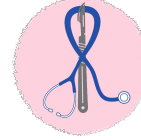


Lipoprotein Metabolism





Revised & Reviewed
Abdulaziz & Bahammam
Faye Weel Sondi



MED441
KING SAUD UNIVERSITY

3

Cardiovascular
Block - KSU

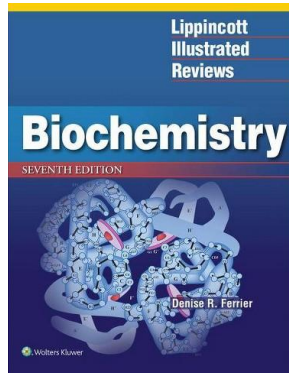
-  Main text
-  Important
-  Notes
-  Extra

[Editing File](#)

We **HIGHLY** recommend that to watch this video below
to make this lecture more easier & we suggest this
book for you if you want more details



شرح بالعربي - Lipoproteins
BY Science Bites



**Biochemistry Lippincott
Illustrated Reviews 7th Edition**
BY Denise R. Ferrier

Chapter 18
Pages 656-670



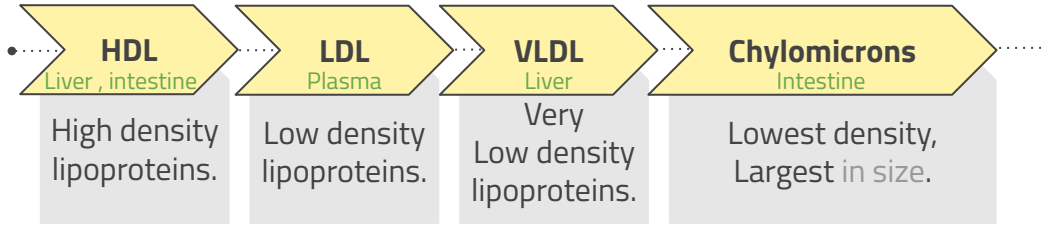
Objectives

- ✦ Define and list the types, structure and composition of lipoproteins.
- ✦ Understand various functions of lipoprotein particles.
- ✦ Compare the functions of lipoprotein particles and their implications in disease.
- ✦ Understand the metabolism of chylomicrons, VLDL and LDL particles.
- ✦ Discuss the functions of lipoprotein lipase and its role in disease.
- ✦ List the diseases due to imbalance in the metabolism of lipoproteins.

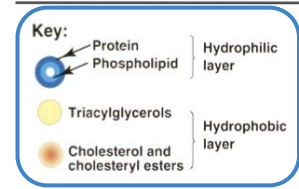
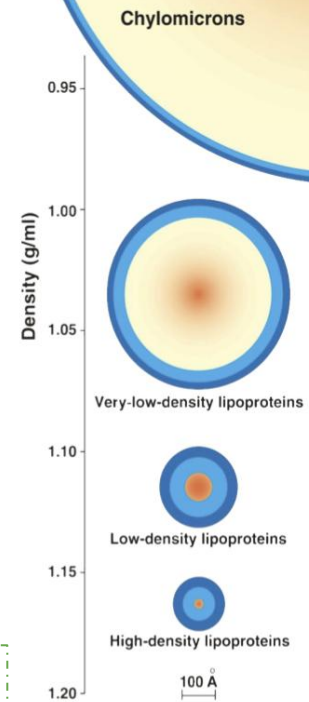
Lipoproteins

- Lipids are hydrophobic macromolecule, so they need to be transported in plasma as **lipoprotein particles**.
- Function: Lipoproteins keep lipid contents soluble while transporting them to and from the tissues.
- Plasma lipoproteins are spherical in shape, they contain:
 - lipid (contains different type like TAGs, cholesterol, cholesteryl ester, phospholipids).
 - Special type of proteins (apolipoprotein).

Types of lipoprotein: (water has more density than lipids)



As you can see in the figure: **Chylomicrons & VLDL** are mainly carrying TAGs, **LDL** mainly carrying cholesterol & cholesteryl esters, and **HDL** mainly carrying both TAGs & cholesterol & cholesteryl esters.

