بسم الله الرحمن الرحيم

Lipoprotein Metabolism

By

Reem M. Sallam, M.D., MSc., Ph.D.

Introduction

Lipid compounds:

Relatively water insoluble

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

Lipoprotein Structure

Protein part: Apoproteins or apolipoproteins

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

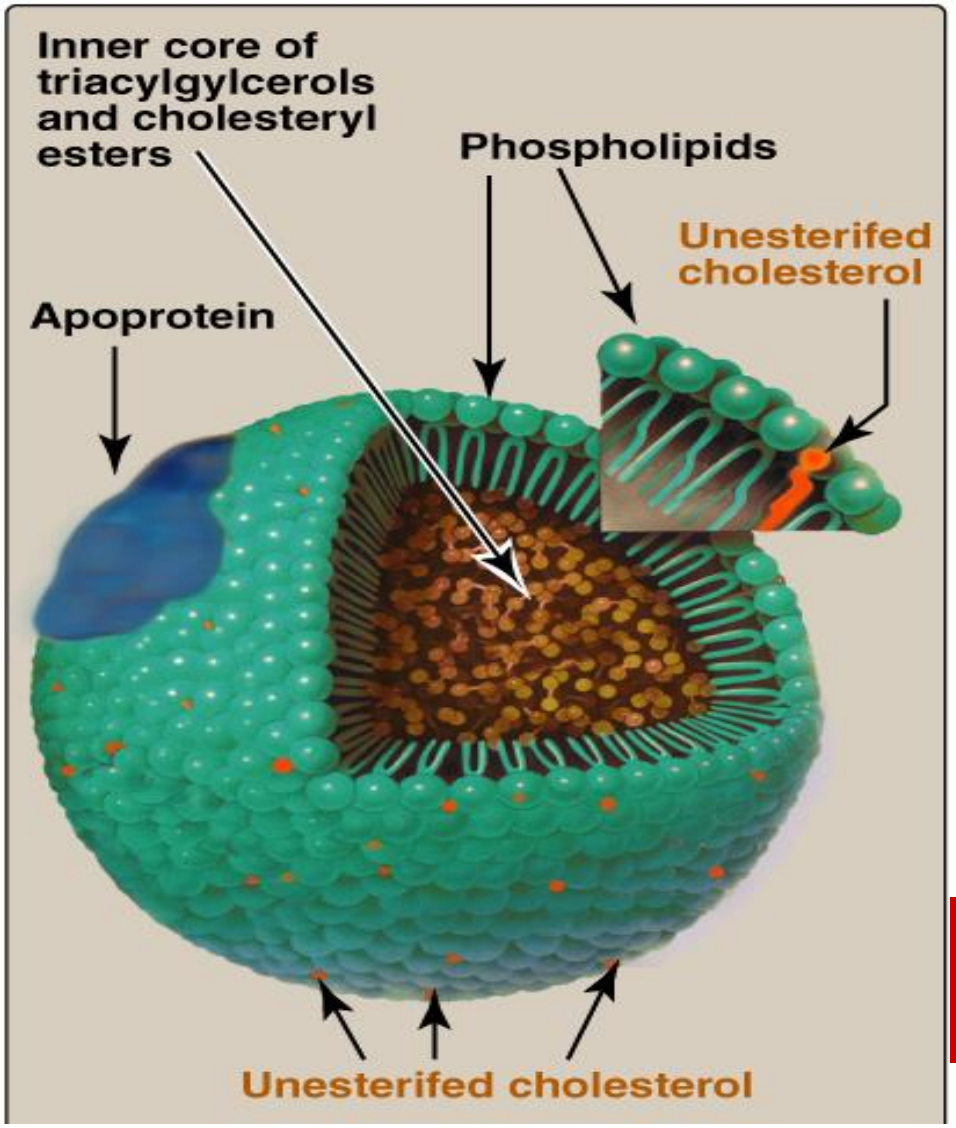
Functions:

- Structural and transport function
- Enzymatic function
- Ligands for receptors

Lipid part:

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

Spherical molecules of lipids and proteins (apoproteins)



Outer coat:

- Apoproteins
- Phospholipids
- Cholesterol (Unesterified)

Inner core:

- TG
- Cholesterol ester (CE)

