Biochemstry Team

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Lipoprotein Metabolism

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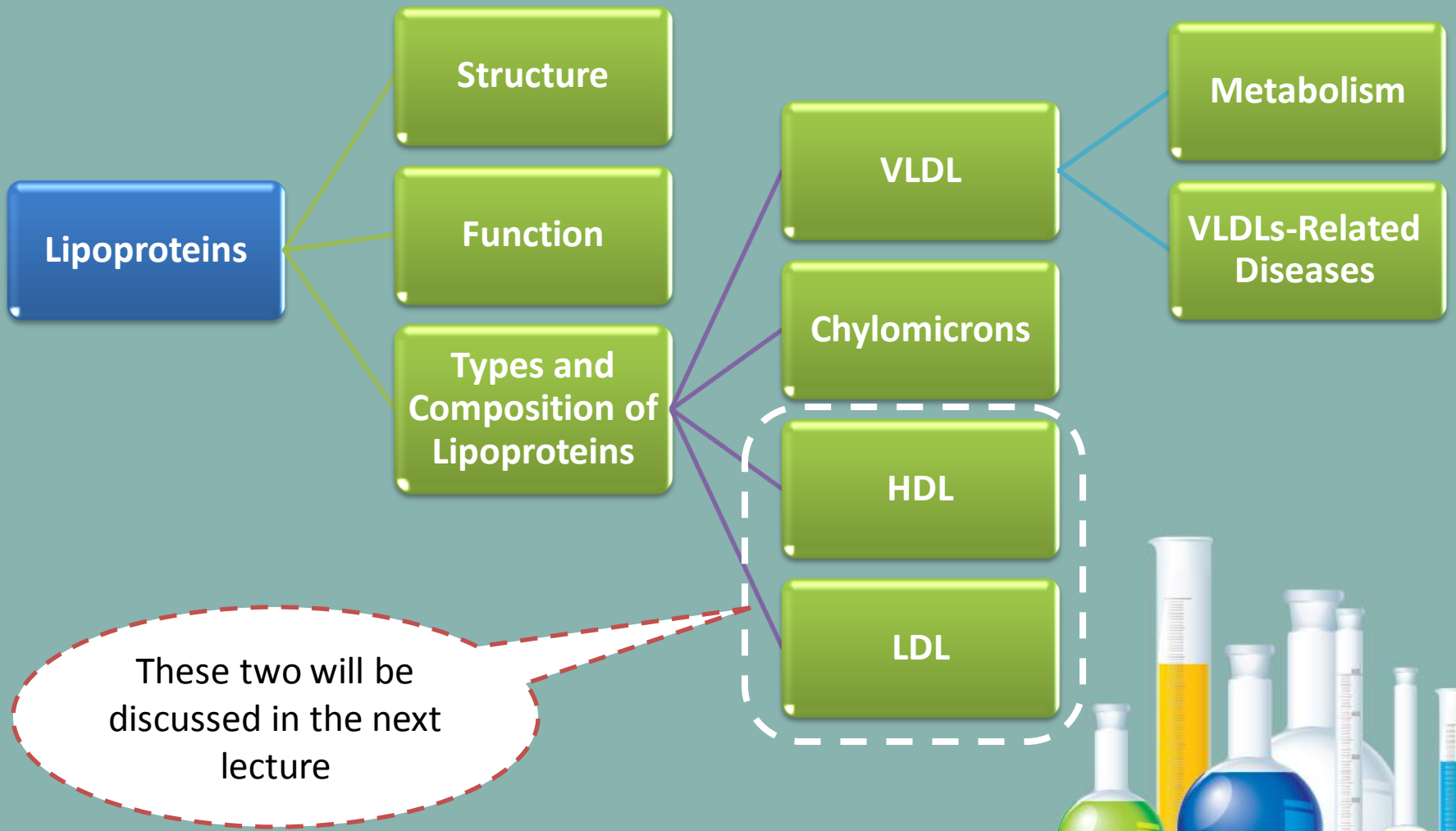
Objectives:
Not be given ☹

Red = imp

Blue = explain

Green= addition notes

Mind mab


Lipoproteins
Structure
Function
Types and Composition of Lipoproteins
VLDL
Chylomicrons
HDL
LDL
Metabolism
VLDLs-Related Diseases
These two will be discussed in the next lecture

Introduction

Lipid compounds:

