

Lipoprotein Metabolism and Disorders

Semester 4th –UG

BY

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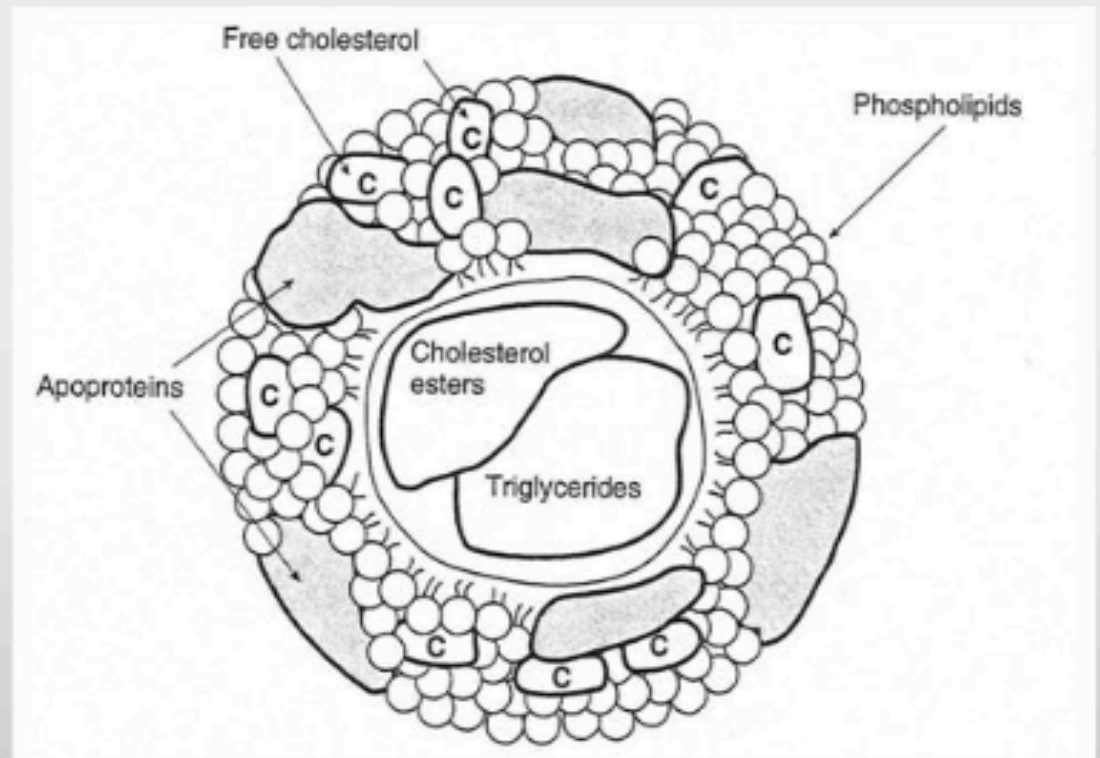
Tue-18th June-19

Lipoprotein Metabolism

All the lipids contained in plasma, including fat, phospholipids, cholesterol, cholesterol ester and fatty acid, exist and transport in the form of lipoprotein

