

Hyperlipidemia

Pronunciations: (Hy-per-lip-id-emia)

Hyperlipidemia (or hyperlipoproteinemia) is a general term for elevated plasma lipid levels in the bloodstream. Lipids include cholesterol, triglycerides, phospholipids, and cholesterol esters. There are several different forms of hyperlipidemia: hyperlipoproteinemia (elevated lipoprotein [VLDL, LDL] levels), hypercholesterolemia (elevated cholesterol levels), and hypertriglyceridemia (elevated triglyceride levels). Accumulation of lipids may accelerate atherosclerosis, which eventually leads to fatty streaks and plaque build up in the arterial walls.

Causes

In general, the etiology of hyperlipidemia is usually related to delayed or defective clearance or overproduction of VLDL, which subsequently turns to LDL. In addition, a reduction in the number or function of LDL receptors caused by genetic or dietary (i.e., saturated fat) factors may delay clearance from the blood. The primary causes of hyperlipidemia may be genetic, such as with familial diseases which lead to an increase in LDL levels. Genetics factors may be associated with absent or nonfunctional LDL receptors (familial hypercholesterolemia), defective apolipoprotein fractions (familial apolipoprotein B¹ and familial dysbetalipoproteinemia), lecithin acyltransferase deficiency, and other genetic abnormalities that have not yet been identified. Familial hypercholesterolemia is a common lipid disorder caused by defective or absent LDL receptors, resulting in increased LDL levels because clearance from the blood is delayed. Secondary causes of hyperlipidemia are related to dietary and disease risk factors, and drugs that increase lipid levels in the blood. Factors that have been found to be associated with high blood cholesterol include: diets high in fat, saturated fat, and cholesterol; excessive calorie and alcohol intakes; obesity; diabetes mellitus; hypothyroidism; hypopituitarism; nephrotic syndrome; chronic renal failure; certain medications (i.e., oral contraceptives, anabolic hormones); physical activity; and season of the year. Hyperlipidemia is a more common occurrence in men than in women.

Diagnosis

Symptoms:

Hyperlipidemia is discovered during a routine lipid analysis, with no symptoms usually present.

Other symptoms:

Xanthomas (in cases of familial disorders; usually present during adolescence or early adulthood)

Interpretation of Laboratory Tests

The following methods are frequently used to determine if hyperlipidemia may be present. The National Cholesterol Education Program requests that routine blood lipid

assessment occur every 5 years starting at the age of 20². Additional screening should be conducted if the patient has high total cholesterol levels, low HDL levels, or borderline total cholesterol levels and two coronary artery disease risk factors.

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BLOOD TESTS		
Test Name	Normal values	Indicators
Total Cholesterol	Total Cholesterol: < 200 mg/dL (desirable) (< 180 optimal)	200-239 mg/dL = Borderline High (borderline risk for coronary heart disease [CHD]) > 240 mg/dL = Hypercholesterolemia
Total Cholesterol for children	< 180 mg/dL	> 180 mg/dL may lead to premature atherosclerosis
Triglyceride Levels	Less than 150 mg/dL	150-199 mg/dL is Borderline High 200-499 mg/dL is High 500 mg/dL or above is Very High
HDL Cholesterol	≥ 60 mg/dL is desirable	In general, HDL levels < 40 mg/dL increases risk for CHD. Women with levels < 47 mg/dL and men < 37 mg/dL have increased risk.
LDL Cholesterol	< 100 mg/dL (optimal) 100-129 mg/dL (near optimal/above optimal)	130-159 mg/dL Borderline High 160-189 mg/dL High ≥ 190 mg/dL Very High
C-reactive Protein (CRP)	CRP < 1 mg/dl	CRP > 1 mg/dl (> 10 mg/dl often seen) suggests inflammation
TESTS		
Test Name	Indicators	
Skin assessment	Xanthelasmas and xanthomas are fatty deposits under the skin surface commonly found in patients with metabolic disorders, such as elevated blood lipids and genetic disorders such as familial hypercholesterolemia. A biopsy will show fatty deposits.	

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When interpreting the results, the following guidelines must be considered: 1) as age increases, so do lipid levels; 2) patients must fast for at least 12 hours before having their blood taken because chylomicron clearance can take up to 10 hours. For screening purposes however, measurement of cholesterol does not require a fasted sample; 3) the patient's medical and lifestyle history must be taken into account, therefore patients should be in a steady state (no significant weight loss, drug use, illness, etc); 4) if hyperlipidemia is from secondary causes, improvement on those may improve the lipid profile. If abnormal results are attained, at least 2 more samples should be taken before diagnosing.