Relatively water insoluble(Except ketone bodies)

Therefore, they are transported in plasma (aqueous) as **Lipoproteins**

lipoproteins and Related Clinical Problems

- Atherosclerosis and hypertension
- Coronary heart diseases
- Lipoproteinemias (hypo- and hyper-)
- Fatty liver = (hepatic steatosis)

Lipoprotein Structure

Protein part

: **Apoproteins or apolipoproteins**

Abbreviations: Apo-A, B, C, D, E

Functions:

Structural and transport function (most important)

*Enzymatic function (activation of enzymes)

**Ligands for receptors (for recognition)

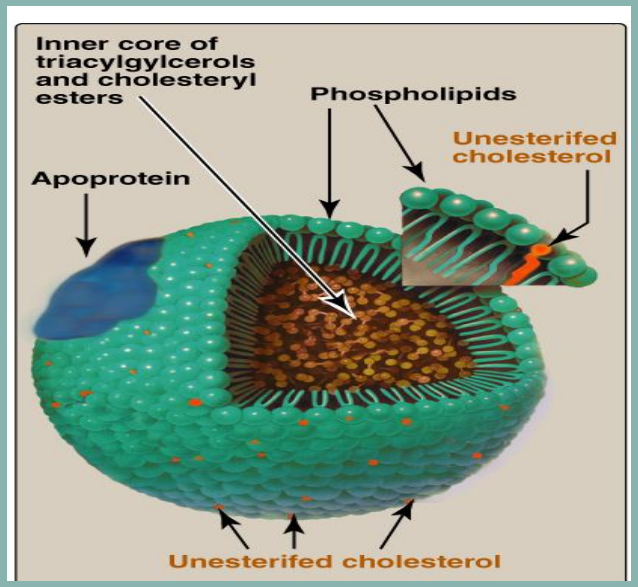
Lipid part:

- According to the type of lipoproteins
- Different lipid components in various combinations

*Enzymatic function They are not enzyme but act as a cofactor, for example, ApoC II cofactor for lipoprotein lipase.

**Ligands for receptors : so, the receptor will identify the Apoprotein.

Spherical molecules of lipids and proteins (apoproteins)



Outer coat (Hydrophilic):

- - Apoproteins
- - Phospholipids
- - Cholesterol(Unesterified) has free hydroxyl group

Inner core (Hydrophobic):

- TG(triacyl glycerol)
- - Cholesterol ester (CE)

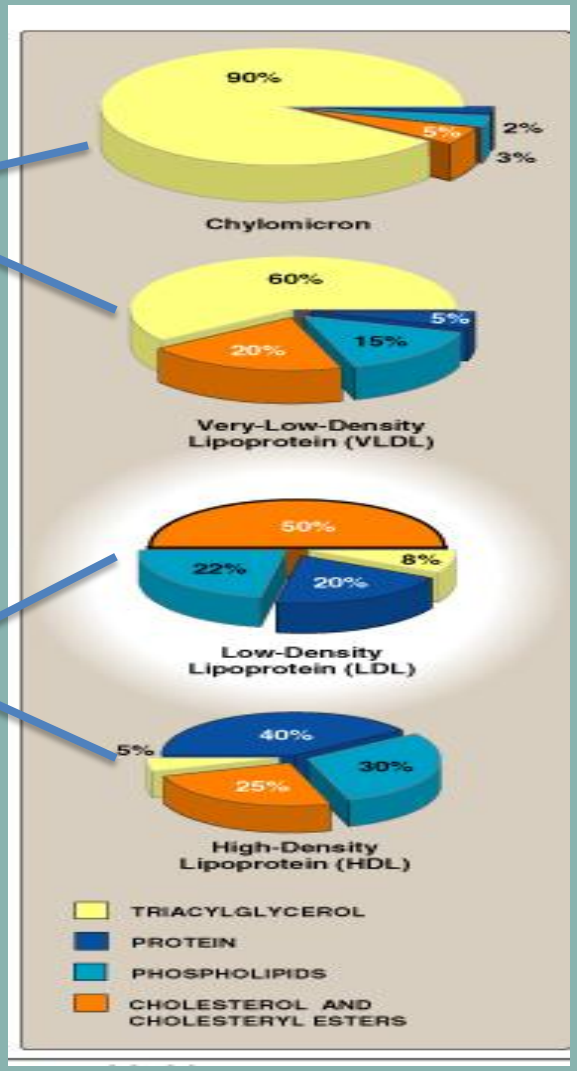
Lipoproteins differ in size, density & electrophoretic mobility according to their composition.