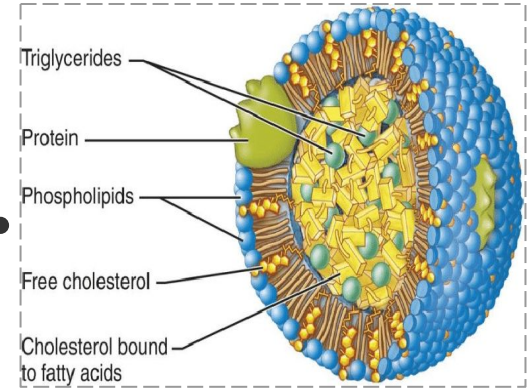
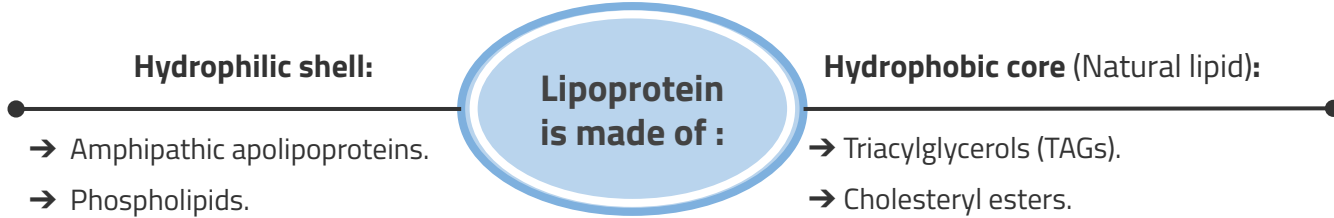


▶ Lipoproteins differ in their

- > lipid and protein composition.
- > Size.
- > Density.
- > Site of origin (synthesis).

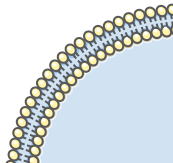
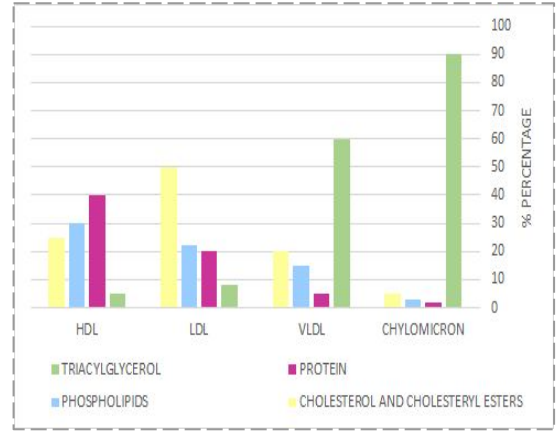


Composition of Lipoprotein



*Because it is required for maintaining the structure of the phospholipid layer outside & it has (OH) at C3 remember?

Cholesterol	Type	TAGs (Triglycerides)
<ul style="list-style-type: none"> ● LDL (Cholesterols = 50% of LDL) ● HDL (Cholesterols = 25% OF HDL) 	Transported By	<ul style="list-style-type: none"> ● Chylomicrons (TAGs = 90% of chylomicrons) ● VLDL (TAGs = 60% of VLDL)



Apolipoproteins

▶ Types:

- Apo B-48, B-100
- Apo C-I, C-II, C-III
- Apo E

▶ Functions:

- 1 Provide recognition sites for cell-surface receptors.
- 2 Provide structure to lipoprotein particles (some types of Apolipoproteins are important to maintain the structure of a lipid).
- 3 Activators or coenzymes for the enzymes involved in lipoprotein metabolism. (some not all)

Chylomicrons

- Assembled (formed) in the intestinal mucosal cells
- The milky appearance of plasma after a meal is due to chylomicrons (as in the picture)

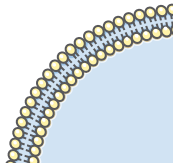
▶ Function:

Is to transports the following to the peripheral tissues:

- 1 Dietary TAGs fats (triacylglycerol) (90%) (exogenous TAGs).
- 2 Cholesterol (C).
- 3 Fat-soluble vitamins (from the diet).
- 4 Cholesteryl esters (CE).



After taking meal | Fasting patients plasma



Very low density lipoprotein (VLDL):

- Produced and secreted by the **Liver**.