Lipoprotein Structure

Types of Lipoproteins

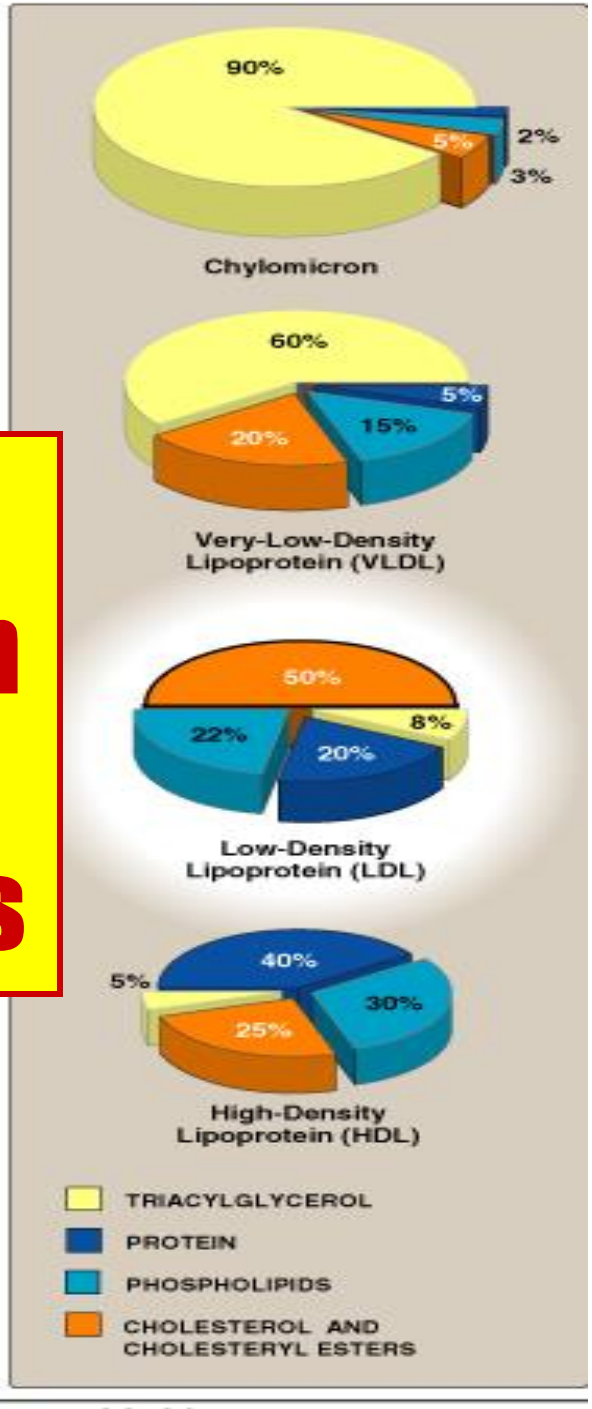
- **What's different in various types of lipoproteins?**

