. Additionally, many patients are interested in “natural” methods to lower cholesterol. If this is the case, work with them and do not dismiss their ideas out of hand. Some products have small ef-

fects on total and LDL cholesterol on the order of 3% to 5% and work best when used to replace foods high in saturated fat. For example:

- Soluble fiber-containing foods: oatmeal (regular not instant), beans, apples, citrus
- Soy-based foods: tofu, soy milk or soy nuts
- Fish: salmon, herring, oysters, halibut, canned light tuna
- Foods high in unsaturated oils: walnuts, almonds, avocados, olive oil

If additional LDL cholesterol lowering is needed, supplemental *plant stanols and sterols*, which are derived from nonfood plant-based sources, may be indicated. These products (generally, margarines, yogurts, and salad dressing) are widely available and clearly labeled in grocery stores. They can also be obtained in tablet form over the counter. When ingested at a dose of 3 gm per day, plant stanols and sterols interfere with cholesterol absorption in the gut and inhibit the enterohepatic recirculation of cholesterol. This, in turn, stimulates the liver to upregulate

TABLE 6

Pharmacotherapeutic agents used in hyperlipidemia

Drug Class	Examples	Action	Contraindications and Side Effects
Statin	Atorvastatin Fluvastatin* Lovastatin Pravastatin Rosuvastatin* Simvastatin	Inhibits hepatic cholesterol synthesis	Myalgia, myositis, raised aspartate aminotransferase (AST — formerly SGOT) and alanine aminotransferase (ALT — formerly SGPT)
Niacin	Extended-release niacin*	Lowers very low density lipoprotein synthesis	Flushing, raised AST and ALT
Fibrate	Gemfibrozil* Fenofibrate*	Lowers very low density lipoprotein synthesis	Dyspepsia, constipation, myositis, anemia
Bile acid sequestrant	Cholestyramine Colesevelam*	Binds intestinal bile acids, interrupts entero-hepatic recirculation	Gas, bloating, constipation, cramps
Cholesterol absorption inhibitor	Ezetimibe*	Inhibits cholesterol absorption from small intestine	Gas, bloating, constipation

*Not FDA approved for patients under age 18.

LDL receptors and lower plasma LDL cholesterol. Up to 10% LDL cholesterol lowering is seen in clinical trials in children and adults.

For the patient with hypertriglyceridemia, if the TLC diet is not enough to reach target triglyceride values, omega-3 oils derived from marine sources can be given. A dosage of 1 gm to 3 gm per day of combined eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in capsule or liquid form has been shown to be effective in reducing hypertriglyceridemia and inflammation.

CONCLUSION

Hyperlipidemia and its management give pediatricians a unique opportunity to practice prevention with their adolescent patients in an area that is less emotionally charged than sexuality and drug use but is every bit as important in terms of long-term morbidity and mortality. All teens and their families should be made aware of their risk status and the ways to reduce their risk. This necessitates a focused family history, a random cholesterol test or fasting lipid profile when indicated, and counseling based on the findings.

Therapeutic lifestyle change (TLC) is

an effective approach to lipid management that accommodates opportunities for other types of health risk counseling. In a patient with heterozygous FH, if lipid levels are not controlled by TLC after a period of 1 to 2 years, pharmacotherapy may be initiated. Milder types of lipid disorders can be followed longer (into adulthood) without drug treatment.

ACKNOWLEDGMENT

The editors would like to acknowledge technical review by Rae-Ellen W. Kavey, MD, MPH, senior medical officer and coordinator, Pediatric Cardiovascular Risk Reduction Program, National Heart, Lung and Blood Institute, National Institutes of Health.

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Supported through an
educational grant from

