LIPOPROTEINS METABOLISM

"DON'T STOP WHEN YOU'RE TIRED, STOP WHEN YOU'RE DONE"

Color index:

- Important
- Extra explanation

*** Please check out this link to know if there are any changes or additions.**

OBJECTIVES:

- Know the composition of plasma lipoproteins (chylomicrons, VLDL, LDL and HDL).
- Recognize the metabolism and function of plasma lipoproteins .
- Identify the functions of apolipoproteins.
- Outline the clinical aspects of abnormal lipoprotein metabolism.

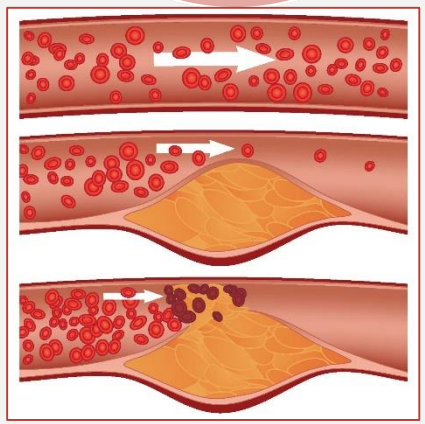
Introduction to lipoproteins:

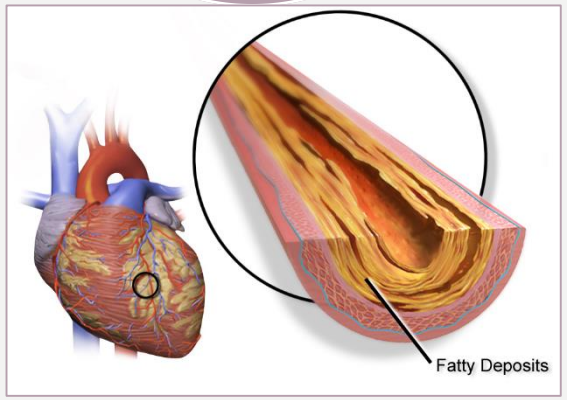
- **why do we need lipoproteins compounds?**

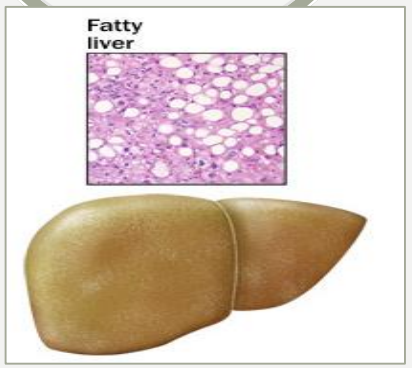
Lipid compounds are relatively water insoluble, therefore, they are transported in the plasma (aqueous) as "**Lipoproteins**".

Lipoproteins and related clinical problems:

Atherosclerosis And hypertension → Coronary heart diseases → Hyper\hypo Lipo-proteinemias → Fatty liver.







Introduction to lipoproteins

LIPOPROTEINS STRUCTURE:

Lipoproteins are composed of two parts:

Protein part:

- **Called:** Apoproteins or Apolipoproteins.

- Abbreviations:

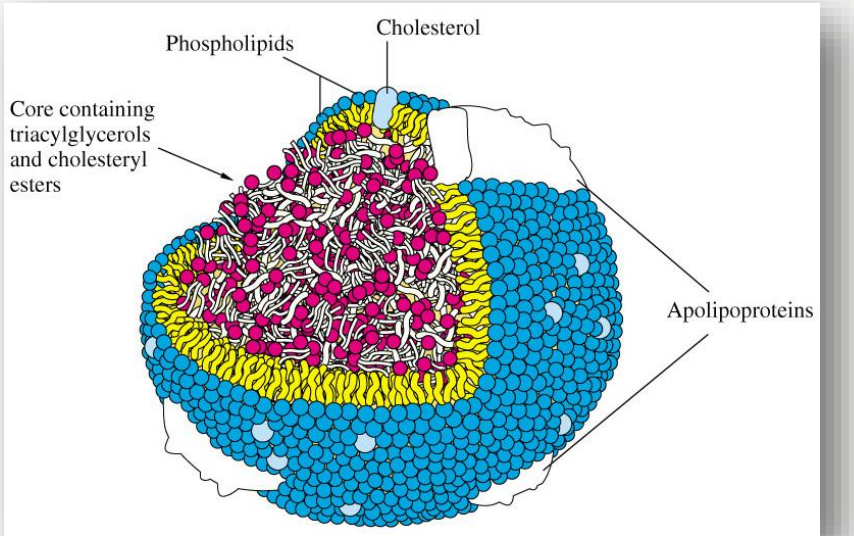
Apo-A, B, C, D, E.