Common Current Treatments

The mainstay of treatment for hyperlipidemia is first dietary and lifestyle alterations, followed by reassessment and determination if drug therapy is necessary. Treatment decisions should be based on LDL levels. If a mild elevation of LDL is evident, dietary therapy should be tried for at least 6 months prior to prescribing medication. For more severe cases of hypercholesterolemia (LDL \geq 190 mg/dL or if coronary artery disease is present), then medications may be needed sooner. Patients with familial hypercholesterolemia will most likely require medication, starting in early childhood. Furthermore, a detailed family history should be evaluated and willingness to change lifestyle factors should be considered because these factors may necessitate more aggressive therapy.

Medications

The following table lists some classes and examples of medications commonly prescribed to patients at risk or suffering from hyperlipidemia. The order of medications listed in the table is not intended to represent subsequent treatments; complementary medications may be needed to address multiple symptoms.

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LIPID LOWERING MEDICATIONS		
Indication	Class/Examples	Notes
Elevated Lipid Levels	HMG CoA Reductase Inhibitors (Statins): -Lovastatin -Pravastatin	May increase liver enzymes and myopathy occurrence
Elevated Lipid Levels	Bile Acid Sequestrants: -Cholestyramine -Colestipol	Can produce GI distress and impair the absorption of other drugs
Elevated Lipid Levels	Fibrinates -Clofibrate -Gemfibrozil	Gallstone, dyspepsia, and myopathy may occur.
Elevated Lipid Levels	Nicotinic Acid	Flushing of the skin very common. May increase the risk for gout and hepatotoxicity.
Elevated Lipid Levels	Fish Oil: Eicosapentaenoic Acid (EPA) and Docosahexaenoic Acid (DHA)	2 to 4 grams each day effective in lowering TG levels. May lower total and LDL cholesterol.

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Dietary Interventions

The primary nutritional goal in the treatment of hyperlipidemia is to reduce cholesterol and saturated fat intake. Saturated fat should not be more than 10% of total calories and cholesterol should not be more than 300 mg/day. Saturated fat should be replaced with either monounsaturated fats (i.e., olive oil) or polyunsaturated fats. Monounsaturated fats lower LDL cholesterol levels and may increase HDL levels. Polyunsaturated fats lower LDL levels, but in high amounts may actually lower HDL levels as well. Ingestion of at least one gram each day of EPA and DHA has been shown beneficial in reducing triglyceride levels. It is preferable to ingest these compounds through fatty fish (i.e. mackerel, herring) but capsule forms are also acceptable because cost may be a factor. Products such as Benecol® containing plant stanol esters have been shown to reduce cholesterol levels. Increasing soluble fiber (i.e., oatmeal) has been shown to reduce cholesterol levels, although the impact of this is negligible. Incorporation of such products into the diet requires minimal effort.

Weight control is very important, therefore, a weight loss regimen may be warranted to reduce blood lipid levels. Obesity and excessive caloric intake may reduce HDL levels and increase LDL levels because of increased lipoprotein (i.e., VLDL and LDL) synthesis. Vegetarian diets have shown many benefits as well. Individuals on these diets tend to have lower bodyweights and less of a risk for developing heart disease. Risk factors (eg, smoking, hypertension) need to be aggressively handled because the effectiveness of following a low fat and cholesterol diet will be limited, until these factors are removed. Alcohol, especially red wine in moderation, may reduce lipid levels, but intake should be monitored because in high quantities alcohol raises triglyceride levels. According to the American Heart Association and NCEP, the Step 1 and Step 2 diets are effective at lowering LDL and TC levels.

What to Tell the Patient and Family

When the patient's symptoms have subsided, it is important to emphasize the avoidance of foods high in saturated fat and cholesterol. Additional therapies may be warranted as well. For example: a smoking cessation program, weight reduction program, and overall dietary adherence may be needed. It is also important to instruct the whole family on all aspects of the diet and additional therapies. This applies to spouses or partners of patients.

References

1. Innerarity TL, Mahley RW, Weisgraber KH, Bersot TP, Krauss RM, Vega GL, Grundy SM, Friedl W, Davignon J, McCarthy BJ. Familial defective apolipoprotein B-100: a mutation of apolipoprotein B that causes hypercholesterolemia. *J Lipid Res* 1990, 31:1337-49.
2. National Cholesterol Education Program. Third report of the expert panel on detection, evaluation, and treatment of high blood cholesterol in adults. Final

Christopher Theberge

Report. NIH Pub. No. 52-0215. Bethesda, MD: National Heart, Lung, and Blood Institute, 2002; 284 pages.