- **Mainly composed of the following:**

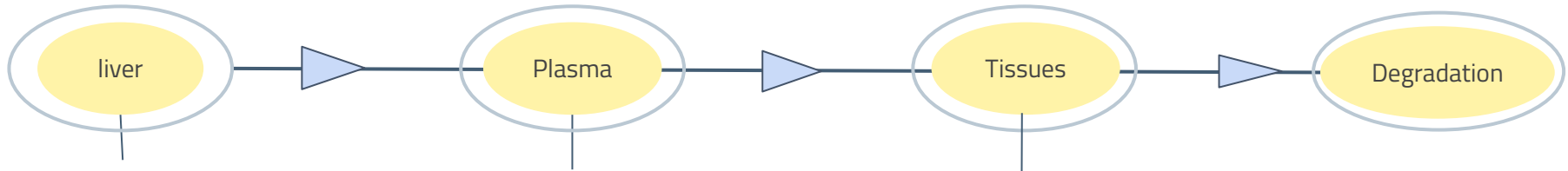
- Endogenous TAGs (60%).
- Some cholesterol (both free and esterified).

- Imbalance in hepatic TAG synthesis and secretion of VLDL can lead to:

- Obesity.
- Type 2 diabetes mellitus.



- **Lipoprotein lipase:** extracellular component found in tissues and its hanging from capillary wall "where VLDL is present"
- It is activated by **Apo C2** , So if there is deficiency in Apo C2, degradation won't happen

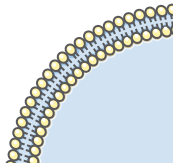


VLDL carries these lipids (TAGs & cholesterol) **from the liver to peripheral tissues**

TAGs will be delivered to the peripheral tissues by VLDL

It will be degraded by an enzyme called **Lipoprotein lipase (LPL)** into:

- Free FAs
- Glycerol





VLDL metabolism



The difference between VLDL and chylomicron metabolism:
-chylomicron site of origin: intestine.
-it takes Apo E and Apo C from HDL.
-after unloading of TAGs at tissues and giving up Apo C, chylomicron remnants (taken up by liver via Apo E) are produced instead of LDL

01

Liver secretes nascent newly formed/ immature endogenously synthesized TAG-rich VLDL particles.

02

In the circulation apo C-II and apo E are transferred from HDL to nascent VLDL and when it has apo B-100 + apo C-II it is called mature VLDL.

03

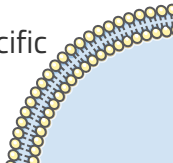
When the mature VLDL reaches the peripheral tissue, extracellular lipoprotein lipase, activated by apo C-II, degrades TAG in VLDL into free FAs & Glycerol, This explains the lower TAG content of LDL and HDL.

