Hyperlipidemia

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Outline

• The story of lipids
• Definition of hyperlipidemia
• Classification of hyperlipidemia
• Causes of hyperlipidemia
• Tests for Hyperlipidemia
• Whom to Screen for Dyslipidemia?
• Medications for Hyperlipidemia
The story of lipids

- Chylomicrons transport fats from the intestinal mucosa to the liver.
- In the liver, the chylomicrons release triglycerides and some cholesterol and become low-density lipoproteins (LDL).
- LDL then carries fat and cholesterol to the body’s cells.
- High-density lipoproteins (HDL) carry fat and cholesterol back to the liver for excretion.
• When oxidized LDL cholesterol gets high, atheroma formation in the walls of arteries occurs, which causes atherosclerosis.
• HDL cholesterol is able to go and remove cholesterol from the atheroma.
• Atherogenic cholesterol $\rightarrow$ LDL, VLDL, IDL
**Chylomicrons**- transport dietary lipids from the gut to the adipose tissue and liver

**Chylomicron remnants**- produced from Chylomicrons by lipoprotein lipases in endothelial cells and transport cholesterol to the liver

**VLDL**- made in the liver and secreted into plasma deliver triglycerides to adipose tissue in the process get converted to IDL and LDL

**LDL**- (bad cholesterol) delivers cholesterol to peripheral tissues via receptors and is **phagocytosed** by macrophages thus delivering cholesterol to the plaques (atheromas)

**HDL**- (good cholesterol) produced in gut and liver cells, HDL transports cholesterol from atheromas to the liver (**reverse cholesterol transport**)
• **Definition**

• Hyperlipidemia is defined as an elevation of one or more of the following: cholesterol, cholesterol esters, phospholipids, or triglycerides. Hyperlipoproteinemia describes an increased concentration of the lipoprotein macromolecules that transport lipids in the plasma.
Classification of hyperlipidemia

- Hyperlipidemias may basically be classified as either familial (also called primary) caused by specific genetic abnormalities, or acquired (also called secondary) when resulting from another underlying disorder that leads to alterations in plasma lipid and lipoprotein metabolism. Also, hyperlipidemia may be idiopathic, that is, without known cause.
Hyperlipidemias are also classified according to which types of lipids are elevated, that is hypercholesterolemia, hypertriglycerideridemia or both in combined hyperlipidemia. Elevated levels of Lipoprotein(a) may also be classified as a form of hyperlipidemia.

Relative prevalence of familial forms of hyperlipidemia
Hyperlipoproteinemia type I

Type I hyperlipoproteinemia exists in several forms:

Lipoprotein lipase deficiency (Type Ia), due to a deficiency of lipoprotein lipase (LPL) or altered apolipoprotein C2, resulting in elevated chylomicrons, the particles that transfer fatty acids from the digestive tract to the liver.

- Familial apoprotein CII deficiency (Type Ib), a condition caused by a lack of lipoprotein lipase activator.
Type I hyperlipoproteinemia usually presents in childhood with eruptive xanthomata and abdominal colic. Complications include retinal vein occlusion, acute pancreatitis, steatosis and organomegaly, and lipaemia retinalis.
<table>
<thead>
<tr>
<th>Type</th>
<th>Synonyms</th>
<th>Defect</th>
<th>Increased lipoprotein</th>
<th>Main symptoms</th>
<th>Treatment</th>
<th>Serum appearance</th>
<th>Estimated prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type II</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>a</td>
<td><em>Familial hypercholesterolemia</em></td>
<td>LDL receptor deficiency</td>
<td>LDL</td>
<td>Xanthelasma, arcus senilis, tendon xanthomas</td>
<td>Bile acid sequestrants, statins, niacin</td>
<td>Clear</td>
<td>1 in 500 for heterozygotes</td>
</tr>
<tr>
<td>b</td>
<td><em>Familial combined hyperlipidemia</em></td>
<td>Decreased LDL receptor and increased ApoB</td>
<td>LDL and VLDL</td>
<td></td>
<td>Statins, niacin, fibrate</td>
<td>Clear</td>
<td>1 in 100</td>
</tr>
<tr>
<td><strong>Type III</strong></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td><em>Familial dysbetalipoproteinemia</em></td>
<td>Defect in Apo E 2 synthesis</td>
<td>IDL</td>
<td>Tubo-Eruptive Xanthomas &amp; Palmar Xanthomas</td>
<td>Fibrate, statins</td>
<td>Turbid</td>
<td>1 in 10,000</td>
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<tr>
<td><strong>Type IV</strong></td>
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<tr>
<td></td>
<td><em>Familial hypertriglyceridemia</em></td>
<td>Increased VLDL production and Decreased elimination</td>
<td>VLDL</td>
<td>Can cause pancreatitis at high triglyceride levels</td>
<td>Fibrate, niacin, statins</td>
<td>Turbid</td>
<td>1 in 100</td>
</tr>
<tr>
<td><strong>Type V</strong></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Increased VLDL production and Decreased LPL</td>
<td>VLDL and Chylomicrons</td>
<td></td>
<td>Niacin, fibrate</td>
<td>Creamy top layer &amp; turbid bottom</td>
<td></td>
</tr>
</tbody>
</table>
Acquired (secondary)