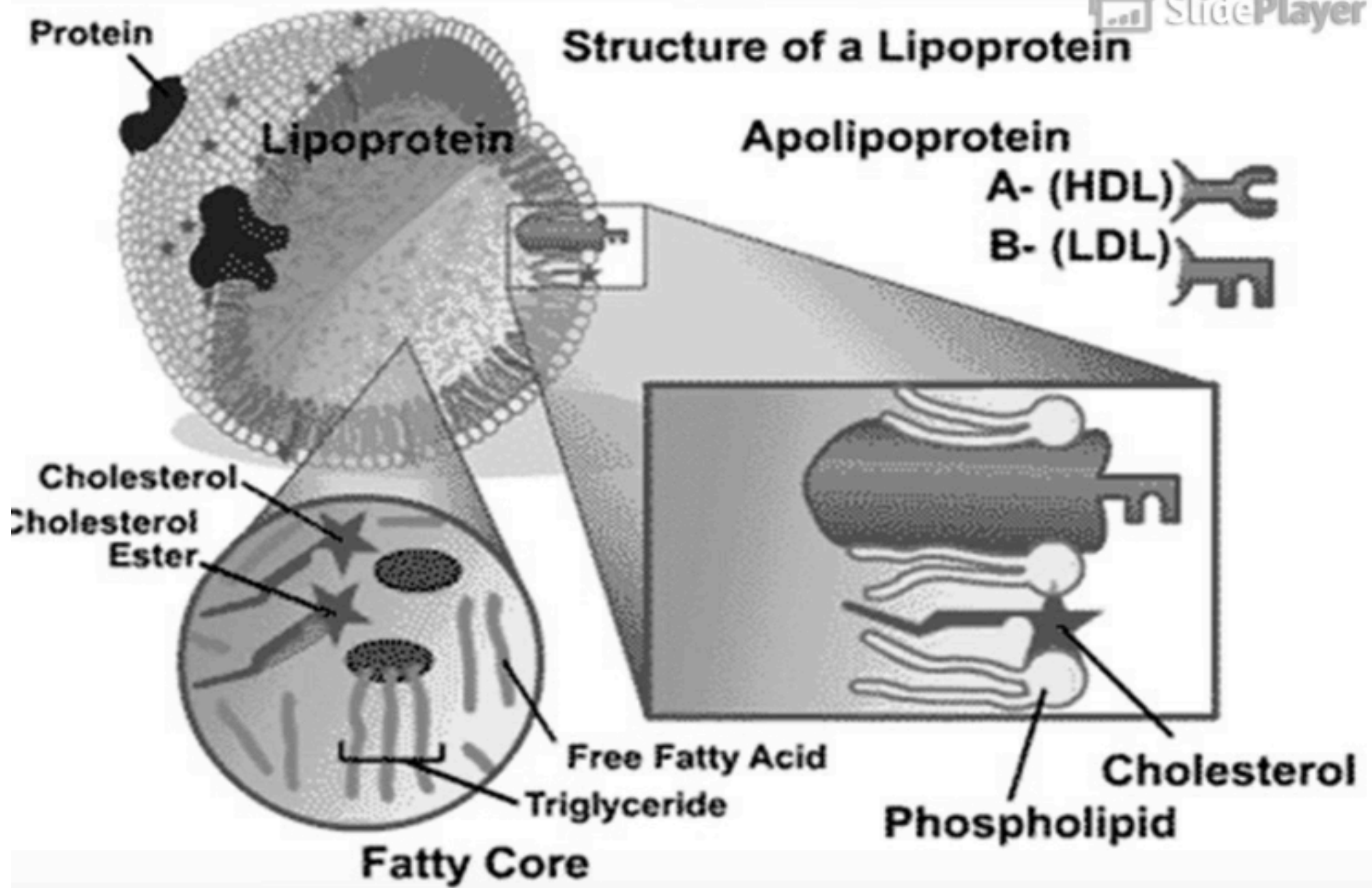
Structure

- Non-covalent assemblies of lipids and proteins
- LP core
 - Triglycerides
 - Cholesterol esters
- LP surface
 - Phospholipids
 - Proteins
 - cholesterol

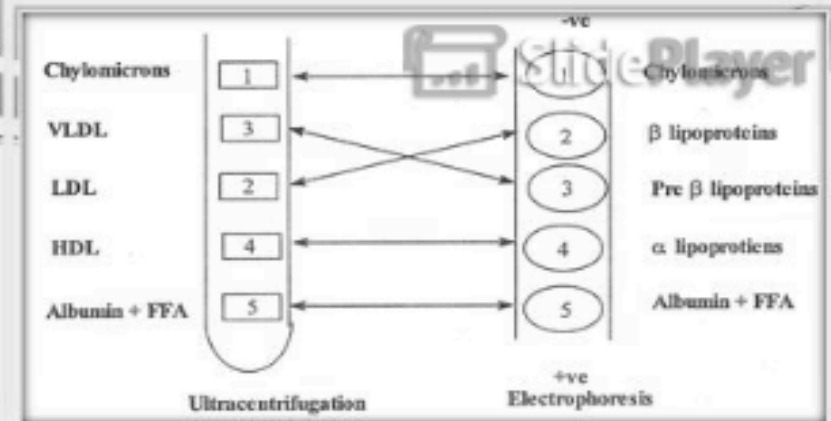


Function as transport vehicles for triacylglycerols and cholesterol in the blood

Structure of a Lipoprotein



Lipoprotein Nomenclature, Composition and separation



Major Protein	apoB 48	apoB 100	apoB 100	apoA-I
Major Lipid	TG	TG	CE	CE



1. Electrophoresis method:

CM (chylomicron) low
 ↓
 β-Lipoprotein high
 pre β-Lipoprotein
 α- Lipoprotein

2. Ultra centrifugation method :

CM (chylomicron) fast
 ↓
 very low density lipoprotein (VLDL)
 low density lipoprotein (LDL)
 high density lipoprotein (HDL) slow

Lipids are Transported as Lipoproteins

- All lipids in plasma are transported in the form of lipoproteins .
- Transport dietary lipids from intestine to liver (exogenous)  Chylomicrons
- Transport lipids from liver to peripheral tissues (endogenous)  VLDL (very low density lipoproteins)

Apolipoproteins (apoproteins)

- They are the protein components of lipoproteins
- Consisting:
- 60% of some lipoproteins (HDL)
- and 1% of some lipoproteins (chylomicrons)
- The **major apoprotein** of HDL is designated **A**, and of LDL is **apo-B** which is also found in VLDL and chylomicrons

Functions of Apo-lipoproteins

1. To combine and transport lipids
2. To recognize the lipoprotein receptors
 - Apo-B₁₀₀ is the ligand for LDL-receptors
 - Apo-A₁ is the ligand for HDL receptor.
3. Activators for certain enzymes involved in lipoprotein metabolism
 - Apo C II activates lipoprotein lipase and
 - Apo-A₁ activates LCAT (Lecithin Cholesterol Acyltransferase, formation of cholesterol esters in lipoproteins).