- **Functions:**

- Structural and transport function (by facilitating lipids transportation in the circulation)
- Enzymatic Function (sometimes they act as coenzymes).
- Ligands for receptors (will be discussed later).

Lipid part:

- It differs according to the type of lipoproteins.
- Different lipid components in various combinations.



Lipoproteins structure

LIPOPROTEINS STRUCTURE

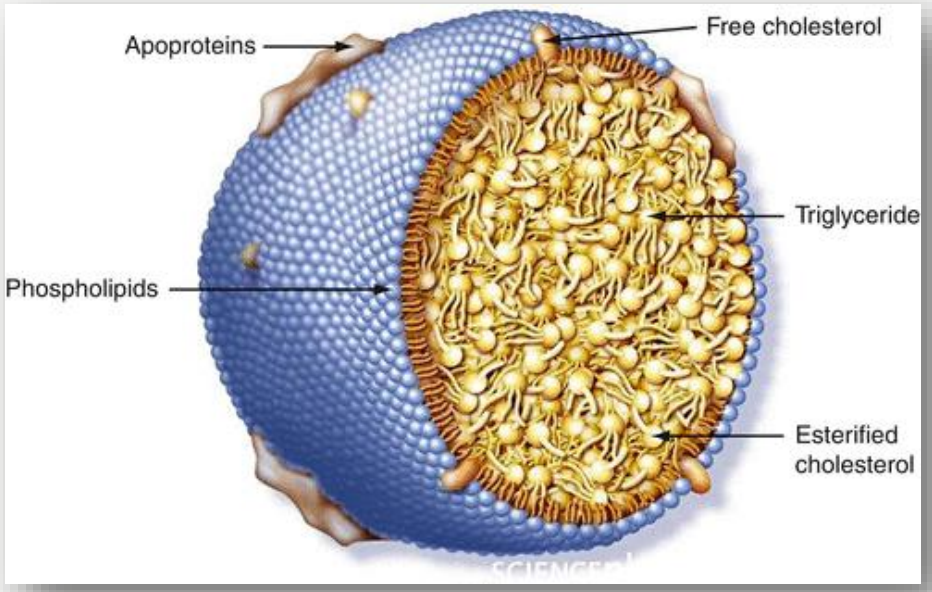
They are Spherical molecules of lipids and proteins (apoproteins)

Inner core :

- Triacylglycerol
- \+
- Cholesteryl esters

outer core :

- Apoproteins
- \+
- phospholipids
- \+
- Cholesterol (free-unesterified)



Explanation:
Lipoproteins are composed of a lipid core (containing triacylglycerol and cholesteryl esters) surrounded by a shell of: (amphipathic apolipoproteins, phospholipids, and unesterified “free” cholesterol) . These amphipathic compounds are oriented so that their polar portions are exposed on the surface of the lipoproteins, thereby rendering the particle soluble in aqueous solution