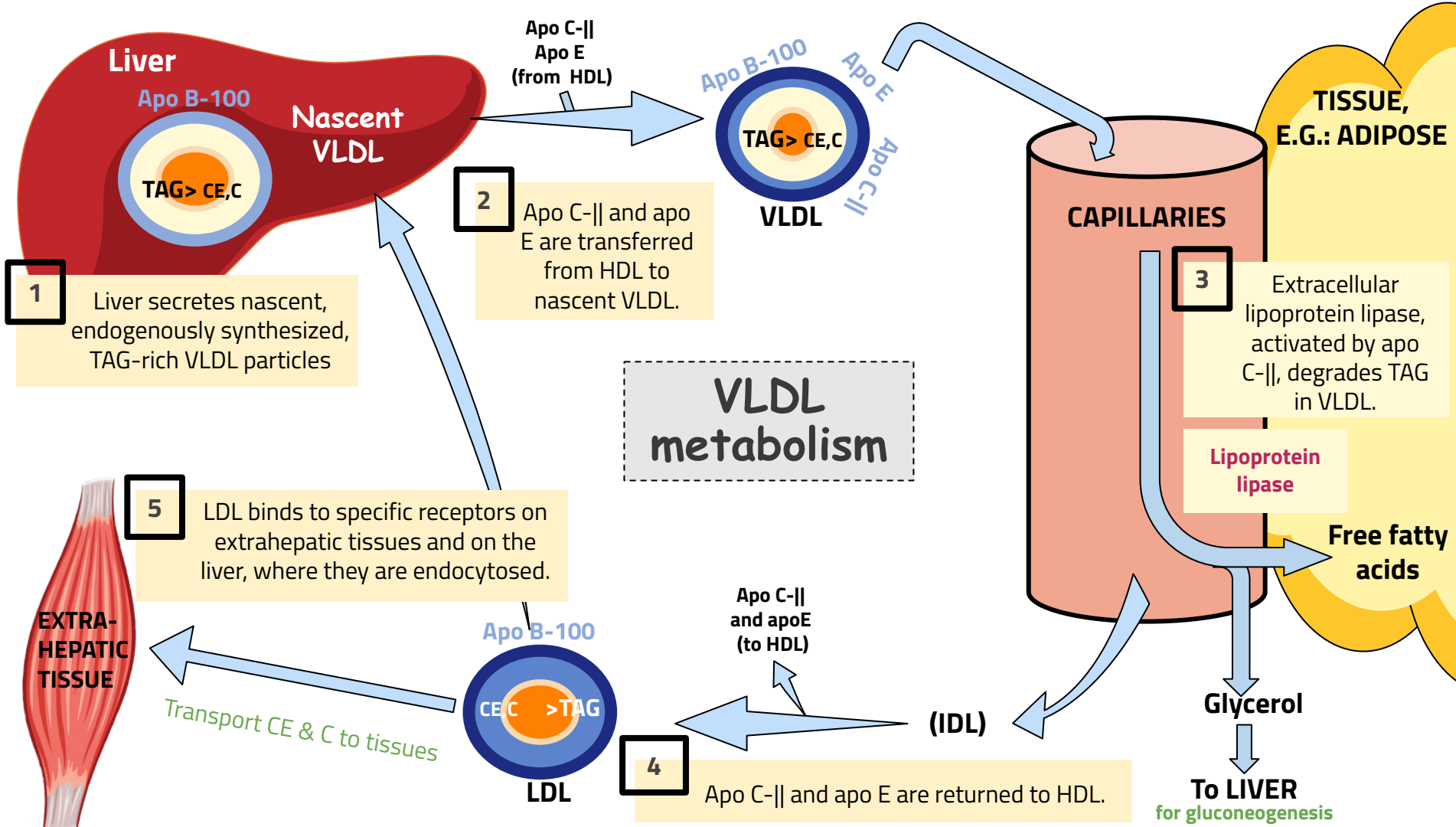
04

Apo C-II and apo E are returned to HDL.

05

Now the molecule just having apo B-100, and carrying much less TAGs and become LDL then LDL binds to specific receptors on extrahepatic tissues and on the liver, where they are endocytosed.





VLDL metabolism

1

Release from the liver:

- ❖ As nascent particles containing:
 - TAGs and cholesterol.
 - Apo B-100.
- ❖ Obtain apo C-II and apo E from circulating HDL particles.
- ❖ Apo C-II is required for activation of LPL.

2

Modification in the circulation:

- ❖ TAGs in VLDL are degraded by lipoprotein lipase (LPL).
- ❖ VLDL becomes smaller and denser.
- ❖ Surface components (apo C and E) are returned to HDL → LDL is produced.
- ❖ VLDL transfers TAGs to HDL in exchange for cholesteryl esters.
- ❖ This exchange is catalyzed by cholesteryl ester transfer protein (CETP).

Conversion to LDL:

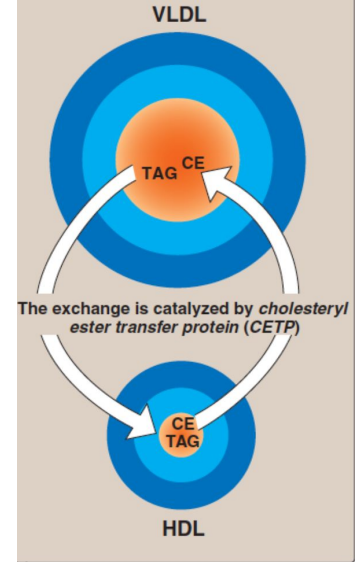
- ❖ After modifications, VLDL is converted to:
 - LDL.
 - IDL (Intermediate density lipoprotein) (taken up by liver cells thru apo E).
 - VLDL remnants.

3

Apo E

- ❖ Apo E exists in three isoforms:
 - Apo E-2 (Poorly binds to receptors).
 - Apo E-3.
 - Apo E-4.

2) modification in the circulation



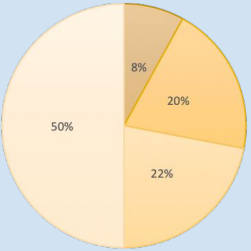
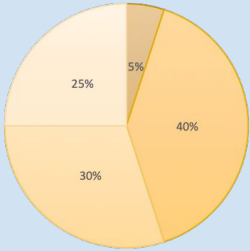
Some of the TAGs are transferred to HDL in exchange of CE and this catalyzed by CETP.

