

Quick Recertification Series

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LIPID DISORDERS

GENERAL FEATURES

- More than 25% of the adult US population has hyperlipidemia. Despite wide promotion of the National Cholesterol Education Program Adult Treatment Panel (ATP) III guidelines, control of hyperlipidemia remains suboptimal.
- A strong familial tendency toward hyperlipidemia exists, and 70% of patients with lipid abnormalities have a family history of a lipid disorder.
- Lipoproteins are classified into five subclasses: chylomicrons, very-low-density lipoprotein, intermediate-density lipoprotein, low-density lipoprotein (LDL), and high-density lipoprotein (HDL).
- LDL cholesterol (LDL-C) is the major carrier of cholesterol to peripheral tissues. The reverse transport lipoprotein, HDL cholesterol (HDL-C), carries cholesterol back to the liver to be excreted as bile salts. HDL-C is referred to as the *good cholesterol*.
- Risk of atherosclerotic vascular disease increases with increasing levels of LDL-C in both sexes and for people from different racial and ethnic groups.
- LDL-C promotes atherosclerosis by damaging the endothelium, altering vascular tone, increasing platelet aggregation, activating pro-inflammatory signaling pathways, and inducing growth factors.
- Risk of coronary heart disease (CHD) increases with decreasing levels of HDL-C.
- Lowering LDL-C level in patients with CHD significantly reduces mor-

tality and recurrence of cardiovascular events.

- Several types of primary familial hypercholesterolemia are caused by genetic disorders of lipid metabolism. Patients with certain genetic lipid disorders should be referred to a lipid specialist.
- Secondary causes of hyperlipidemia include obesity, hypothyroidism, diabetes, chronic renal failure, nephrotic syndrome, obstructive liver disease, and certain medications.

CLINICAL ASSESSMENT

- History
 - Ascertain family history of hyperlipidemia, premature MI, or sudden cardiac death; delineate other cardiovascular risk factors, such as smoking, alcohol intake, diet, physical activity, and diabetes.
 - Patients with mild hyperlipidemia are usually asymptomatic.
 - Symptoms of angina, transient ischemic attack, fatigue, and dyspnea suggest atherosclerotic vascular involvement.
 - Patients with severe hypertriglyceridemia may complain of nausea, vomiting, and abdominal pain related to pancreatitis.
- Physical examination
 - Few clinical findings are seen in patients with hyperlipidemia, and often physical examination findings are within normal limits.
 - BP, waist circumference, weight, signs of vascular compromise, and presence of corneal opacification should be noted.
 - Xanthomas are occasionally seen in patients with familial lipid disorders or extremely high cholesterol levels.

DIAGNOSIS

- Medical history and the results of fasting lipid panels (total cholesterol, HDL-C, LDL-C, and triglyceride levels) establish the diagnosis.

- Recommendations for routine laboratory screening vary. The US Preventive Services Task Force recommends routine screening for lipid disorders in men 35 years and older and women 45 years and older. Younger adults (men aged 20-35 years and women aged 20-45 years) should be screened for lipid disorders if they have other risk factors for CHD.
- The optimal interval for screening is uncertain. A fasting lipoprotein profile every 5 years is customary for patients without risk factors for CHD and repeatedly normal lipid levels. Testing should be performed more frequently for patients who have consistently borderline-high lipid levels.
- Evaluating lipid fractions and assessing the patient's risk for CHD is critical to guiding therapeutic decisions.
- Absolute risk for patients without CHD or other clinical forms of atherosclerotic disease is calculated by counting categorical risk factors.
- Major risk factors for the development of atherosclerotic heart disease that modify LDL-C goals are:
 - Age (men ≥ 45 years; women ≥ 55 years)
 - Family history of sudden death before age 55 years in the father or first-degree male relative or before 65 years in the mother or first-degree female relative
 - Cigarette smoking
 - Hypertension (BP $\geq 140/90$ mm Hg or taking antihypertensive medication)
 - HDL-C < 40 mg/dL (a risk factor is subtracted if the HDL-C is > 60 mg/dL because of the known cardioprotective benefit of this lipoprotein).
- The presence of one or fewer categorical risk factors warrants a target LDL-C level < 160 mg/dL.
- If two or more risk factors are present, determine the patient's 10-year

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risk for CHD using the Framingham scoring system (available at <http://hp2010.nhlbihin.net/atp3iii/calculator.asp?usertype=prof>). Target LDL-C levels are:

- <100 mg/dL if the 10-year risk for CHD is $\geq 20\%$
- <130 mg/dL if the 10-year risk for CHD is $< 20\%$
- Counting risk factors to determine the intensity of cholesterol-lowering therapy is unnecessary in patients with established atherosclerotic disease. These patients are considered high risk and warrant a target LDL-C level ≤ 100 mg/dL.