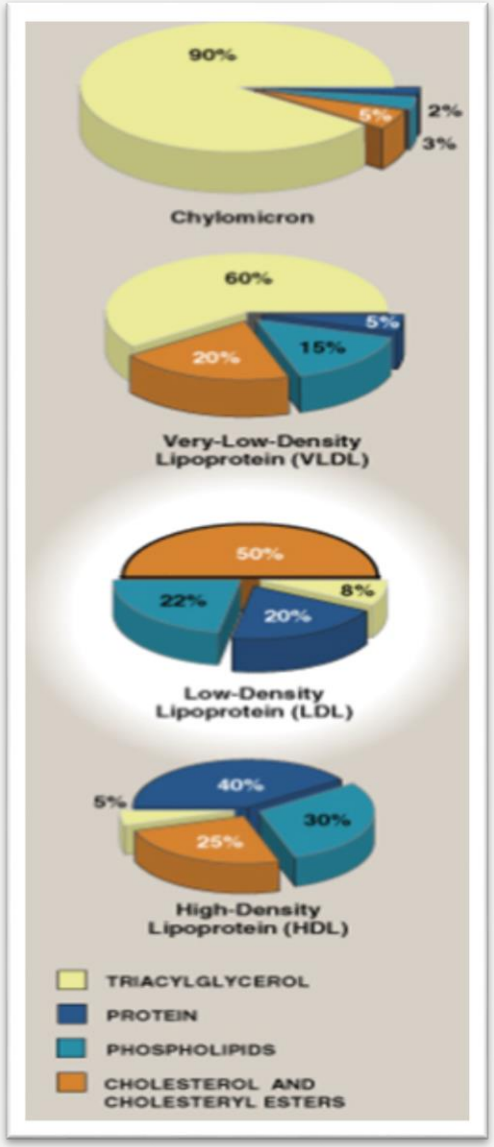
TYPES OF LIPOPROTEINS

❖ 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 (a method that has been developed for the separation of plasma lipoproteins).

Type:	What does it transport?	Size:	Density:	% of lipids:	% of proteins + phospholipids:
Chylomicrons	Dietary (exogenous) triacylglycerol	Highest ↑ Increases	decreases ↓ Highest	Highest ↑ Increases	decreases ↓ Highest
Very low density lipoprotein (VLDL)	Endogenous triacylglycerol (Hepatic synthesis)				
Low density Lipoprotein (LDL)	Free cholesterol				
High density Lipoprotein (HDL)	Esterified cholesterol				



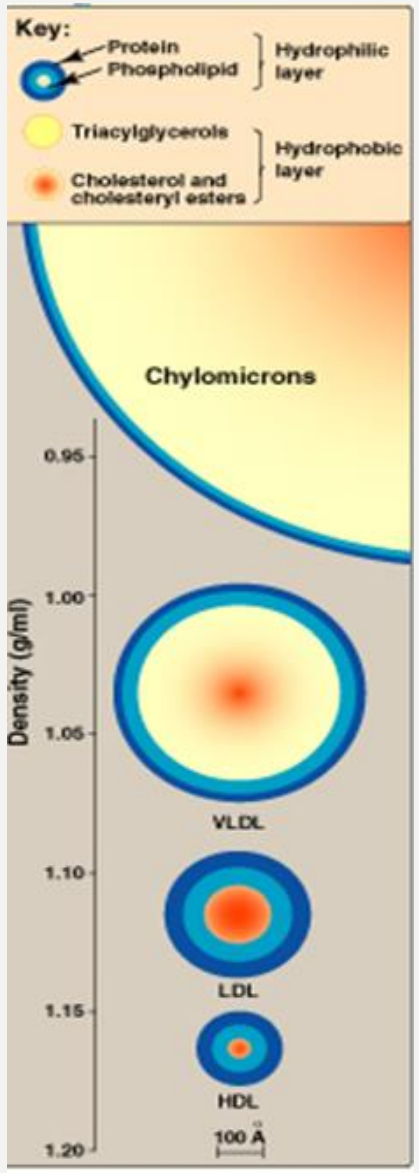
لتسهيل الفهم:

من إسم المركب نستطيع أن نعرف الدنستي حقته ، ومن خلال الدنستي نستطيع أن نعرف :

- **نسبة البروتين والفسفوليبدز من خلال:** قاعدة بسيطة جداً « كلما زادت نسبة البروتين والفسفوليبدز (أو قلت نسبة الترایاسایل جلیسرول)».
- **سایز المركب:** بناء على معلوماتنا السابقة عن الكثافة أو الدنستي ، التي تعني بشكل مجازي مقدار تراص الجزيئات مع بعضها ، فكلما صغر الحجم كلما كانت متراصه.

مو مطلوب نعرف النسب ، لكن لازم نعرف من الي عنده بروتين أكثر و فوسفوليبدز اكثر و هكذا