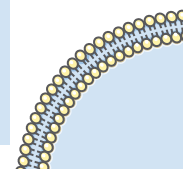


Low density lipoproteins (LDL) & High density lipoproteins (HDL)

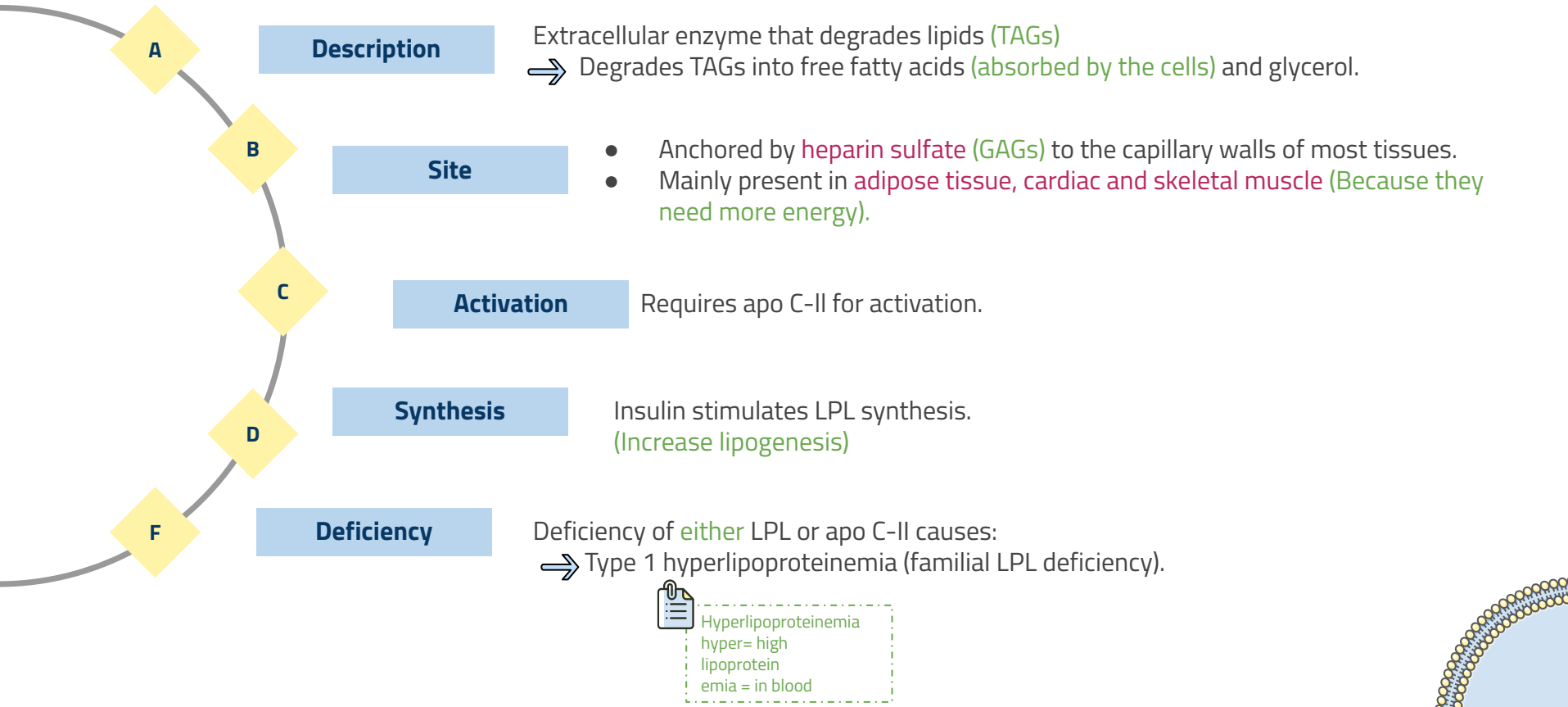


* It is a structural protein & acting as a surface receptor.

(LDL) (Bad cholesterol)		(HDL) (Good cholesterol)
Produced from VLDL particles.	Production	Produced in the liver and intestine .
<ul style="list-style-type: none">● Mainly cholesterol and cholesteryl esters.● Apo B-100 lipoprotein.	Contents	<ul style="list-style-type: none">● Mainly proteins, phospholipids, cholesterol, cholesteryl esters.● Apo A-1, C-2, and E lipoproteins.
<ul style="list-style-type: none">● Provides cholesterol to peripheral tissue.● LDL binds to cell surface receptors thru Apo B-100 (receptor-mediated endocytosis*).	Functions	<ul style="list-style-type: none">● Take up cholesterol from peripheral tissues to the liver.
 <p>50% 22% 20% 8%</p> <p>■ triacylglycerol ■ protein ■ phspholipids ■ cholesterol and cholesteryl esters</p>	Chart	 <p>40% 30% 25% 5%</p> <p>■ triacylglycerol ■ protein ■ phspholipids ■ cholesterol and cholesteryl esters</p>