They differ in lipid and protein composition and therefore, they differ in

- Size and density

- Electrophoretic mobility

Types and Composition of Lipoproteins

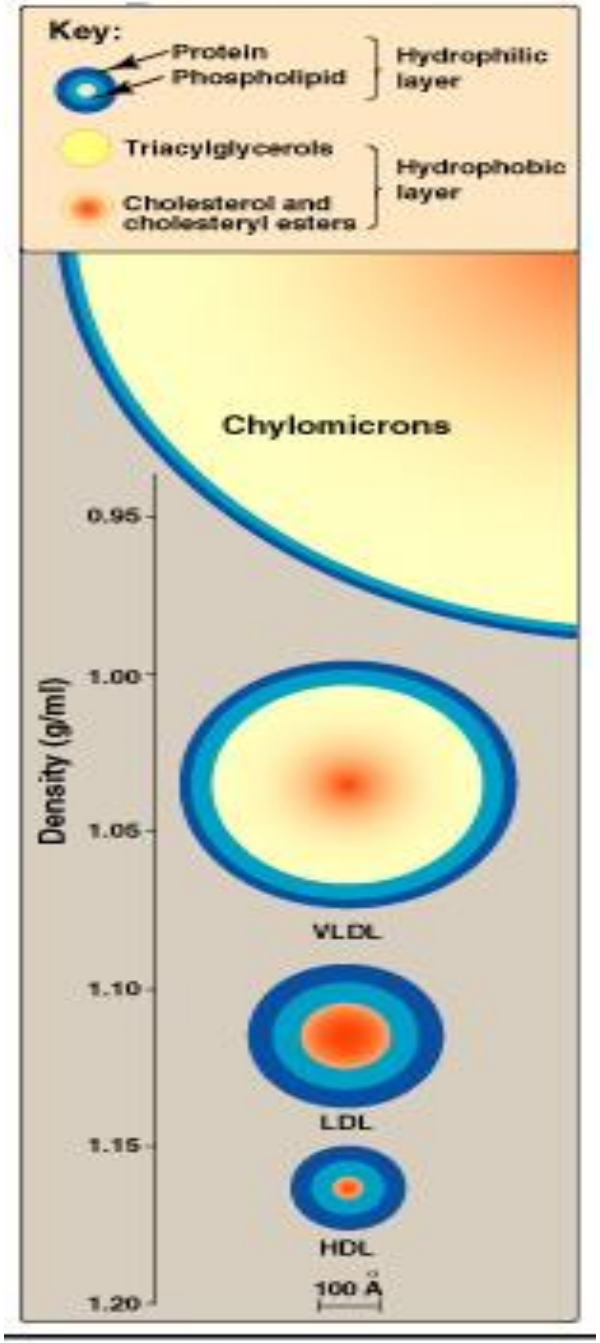


Chylomicrons

Very low density Lipoprotein (VLDL)

Low density Lipoprotein (LDL)

High density Lipoprotein (HDL)



Ultracentrifugation of Lipoproteins

Lipoprotein Electrophoresis

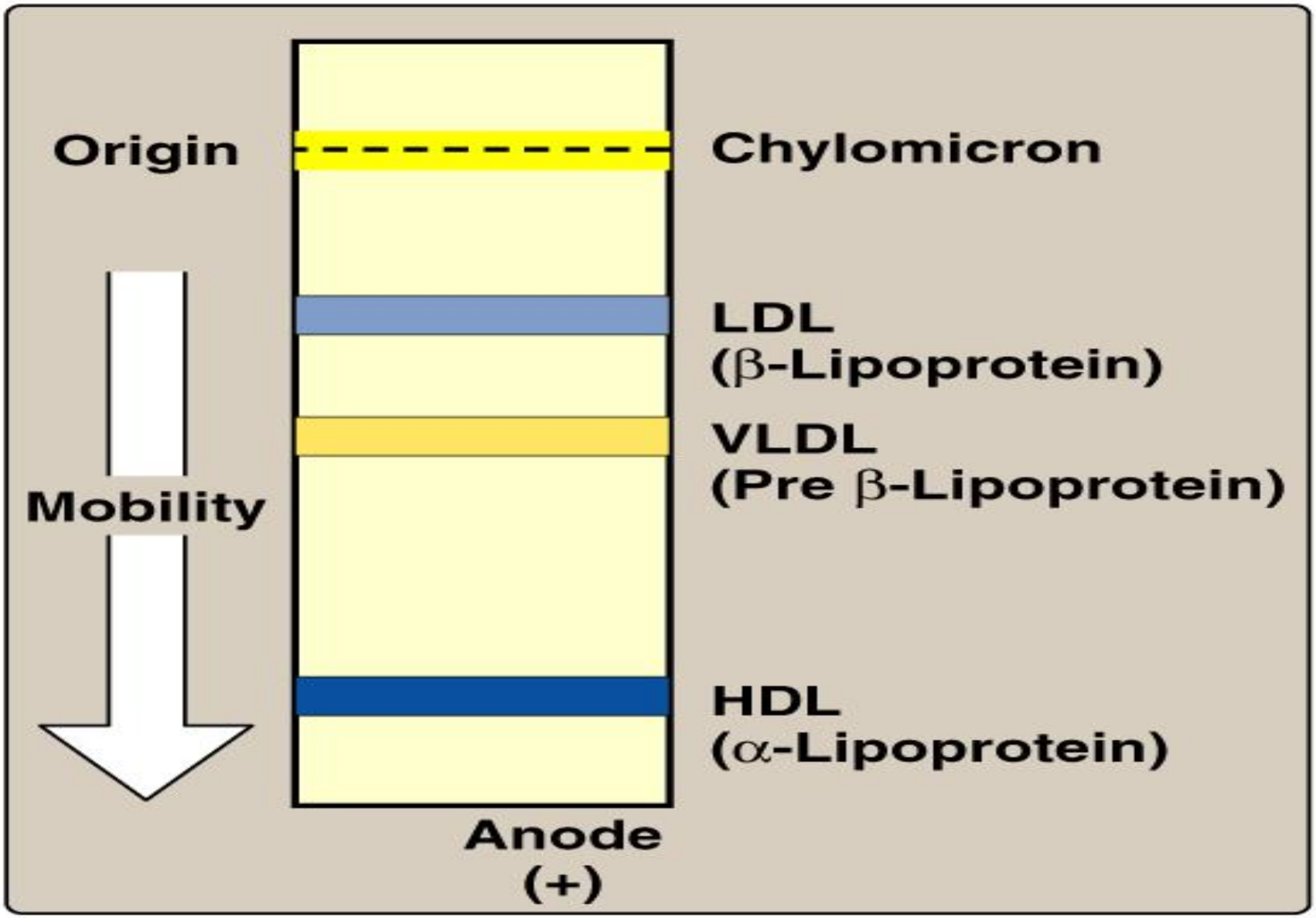


Figure 18.15

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)