Lipids are low in density but big in size
Proteins have high density but small size

Types and Composition of Lipoproteins

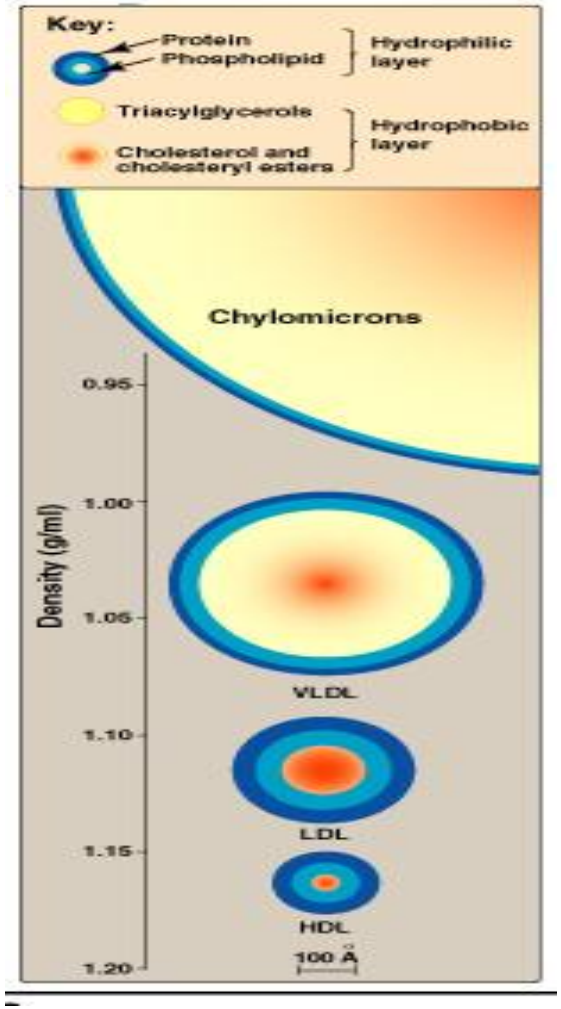
Chylomicrons + VLDL are MAINLY composed of triacylglycerol

• LDL + HDL Rich of cholesterol.
LDL mainly has free cholesterol.
HDL manily has esterified cholesterol



Chylomicrons(largest size , lowest density)
Very low density Lipoprotein (VLDL)
Low density Lipoprotein (LDL)
High density Lipoprotein (HDL)
(smallest size , hightest density)

Ultracentrifugation & Electrophoresis of Lipoproteins



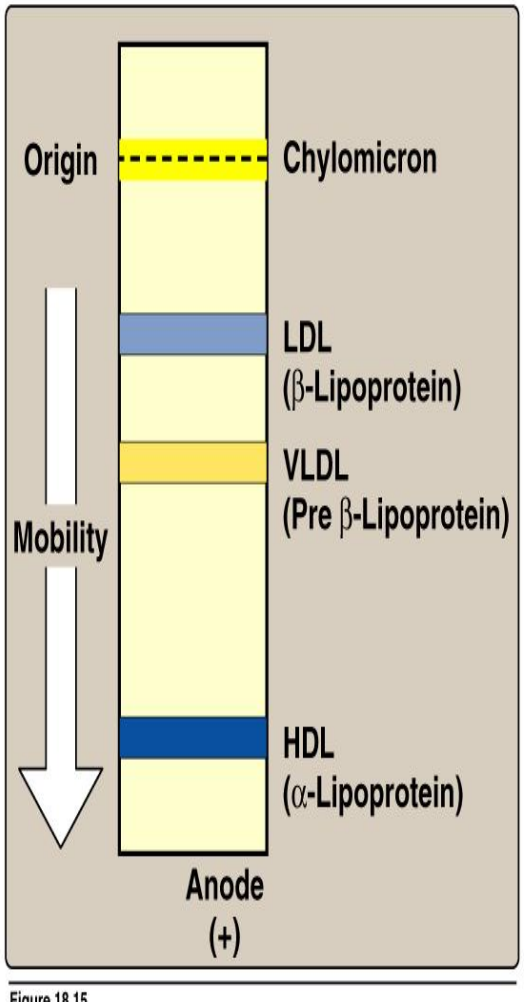


Figure 18.15

Chylomicron → very big to the extent it does not move

*LDL & VLDL → VLDL is more mobile although LDL is smaller in size. Why?