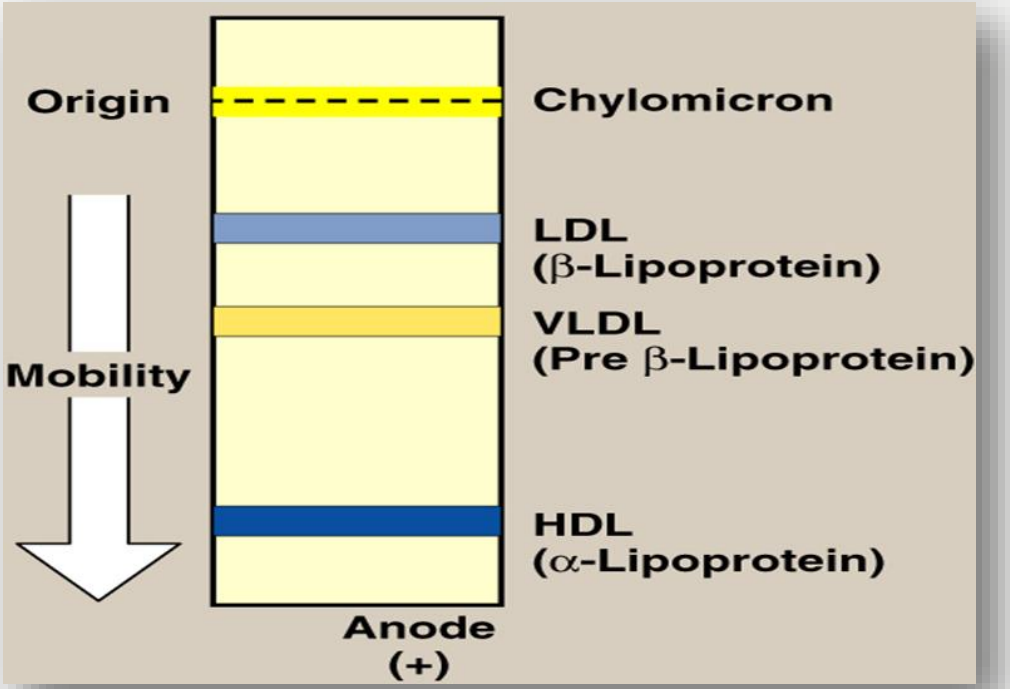
ULTRACENTRIFUGATION OF LIPOPROTEINS:



Centrifugation is the process of separating substances of different densities by the use of a centrifuge

يعني ناخذ عينة دم ونضعها في سينترفيوج وراح تظهر اللايبوبروتينز على شكل طبقات كما في الصورة

LIPOPROTEINS ELECTROPHORESIS:



- Lipoproteins are classified into 4 groups according to **migration in electric field** (electrophoresis) the migration always from positive to negative:
  - **Chylomicrons.**
  - **B-Lipoprotein. (LDL)**
  - **Pre β-Lipoprotein. (VLDL).**
  - **α-Lipoprotein. (HDL)** (it's called alpha because it's the fastest in migration)

د.عمرو نبه أن: ممكن يسألونا عن ترتيب أنواع اللايبوبروتينز من الانود للكاثود ، أو العكس)

electrophoresis

CHYLOMICRONS

Chylomicrons	
Assembled in:	Intestinal Mucosa.
Density:	Lowest Density.
Size:	Largest Size.
% of Lipids:	Highest.
% of proteins:	Lowest.
Triacylglycerol:	Highest triacylglycerol (dietary origin)
Function:	It carries **dietary lipids** to peripheral tissues
Responsible for:	It responsible for physiological **milky appearance of plasma** (**Up to 2 hours after meal**)

Because these particles are 99% lipids, they have a buoyant density less than that of whole plasma and float to the top of the tube. Being large in size, chylomicrons refract light causing a milky appearance.

- كيف نتذكر وظيفته؟

اللي هي :

Carrying dietary lipids to the peripheral tissues

ChyloMICRONS

MACRONS ← تشبه

"Macron is a French sweet"

يعني يدخل بالدايت ☺

Note:

The milky appearance of plasma becomes pathological if it appears **after** 2 hours.