TREATMENT

- Treat causes of secondary hyperlipidemia and adjust medications, such as corticosteroids and progestins.
- Treatment decisions for primary hyperlipidemia should take into account overall CHD risk rather than lipid levels alone. Level of CHD risk guides the initiation of therapeutic lifestyle changes (TLCs) and medication selection.
- All patients with hyperlipidemia should be counseled on TLCs, including lowering intake of dietary saturated fats ($< 7\%$ of calories) and cholesterol (< 200 mg/d), increasing intake of soluble fiber (10-25 g/d) and plant stanols/sterols (2 g/d), weight reduction, smoking cessation, and exercise.
- LDL-C should be the primary target of lipid-lowering therapy. ATP III guidelines suggest measuring lipoprotein levels every 6 weeks until target levels are achieved, then every 6 to 12 months thereafter.
- Statins are the preferred lipid-lowering agents. They inhibit the rate-limiting enzyme responsible for producing cholesterol.
 - On average, statins reduce circulating LDL-C as much as 35%, with

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a slight decrease in triglyceride levels and a modest increase in HDL-C. These agents are the only drugs that definitively improved mortality and morbidity in primary and secondary prevention trials.

- Although generally well-tolerated, statins can cause myalgias and elevate liver enzymes; however, the risk of rhabdomyolysis or significant clinical myositis is quite low. Obtain baseline creatinine kinase and transaminase levels before starting therapy. Monitor liver function 3 and 6 months after therapy is initiated and every 6 to 12 months thereafter if laboratory test results are within normal limits.
- Ezetimibe (Zetia), the first of a new class of drugs that inhibits cholesterol absorption in the intestines, is indicated for patients who fail to achieve target LDL-C levels on statin monotherapy. However, the effect of ezetimibe on the development of atherosclerosis is not yet known.
- Administer bile acid sequestrants as adjunctive therapy in patients with markedly elevated LDL-C levels. Use may be limited by side effects such as bloating, nausea, and constipation.
- Niacin is used in combination with statins to lower triglyceride and LDL-C levels and increase HDL-C levels.
- Patients with hyperlipidemia and hypertriglyceridemia frequently require combination therapy. Adding a fibrate, niacin, or ezetimibe to a statin will lower LDL-C and triglyceride levels more effectively than statin monotherapy.
- Fibrates raise HDL-C levels and lower triglyceride levels; their main indication is for hypertriglyceridemia when TLCs alone are ineffective. Fenofibrate can be safely added to a statin regimen. Fish oils with omega-3 fatty acids can be an effective adjunct for patients with hypertriglyceridemia.
- Costs of therapy, drug interactions, adverse effects, and patient preferences should always be discussed and considered.

QUESTIONS & ANSWERS

1. Laboratory test results for a 48-year-old hypertensive man, a chronic smoker whose father died as a result of an MI at age 52 years, are total cholesterol, 275 mg/dL; HDL-C, 25 mg/dL; calculated LDL-C, 180 mg/dL; and triglycerides, 150 mg/dL. He works two jobs to support his family, gets minimal exercise, and eats fast food on a regular basis because of time constraints. What should his target LDL-C level be?

- a. <100 mg/dL
- b. <130 mg/dL
- c. <160 mg/dL
- d. <200 mg/dL

Answer: a

Explanation: This patient has multiple risk factors for coronary heart disease (CHD) and a $> 20\%$ 10-year risk for CHD, according to the Framingham score table. His LDL-C goal should be < 100 mg/dL.

2. How would you manage this patient's treatment?

- a. Recommend therapeutic lifestyle changes (TLCs) and reevaluate in 6 months
- b. Recommend TLC measures and initiate statin therapy
- c. Refer to a lipid specialist
- d. Prescribe a combination regimen of a statin and niacin

Answer: b

Explanation: The Adult Treatment Panel III guidelines advise that when two or more risk factors are present and the patient's 10-year CHD risk is $> 20\%$, lipid lowering drug therapy should be started in addition to TLCs if the LDL-C level is ≥ 130 mg/dL.

- Patient education and close monitoring that improves adherence are essential for optimal hyperlipidemia management.
- Clinicians can access the Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults Treatment Panel III: Executive Summary at <http://www.nhlbi.nih.gov/guidelines/cholesterol/atp3xsum.pdf>.

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