VLDL is more negative in charge so is attracted more to the +ve anode

HDL → fast molecule

movement in gel media

Mainly depends on size with some exceptions*

Plasma Lipoproteins

For triacylglycerol transport (TG-rich):

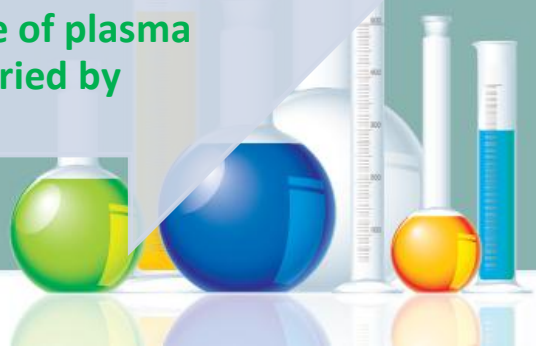
- - Chylomicrons: TG of dietary origin
- - VLDL: TG of endogenous (hepatic) synthesis

For cholesterol transport (cholesterol-rich):

- LDL: Mainly free cholesterol
- HDL: Mainly esterified cholesterol

Chylomicrons

- Assembled in intestinal mucosal cells
- • Lowest density, largest size
- Highest % of lipids and lowest % proteins
- Highest triacylglycerol (dietary origin)
- Carry dietary lipids to peripheral tissues
- Responsible for physiological milky appearance of plasma (up to 2 hours after meal) milky appearance of plasma is Because of dietery TAG carried by chylomicrons



Very Low Density Lipoproteins VLDLs

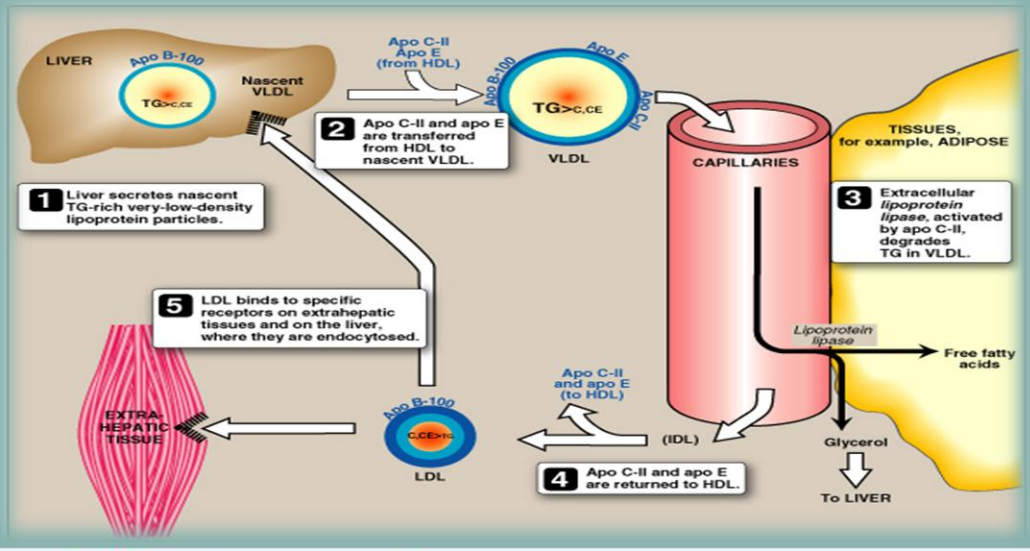
- Assembled in liver
- High triacylglycerol (hepatic origin)
- Carry lipids from liver to peripheral tissues
- Nascent VLDL: contains *Apo B-100
- **Mature VLDL: Apo B-100 plus Apo C-II and Apo E (from HDL)

Metabolism of VLDLs

- Assembled and secreted by liver
- Mature VLDLs in blood
- Modifications of circulating VLDLs
- End products: IDL and LDL

*Abo-B 48 in the wall of chylomicrons

**Modification and maturity : dynamic interaction between lipoprotein



Nascent VLDL → (take apo-C II and apo-E) from HDL and become mature → TG is degraded by <u>extracellular</u> lipoprotein lipase " in the endothelial lining of the walls of capillaryies" : to glycerol (goes to liver) and FA (goes to tissues)