- Acquired hyperlipidemias (also called secondary dyslipoproteinemias) may result in increased risk of premature atherosclerosis or, when associated with marked hypertriglyceridemia, may lead to pancreatitis and other complications of the chylomicronemia syndrome. The most common causes of acquired hyperlipidemia are:
- diabetes mellitus
- Use of drugs such as diuretics, beta blockers, and estrogens
- Other conditions leading to acquired hyperlipidemia include:
  - Hypothyroidism
  - renal failure
  - nephrotic syndrome
  - alcohol usage
  - Some rare endocrine disorders and metabolic disorders
Causes of Hyperlipidemia

- Diet
- Hypothyroidism
- Nephrotic syndrome
- Anorexia nervosa
- Obstructive liver disease
- Obesity
- Diabetes mellitus
- Pregnancy

- Obstructive liver disease
- Acute hepatitis
- Systemic lupus erythematosus
- AIDS (protease inhibitors)
Tests

• Because hyperlipidemia usually doesn't cause symptoms, you will need a blood test for a diagnosis. The National Cholesterol Education Program recommends that people get this test every 5 years after age 20.
The physician will compare your results to established ranges. The ranges help the physician diagnose hyperlipidemia and then decide whether you will need lifestyle modification, medical treatment, or both as treatments. The physician will also determine whether you might have atherosclerosis or other risk factors for heart disease.
Most blood tests measure levels of LDL (sometimes called "bad") cholesterol, HDL (sometimes called "good") cholesterol, total cholesterol (LDL plus HDL), and triglycerides. To have a low risk of heart disease, your desirable lipid levels are:

- LDL less than 130 mg/dL
- HDL greater than 40 mg/dL (men) or 50 mg/dL (women)
- Total cholesterol less than 200 mg/dL
- Triglycerides less than 200 mg/dL
# Medications for Hyperlipidemia

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Agents</th>
<th>Effects (% change)</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>HMG CoA reductase inhibitors</td>
<td>Lovastatin, Pravastatin</td>
<td>↓LDL (18-55), ↑HDL (5-15) ↓Triglycerides (7-30)</td>
<td>Myopathy, increased liver enzymes</td>
</tr>
<tr>
<td>Cholesterol absorption inhibitor</td>
<td>Ezetimibe</td>
<td>↓LDL (14-18), ↑HDL (1-3) ↓Triglyceride (2)</td>
<td>Headache, GI distress</td>
</tr>
<tr>
<td>Nicotinic Acid</td>
<td></td>
<td>↓LDL (15-30), ↑HDL (15-35) ↓Triglyceride (20-50)</td>
<td>Flushing, Hyperglycemia, Hyperuricemia, GI distress, hepatotoxicity</td>
</tr>
<tr>
<td>Fibric Acids</td>
<td>Gemfibrozil, Fenofibrate</td>
<td>↓LDL (5-20), ↑HDL (10-20) ↓Triglyceride (20-50)</td>
<td>Dyspepsia, gallstones, myopathy</td>
</tr>
<tr>
<td>Bile Acid sequestrants</td>
<td>Cholestyramine</td>
<td>↓LDL</td>
<td>GI distress, constipation, decreased absorption of other drugs</td>
</tr>
</tbody>
</table>

Note: HDL stands for High-Density Lipoprotein, LDL stands for Low-Density Lipoprotein, and triglycerides are a type of fat in the blood.
Whom to Screen for Dyslipidemia?

Influenced by cardiac risk factors:

- By age alone:
  - Men over age 40
  - Women over age 50 (or post-menopausal)
- Other risk factors (at any age):
  - DM, HTN, Smoking, Abdominal Obesity
  - Family history of early cardiovascular disease
- Physical signs of hyperlipidemia (at any age):
  - Xanthomata, xanthelasmas, arcus corneae, etc
- Evidence of existing atherosclerosis (at any age)
Manifestations of Dyslipidemia

Eruptive xanthomata on the forearm of a patient with severe ↑TGs

Xanthelasmas and tendon xanthomata in patients with severe ↑LDL (the patient at the bottom has heterozygous familial hypercholesterolemia)
Thank You