Chylomicrons

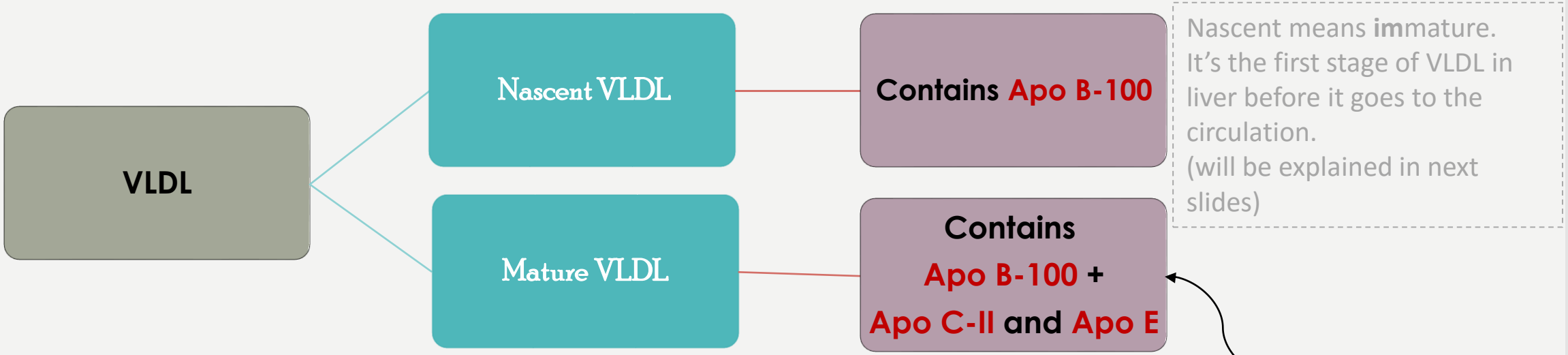
Very Low Density Lipoproteins (VLDLs)

- It Assembled in liver.
- It contains a High amount of triacylglycerol (hepatic cells are the origin of this triacylglycerol).

Remember: the amount of triacylglycerol of VLDL is lower than the amount of it in chylomicrons.

Function :

Carry lipids from **liver** to **peripheral tissues.**



Good and Bad Cholesterol

Metabolism of VLDLs

1- VLDL Assembled and secreted by liver directly into blood as nascent form

Nascent VLDL contains Apo B-100 only

2- Nascent VLDL gets **Apo C-II** & **Apo E** from HDL and turns into mature VLDL.

Apo C-II are a coenzyme which is required to activate lipoprotein lipase.

3- Apo C-II activate lipoprotein lipase

4- Lipoprotein lipase degrade TG into glycerol and fatty acids

TG refers to Triacylglycerol

5- As TG is degraded, VLDLs become **smaller in size & more dense**. Then Apo C-II and Apo-E go back to HDL

6- Exchange of TG with cholesterol ester by cholesterol ester transfer protein

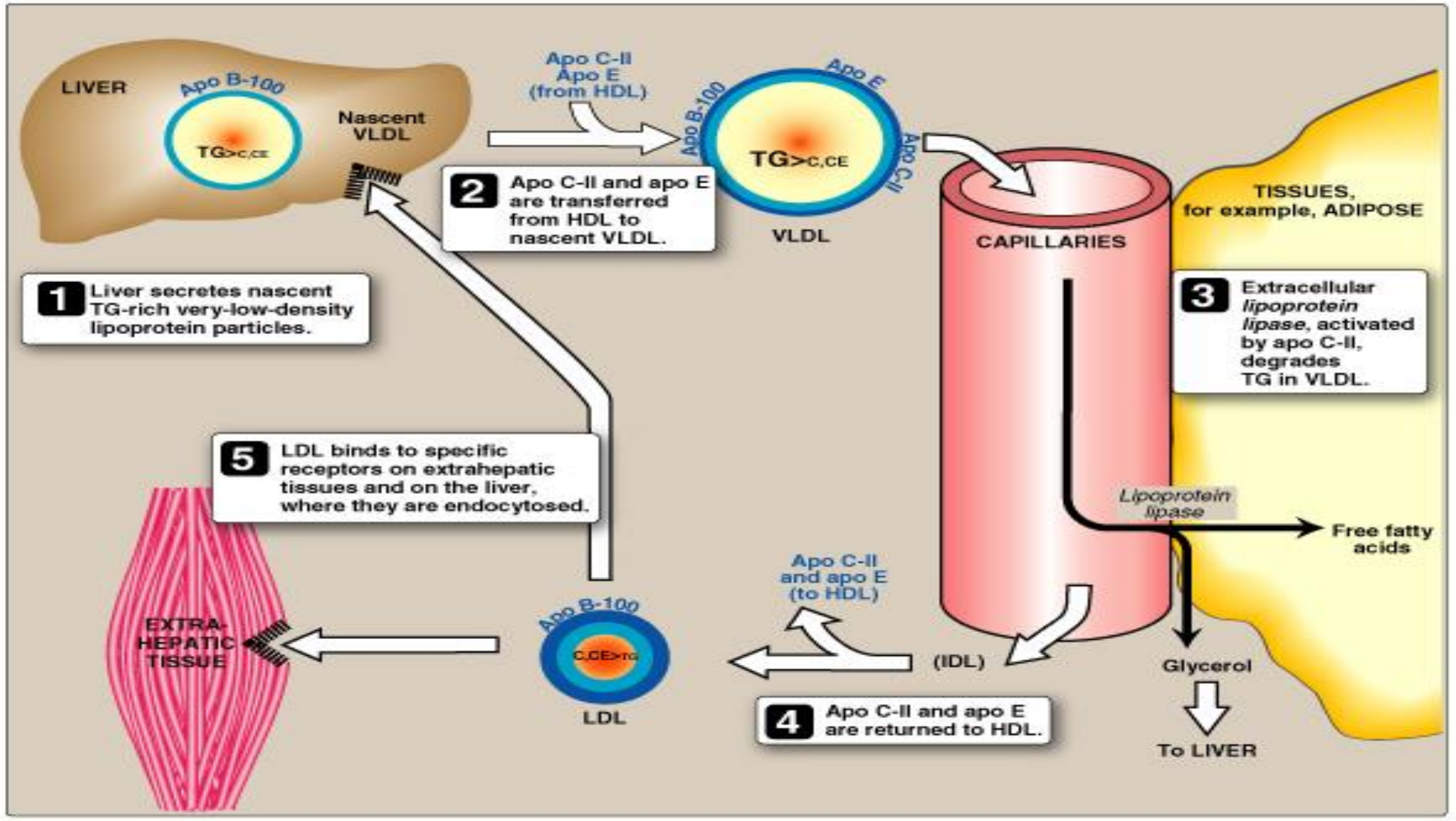
Cholesterol ester transfer protein (also called Apo D) is a protein present on HDL.
It transfers TG from VLDL to HDL, and cholesterol ester from HDL to VLDL.