Metabolism of Lipoproteins

Metabolism Of Chylomicron

FUNCTION :

transport exogenous TG (dietary fat) from the intestine to the peripheral tissues; where TG is used as an energy source or stored in adipose tissue

Step 1:

- Nascent chylomicrons are formed in the intestinal mucosa and pass to the blood stream

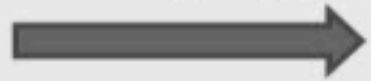
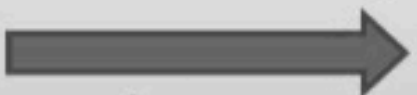
Nascent chylomicrons consists of :

- rich in dietary TG + minimal amount of dietary cholesterol + apoB₁, which is necessary for assembly of the chylomicron.
- The lipid component is very high, thus, it is of least density.

Step 2:


After passage to blood, addition of **apoC** and **apoE** from HDL leads to the formation of mature chylomicrons.


Step 3:

- Capillary lipoprotein lipase (LPL), activated by apoC, hydrolyzes TG present in chylomicrons into  *fatty acids + glycerol + producing chylomicron remnant (chylomicron containing less TG and more cholesterol+ apoE+ apoB)*  which are taken up by the liver through endocytosis.

Step 4

1. Glycerol → is phosphorylated in the liver by glycerol kinase → glycerol 3-phosphate which is used to **synthesize more VLDL**.
2. Free fatty acids → enter the **adipose tissue** to produce **TG for storage**.
In muscle → the fatty acids are oxidized to provide **energy**.
3. ApoC returns to HDL

4. Chylomicron remnants  attach to apoE receptors in the liver and are endocytosed.

5. Dietary cholesterol delivered to the liver via chylomicron remnants is used for  bile acid synthesis.

6. Excess cholesterol is  excreted in bile.

Metabolism of VLDL and production of LDL

1- Synthesis of nascent VLDL

- Nascent VLDL are **synthesized in** the liver.
- They **transport** TG synthesized in the liver (endogenous fats) to peripheral tissues to be available as energy source or for storage.
- also contain **some** cholesterol (17%)
- Its **apoprotein** is apoB-100.

2- Conversion to mature VLDL:

- Nascent VLDL are released into the blood by the liver.
- They receive apo-C11 , E and cholesterol esters from HDL in plasma, converting to mature VLDL.

3-Degradation by plasma lipoprotein lipase (LPL):

- In peripheral tissues, adipose tissue and muscles, VLDL/TG are hydrolyzed by lipoprotein lipase (LPL).
- The LPL (activated by apoC of VLDL) hydrolyses TG/VLDL into fatty acids +glycerol+ VLDL remnants (Intermediate-density lipoproteins (IDL); containing less of TG and more of cholesterol).
- A small part of VLDL remnant is taken up by the liver, by receptor-mediated endocytosis.
- The major fraction of VLDL remnant further loses TG, so as to be converted to LDL.
- This conversion of VLDL to IDL and then to LDL is referred to as: lipoprotein cascade pathway.

Low density lipoproteins (LDL)

- All LDL arise normally from VLDL metabolism.
- Structure of LDL:
- Apo-B₁₀₀ is the only apolipoprotein in LDL particles.
- LDL is a cholesterol-rich particle, because it has minimum TG

The function of LDL:

- 1- transport cholesterol from liver to peripheral tissues
- 2- regulate cholesterol synthesis.
- 3-LDL are important source of cholesterol to extrahepatic tissues.
- 4-. It is the major transport form of cholesterol/blood
- 5- The liver has a major role in controlling LDL cholesterol/ plasma due to:
 - (1) Most of the LDL receptors are present in the liver;
 - (2) The liver synthesizes cholesterol.
 - (3) It removes cholesterol from lipoprotein remnants.
 - (4) It is the only organ that can excrete cholesterol through bile.

It is risk factor;

- High levels of LDL -cholesterol increase the risk of atherosclerosis.


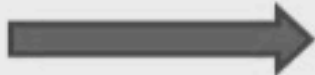
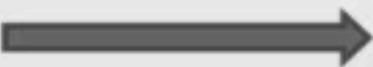
Fates of Free Cholesterol Transported to the Cells by LDL:

- (1) Incorporated into cell membranes.
- (2) Metabolized to steroid hormones.
- (3) Re-esterified and stored.
- (4) excreted through liver.

Metabolism of high density lipoproteins (HDL)

- They are formed by the liver cells and intestinal mucosa.
- These are the smallest and the most dense lipoprotein particles.
- They contain large amount of proteins (50-60%) and very little triglycerides, while the predominant lipid is phospholipid.

Function of HDL

- 1- Removing free cholesterol from extra hepatic tissues  and esterifying it using plasma enzyme called lecithin-cholesterol-acyl transferase (LCAT). The apo A1 of HDL activates LCAT.
- they transport cholesterol esters  to the liver.
- Hepatic lipase (similar to LPL) hydrolyses HDL and cholesterol esters  free Cholesterol, which either:
 - ❖ Enters in the formation of lipoprotein.
 - ❖ Converted to bile acid.
 - ❖ Excreted into bile for removal from the body.