After that VLDL becomes IDL "intermediate density lipoprotein" → loose lipids and give (apo-C II and apo-E) to HDL and become LDL → go to LDL receptor in liver

Lipoprotein lipase

Extracellular enzyme, anchored by heparan sulfate to the capillary walls of most tissues

Predominantly present in **adipose tissue**, **cardiac** & **skeletal** muscle

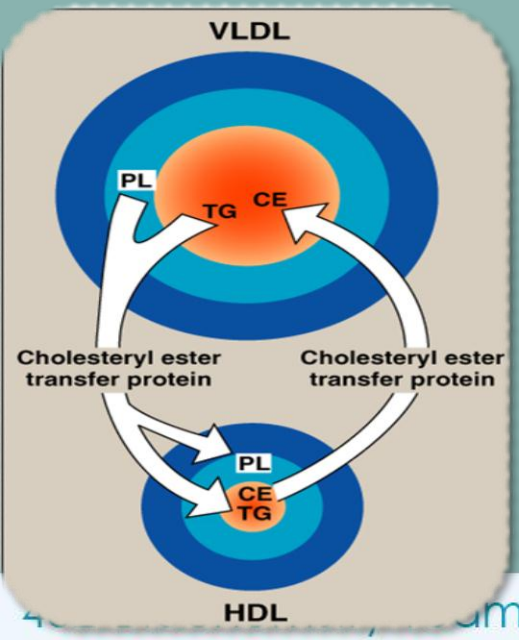
Requires ApoC-II for activation

Degrades TG into glycerol and free fatty acids

Insulin stimulates its synthesis and transfer to the luminal surface of the capillary

If deficient (or if apo C-II is deficient) → type 1 hyperlipoproteinemia = familial lipoprotein lipase deficiency)

Lipid-Transfer Protein



Metabolism of VLDLs: Mature VLDLs

Assembled and secreted by liver directly into blood as nascent form

Mature VLDLs: contain Apo B-100 **plus** Apo C-II and Apo E.

ApoC-II is required for activation of lipoprotein lipase

Lipoprotein lipase is required to degrade TG into glycerol and fatty acids

Modifications of Circulating VLDLs

1- Degradation of TG by lipoprotein lipase → VLDLs become:

- Smaller in size
- More dense

2- Apo C & Apo E return back to HDL

3- Some TG are transferred from VLDL to HDL in exchange with cholesterol ester (By cholesterol ester transfer protein)

VLDL ⟶ IDL (returns Apo E to HDL) ⟶ LDL

* TG-transfer protein : important for the synthesis of chlymicron and VLDL

VLDLs-Related Diseases

Hypolipoproteinemia

Defect in *TG-transfer protein
Apo B-100 cannot be loaded with lipid
Accumulation of TG in liver

Hyperlipoproteinemia

Fatty Liver (hepatic steatosis)

Imbalance between hepatic synthesis of TG
and secretion of VLDLs.
Accumulation of TG in liver

Type I Hyperlipoproteinemia

Familial Lipoprotein lipase deficiency
- Due to deficiency of lipoprotein lipase or its cofactor (Apo C-II)

Shows a dramatic accumulation (≥1000 mg/dl) of chylomicrons in plasma
- Usually associated with acute abdomen due to acute pancreatitis
- ↑ plasma TG even in the fasted state

Type III Hyperlipoproteinemia

- Familialdysbetalipoproteinemia
- Due to Apo E deficiency
- Associated with hypercholesterolemia &premature atherosclerosis

Questions

Which of the following lipoproteins has the largest size?

a.chylomicrons
b.VLDL
c.LDL
d.HDL

which of the following is a function of VLDL?

a. carry dietary lipids to peripheral tissue
b. carry lipids to the liver
c. carry lipids from the liver to peripheral tissue
d. cause hyperlipoproteinemia

A patient with a family history of hypercholestrolemia and premature atherosclerosis most likely has:

a. type III hyperlipoproteinemia
b. type I hyperlipoproteinemia
c. fatty liver
d. heart failure

which of the following is required for lipoprotein lipase activation?

a. Apo B-100
b. Apo CII
c. Apo E
d. Heparin sulfate

Ans:
a,c,a,b

Thank you
Good luck
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