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

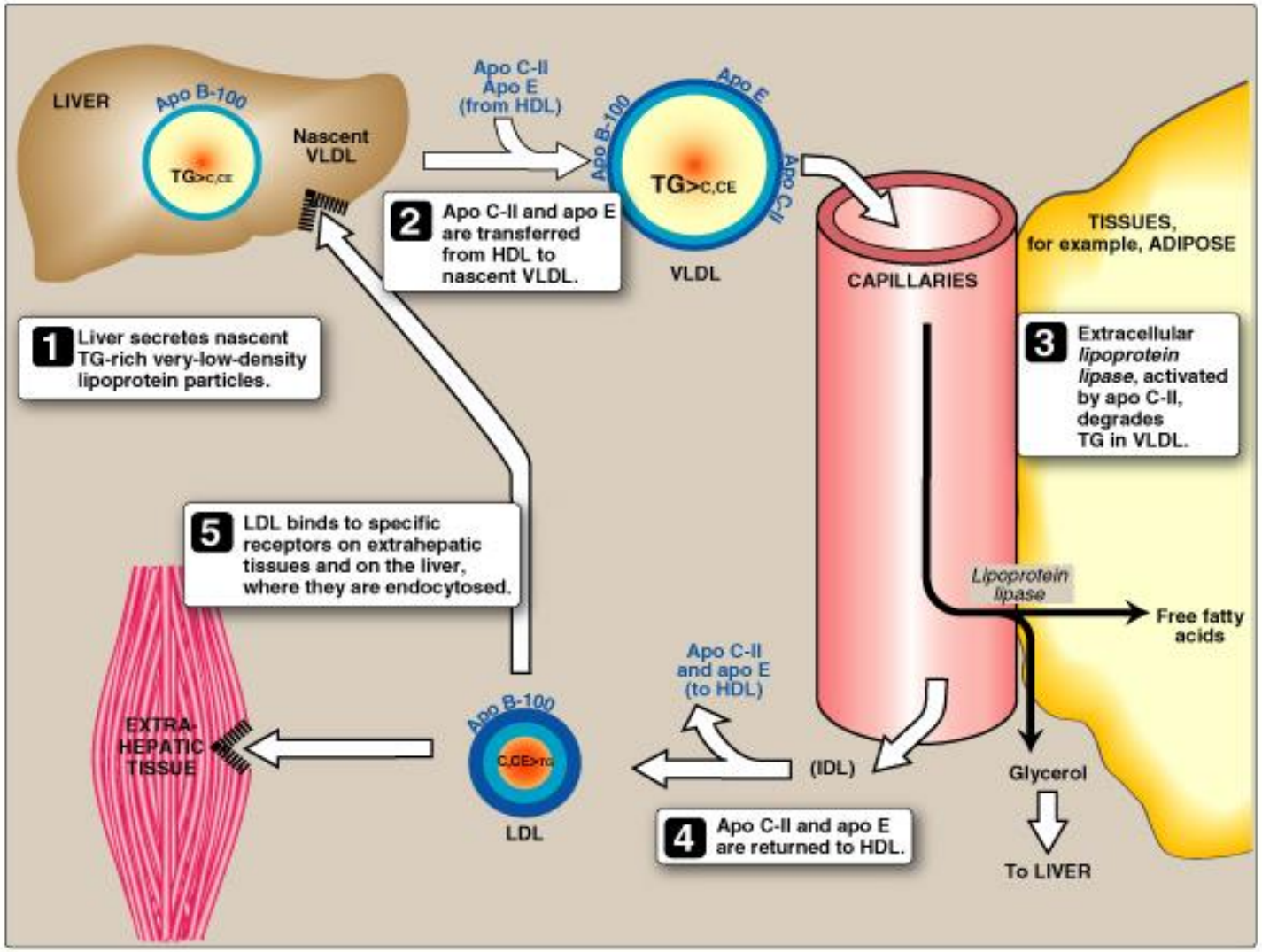
- Assembled and secreted by liver
- Mature VLDLs in blood
- Modifications of circulating VLDLs
- End products: IDL and LDL
- Related diseases:

  Hypolipoproteinemia: Abetalipoproteinemia

  Hyperlipoproteinemias:

    Type I hyperlipoproteinemia

    Familial type III hyperlipoproteinemia



VLDL Metabolism

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**

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)**

Modifications of Circulating VLDLs

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

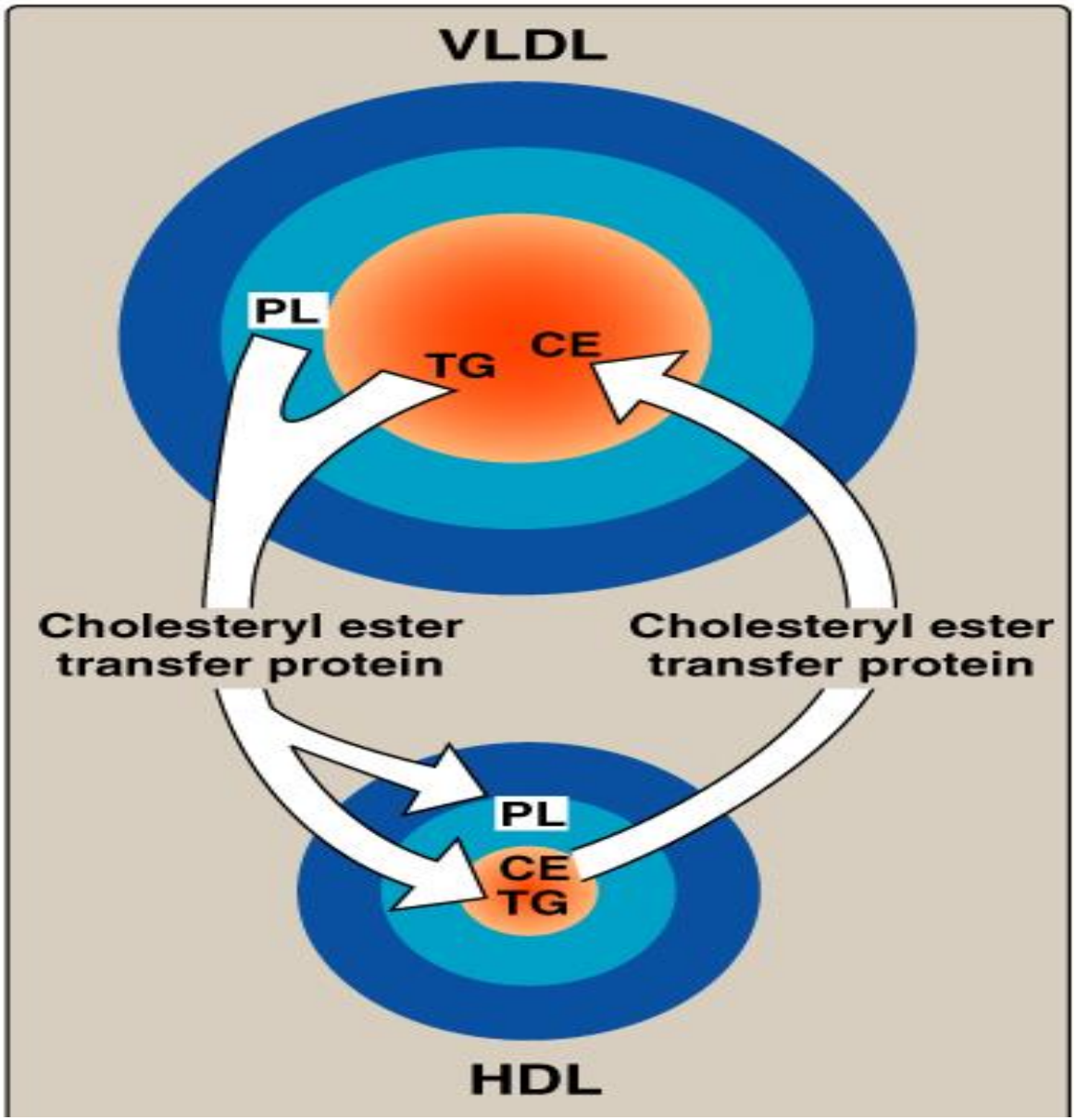
Smaller in size

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



Lipid-Transfer Protein

VLDLs-Related Diseases

1- Hypolipoproteinemia

Abetalipoproteinemia

Defect in TG-transfer protein

Apo B-100 cannot be loaded with lipid

Accumulation of TG in liver

2- Fatty Liver (hepatic steatosis)

Imbalance between hepatic synthesis of TG and secretion of VLDLs.

Accumulation of TG in liver

VLDLs-Related Diseases, *continued…*

3- Hyperlipoproteinemia

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

- - (Familial dysbetalipoproteinemia)
- - due to Apo E deficiency
- - Associated with hypercholesterolemia & premature atherosclerosis

THANK YOU ☺