7- Production of LDL in plasma

VLDL turns into IDL, then when Apo E returns to HDL, IDL will turns into LDL

The steps 5, 6 & 7 are called modification of circulating VLDL.

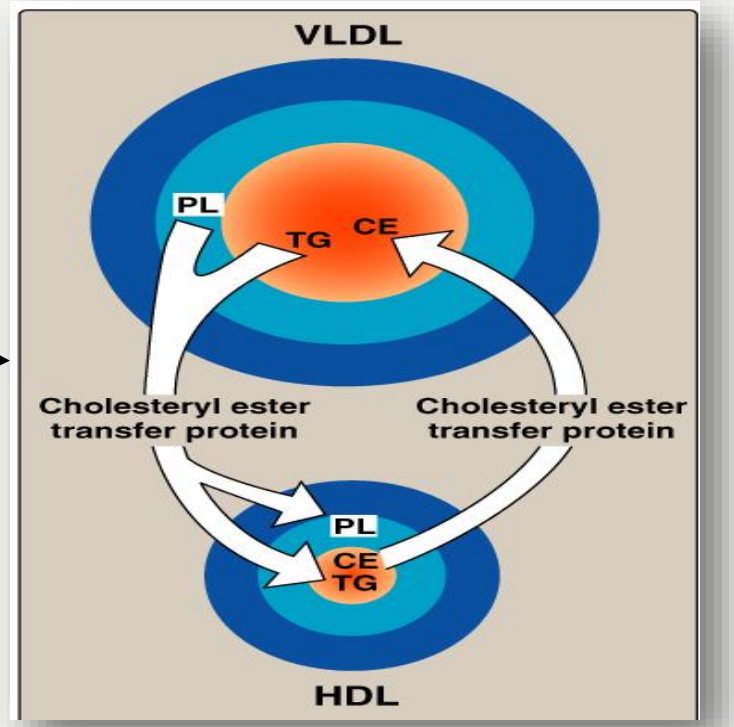
Metabolism of VLDLs



Metabolism of VLDLs

EXTRA:
In the modification of VLDL, the lipoprotein lipase (which presents in the walls of capillaries) will degrade the triacylglycerol (TG) of VLDL and produce fatty acids & glycerol. The VLDL then will turn to IDL (intermediate density lipoprotein, which is a subtype lipoprotein) by giving back the apo C-II to HDL. Then the cholesterol ester transfer protein (Apo D) will transfer TG from VLDL to HDL and cholesterol ester from HDL to VLDL (see the picture below). In the end of this process VLDL will give back apo E to HDL and turn into LDL. LDL will bind to a specific receptors called LDL receptors in liver or in extrahepatic tissues (other tissues) where they are endocytosed (the ligand of LDL receptor is apo B-100, while the ligand of IDL receptor is apo E).