Lipoprotein Lipase (LPL)

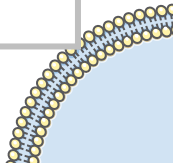




VLDL Diseases

Thanks to 439

Disease	About	Cause	Leads to
Hypolipoproteinemia	-	(A=not or without ; beta= apo B) Abetalipoproteinemia is due to inability to load apo B (B-48 & B-100) with lipids.	<ul style="list-style-type: none">• Few VLDLs and chylomicrons are formed.• TAGs accumulate in liver and intestine (decrease in plasma).
Steatohepatitis	(Fatty liver disease)	Imbalance between: <ul style="list-style-type: none">• TAG synthesis in the liver .• Secretion from the liver.	<ul style="list-style-type: none">• accumulation of TAGs in the liver (fatty liver).
Type I hyperlipoproteinemia	A rare, autosomal recessive disease	Due to familial deficiency of LPL or its coenzyme (apo C-II)	<ul style="list-style-type: none">• Causes excessive accumulation of chylomicrons in plasma (≥ 1000 mg/dl) (hyperchylomicronemia).• High fasting plasma TAGs are observed in these patients.
Type III hyperlipoproteinemia	Also called familial dysbetalipoproteinemia, or broad beta disease	Individuals homozygous for apo E-2 are deficient in clearing: <ul style="list-style-type: none">• Chylomicron remnants.• IDL from the circulation.	<ul style="list-style-type: none">• hypercholesterolemia .• premature atherosclerosis.• Xanthomas: multiple small, yellow skin growths





Take Home Messages

- ✦ Lipoproteins are important for transportation of lipids to and from liver and peripheral tissues
- ✦ Different types of lipoproteins perform different functions in the body
- ✦ Imbalance in the metabolism of lipoproteins leads to accumulation of lipids in the tissues and circulation increasing the risk for atherosclerosis and coronary heart disease

Summary



Click [HERE](#)

Or

Scan the code for the
amazing summary



Quiz

Q1: what is the lowest density lipoprotein but largest in size ?

- A/ VLDL
- B/ LDL
- C/ HDL
- D/ Chylomicrons

Q2: TAGs are transported by ?

- A/ VLDL
- B/ Chylomicrons
- C/ LDL
- D/ A&B

Q3: Where does the chylomicrons assemble ?

- A/ Intestinal mucosal cells
- B/ peripheral tissue
- C/ liver
- D/ kidney

Q: What are the functions of Apolipoprotein ?

Slide 6

Q4: which Apo E isoform binds poorly to receptors ?

- A/ Apo E-1
- B/ Apo E-2
- C/ Apo E-3
- D/ Apo E-4

Q5: which of the following stimulates LPL synthesis ?

- A/ TAGs
- B/ C-II
- C/ Insulin
- D/ heparin sulfate

Q6: which VLDL disease lead to hypercholesterolemia ?

- A/ hypolipoproteinemia
- B/ steatohepatitis
- C/ type I hyperlipoproteinemia
- D/ type III hyperlipoproteinemia

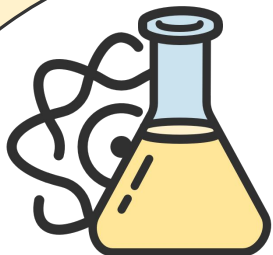
Q: List the lipoprotein types ?

Chylomicrons- VLDL
LDL - HDL

Q: where can LPL be found ?

Adipose tissue,
cardiac and skeletal muscle

Special Thanks to Faisal Alshuaibi



Biochemistry 441

Girls

★ **Leader:** Wareef Almousa

Fay Alluhaidan
Manal Aldhirgham
Fatimah Albenmousa

Haya Alshaloob
Maram Alenzi
Futoon Almotairi

Organizer: Aisha Alhamed

Boys

★ **Leader:** Abdulrahman Alroqi

★ **Sub-leader:** Hamad Aljubayr

Anas Alharbi
Rayan Alahmari
Mohammed Aloufi

Faisal Alazmi
Abdulrahman Badghaish
Ali Almatrri

Reviser: Mohannad Mallat

Organizer: Abdullah Alqarni

Special Thanks to Arwa Almobeirek
for the Great Theme!



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