Objectives

By the end of lecture the student should:

✓ Discuss metabolism of each lipoprotein type.
✓ Mention types, causes, and manifestation of lipoprotein disorders.
✓ Illustrate enzymes involved in lipid transport.
Metabolism of VLDL

**Site:** liver

**Composition:**
- triglycerides 55%,
- phospholipids 20%
- cholesterol ester 15%,
- cholesterol 8%,
- protein 7-10% mainly B 100

**Function:** Transport triglycerides from liver to extrahepatic tissues
Final destruction in liver, extrahepatic tissues (e.g., lymphocytes, fibroblasts) via endocytosis
Metabolism of LDL

**Source:**
From VLDL, some production by liver.

**Composition:**
- 13% triglycerides
- 28% phospholipids
- 48% cholesterol ester
- 10% free cholesterol
- 20% protein mainly apo B\(_{100}\) & E

**Function:**
Carry cholesterol from liver to extra hepatic tissue
Final destruction in liver, extrahepatic tissues (e.g., lymphocytes, fibroblasts) via endocytosis.
Over supply of cholest. (from LDL, HDL, chylomicron remnants) ↓ by:

- (-) **HMG CoA reductase** $\rightarrow \downarrow$ cholesterol synthesis

- (+) **ACAT** (Acyl-CoA cholesterol acyl transferase) which transfer FA form fatty acyl CoA to cholesterol $\rightarrow$ cholest. Ester

- (-) synthesis of new **LDL receptors** $\rightarrow \downarrow$ further entry of LDL into cell.
Metabolism of HDL

Sources:
HDL is synthesized, secreted from liver & intestine

Composition:
- Triglycerides 3%.
- Free cholesterol 5%.
- Cholesterol esters 15%.
- Phospholipids 25%
- Proteins 50% mainly apo A
Cholesterol + Lecithin                             Cholesteryl ester + Lysolecithin
(From tissues)         (From HDL)                                                  (To HDL)                          (To Tissues)

LCAT – apo A₁

Cholesterol + Lecithin                             Cholesteryl ester + Lysolecithin
(From tissues)         (From HDL)                                                  (To HDL)                          (To Tissues)
Functions of HDL:

1- Act as a source for apo C and apo E that are required in the metabolism of chylomicrons & VLDL

2- Removing free cholesterol from extra hepatic tissues and esterifying it using LCAT
   The apo A1 of HDL activates LCAT. Cholesterol ester transferred to HDL, carry cholesterol ester to liver a process known as reverse cholesterol transport

3- Transport phospholipids from liver to tissues
(a)
A group of disorders characterized by increased plasma lipoproteins

According to Fredrickson:
They can be classified into 5 types
Each of which may be familial or acquired
Type I, Hyperlipoproteinemia
The familial type is due to deficiency of lipoprotein lipase enzyme. It is characterized by increased plasma chylomicrons and somewhat VLDL, but LDL and HDL are reduced. There is a marked increase in plasma triacylglycerols and some increase in plasma cholesterol may occur. The plasma is turbid.
Type II, Hyperbetalipoproteinemia
Type II, Hyperbetalipoproteinemia

✓ Characterized by increased plasma LDL
✓ The familial type is caused by reduced LDL metabolism due to defective LDL receptors
✓ There is marked increase in plasma cholesterol (familial hypercholesterolemia)
✓ Plasma is clear
✓ The acquired type occurs in hypothyroidism
Type III, Dysbetalipoproteinemia

- Characterized by increased VLDL (IDL) & chylomicrons remnants
- The plasma is turbid
- There is hypercholesterolemia & hypertriacylglyceridemia
- The familial type is caused by defective apo E necessary for uptake and metabolism of VLDL and chylomicron remnants by liver
<table>
<thead>
<tr>
<th>Type IV, Hyperprebetalipoproteinemia</th>
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<tbody>
<tr>
<td>- Characterized by increased plasma VLDL, triacylglycerols &amp; some increase in plasma cholesterol</td>
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<tr>
<td>- The plasma is turbid</td>
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<tr>
<td>- The familial type is due to increased formation of triacylglycerols from carbohydrates</td>
</tr>
<tr>
<td>- The acquired type occurs in severe type II DM, obesity &amp; alcoholism</td>
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Type V Hyperchylomicronemia & Hyperprebetalipoproteinemia

- Characterized by increased chylomicrons and VLDL → increase triacylglycerols & some what cholesterol
- The plasma is turbid
- The cause of disease is unknown, but may be due to increase formation of apo- B.
- It is usually associated with obesity and glucose hypotolerance
Type VI, hyperalphalipoproteinemia

- characterized by increased HDL & hypercholesterolemia
- It occurs during estrogen therapy.
1. Abetalipoproteinemia

- Familial disease.
- Caused by failure of liver & intestine to synthesize apo B → absence of chylomicrons, VLDL & LDL from blood
- Marked decrease in plasma lipids
- The intestine fails to absorb triacylglycerols → fatty diarrhea
- The liver fails to mobilize fats to the blood → fatty liver
2. Hypobetalipoproteinemia

- Familial disease

- Caused by decreased formation of the apo-B100 by the liver → decreased formation of VLDL & LDL

- Decreased plasma lipids
3. Alphalipoprotein deficiency

• Familial disease

• Caused by failure of the liver to synthesis apo-A

• Cholesterol esters accumulate in tissues (Tangiers disease)

• Plasma triacylglycerols are increased due to deficiency of apo C-II the activator of lipoproteins lipase
• HDL is absent in Tangier disease

** There is an important relationship between atherosclerosis and HDL:

Decreased HDL is associated with atherosclerosis
Increased HDL represents protection against atherosclerosis
Increased LDL/HDL ratio $\rightarrow$ predispose to atherosclerosis
Decreased LDL/ HDL ratio $\rightarrow$ good sign
Lecithin-cholesterol acyl transferase deficiency:

- Familial disease

- Abnormal plasma HDL, LDL and VLDL are present

\[ \text{Cholesterol + Lecithin} \xrightarrow{\text{apo A}_1} \text{Cholesterol ester + Lysolecithin} \]

(from tissues) (from HDL) (to HDL) (to tissues)
Enzymes Involved in Lipid Transport

(1) LCAT:
- Transfer acyl group from lecithin (HDL) to cholesterol forming cholesterol ester & lysolecithin
- Site: plasma
- Activated by apo A₁ (HDL)
(2) Lipoprotein Lipase:
- Site: wall of blood capillaries in all tissues except liver and brain.
- Attached to endothelial cells by heparin sulphate
- It hydrolyses triglycerides present in chylomicrons & VLDL
(3) Hepatic Lipase:
- Site: endothelial cells of the liver,
- Similar action to lipoprotein lipase but it is more specific in hydrolyzing TG in smaller particles as VLDL remnants (IDL) & chylomicrons remnants.
(4) Mobilizing Lipase (Hormone sensitive triglyceride lipase):
- Site: adipose tissue cells,
- controls the release of FA from adipose tissue to plasma.
(5) (HMG COA) reductase enzyme
Control cholesterol biosynthesis (Key enzyme). Activity is controlled by amount of cholesterol cells \(\rightarrow\) which in turn largely depends on cholesterol uptake from the blood.
Questions
Thank You