Lipid transfer protein
(cholesterol ester transfer protein)



Metabolism of VLDLs

Lipoprotein lipase

What is it?

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

Location: Predominantly present in adipose tissue, cardiac & skeletal muscle.

Activated by:

- Requires ApoC-II for activation
- Insulin stimulates its synthesis and transfer to the luminal surface of the capillary.

Function:

Degrades TG into glycerol and free fatty acids

Deficiency:

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

VLDL Related diseases

Hypolipoproteinemia

- It also called **Abetalipoproteinemia.**

- **Happens due to:**

-Defect in TG-transfer protein.

usually Apo B-100 is loaded by TG to form VLDL , the protein responsible of that is called TG-transfer protein.

-When there's a defect in this protein , the Apo B-100 Can't be loaded with lipid (TG) , so the TG will accumulate in liver .

Hyperlipoproteinemia

Fatty Liver (hepatic steatosis)

- Imbalance between hepatic synthesis of TG and secretion of VLDLs →Accumulation of TG in liver → Fatty Liver (hepatic steatosis)

Hepatic steatosis is a benign condition (without inflammation) , but if there was an inflammation it will be called hepatic steatohepatitis which is the dangerous one and may lead to liver failure

VLDL Related diseases

- Hypolipoproteinemia
- Hyperlipoproteinemia
- Fatty Liver (hepatic steatosis)

Type I Hyperlipoproteinemia

- Familial Lipoprotein lipase deficiency or Apo C-II deficiency (or both).
- Usually **associated with** acute abdomen due to acute pancreatitis.

there will be a high amount of VLDL in blood because the enzyme which degrade it is defect.

- **Due to** deficiency of lipoprotein lipase or its cofactor Apo C-II.
- **Shows**
  - a dramatic accumulation (>= 1000 mg\dl) of chylomicrons in plasma.
  - Increased plasma TG even in fasted state.

Type III Hyperlipoproteinemia

- It's **also called** Familial dysbetalipoproteinemia

Dys means that we don't know if it's hyper or hypo, but here it refers to hyperlipoproteinemia.

- it occurs **due to** Apo E deficiency.
- Usually **associated with** Hypercholesterolemia and premature atherosclerosis.

MCQs

1. lipid compounds transported in plasma as:

A. Apoproteins
B. Apolipoprotein
C. cholesterol
D. Lipoproteins

2. Which one of the following has the lowest density :

A. Very low density lipoprotein (VLDL)
B.low density lipoprotein (LDL)
C.High density lipoprotein (HDL)
D. Chylomicrons

3. which one of the following is assembled and secreted by the liver :

A. Very low density lipoprotein (VLDL)
B.low density lipoprotein (LDL)
C.High density lipoprotein (HDL)
D. Chylomicrons

4. accumulation of TG in the liver will cause :

A. liver cirrhosis
B. Fatty liver (Hepatic steatosis)
C. Liver ischemia
D. Hepatic failure

5. Apo CII and Apo E (that are responsible for maturation of VLDL) comes from :

A.LDL
B. HDL
C. Chylomicrons
D.Liver

6. which of the following is LCAT responsible for :

A. Converting cholesterol to cholesterol ester
B. transfer of cholesterol to lipoproteins
C. Degradation of HDL in liver
D. Degradation of chylomicrons

1. D
2. D
3. A
4. B
5. B
6. A

MCQs

7.Patient fasting for 10 hours when we take blood sample we found its milky appearance of plasma what do you think this patient has :

A. Type I hyperlipoproteinemia
B. Type II hyperlipoproteinemia
C. Type III hyperlipoproteinemia
D. hypolipoproteinemia

8. Type III hyperlipoproteinemia caused by :

A. Lipoprotein lipase deficiency
B. Apo CII deficiency
C. Apo E deficiency
D. APo B 100

9. Which type of lipoproteins acts as a reservoir of apolipoproteins for the other lipoproteins:

A. Chylomicrons.
B. VLDL.
C. LDL.
D. HDL.

7. A
8. C
9. D

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