بسم الله الرحمٰن الرحيم

(وَفَوْقَ كُلِّ ذِي عِلْمٍ عَلِيمٌ)

Metabolism | Final 13

Plasma Lipoproteins

Written & Reviewed by : NST member

وَلِلَّهِ الْأَسْمَاءُ الْحُسْنَى فَادْعُوهُ بِهَا

المعنى: الموجد من العدم، والبرء هو التنفيذ وإبراز ما قدره وقرره إلى الوجود على صفة محددة.

الورود: ورد في القرآن (٣) مرات.

الشاهد: ﴿ هُوَ ٱللَّهُ ٱلْخَٰلِقُ ٱلْبَارِئُ ٱلْمُصَوِّرُ ﴾ [الحشر:٢٤].

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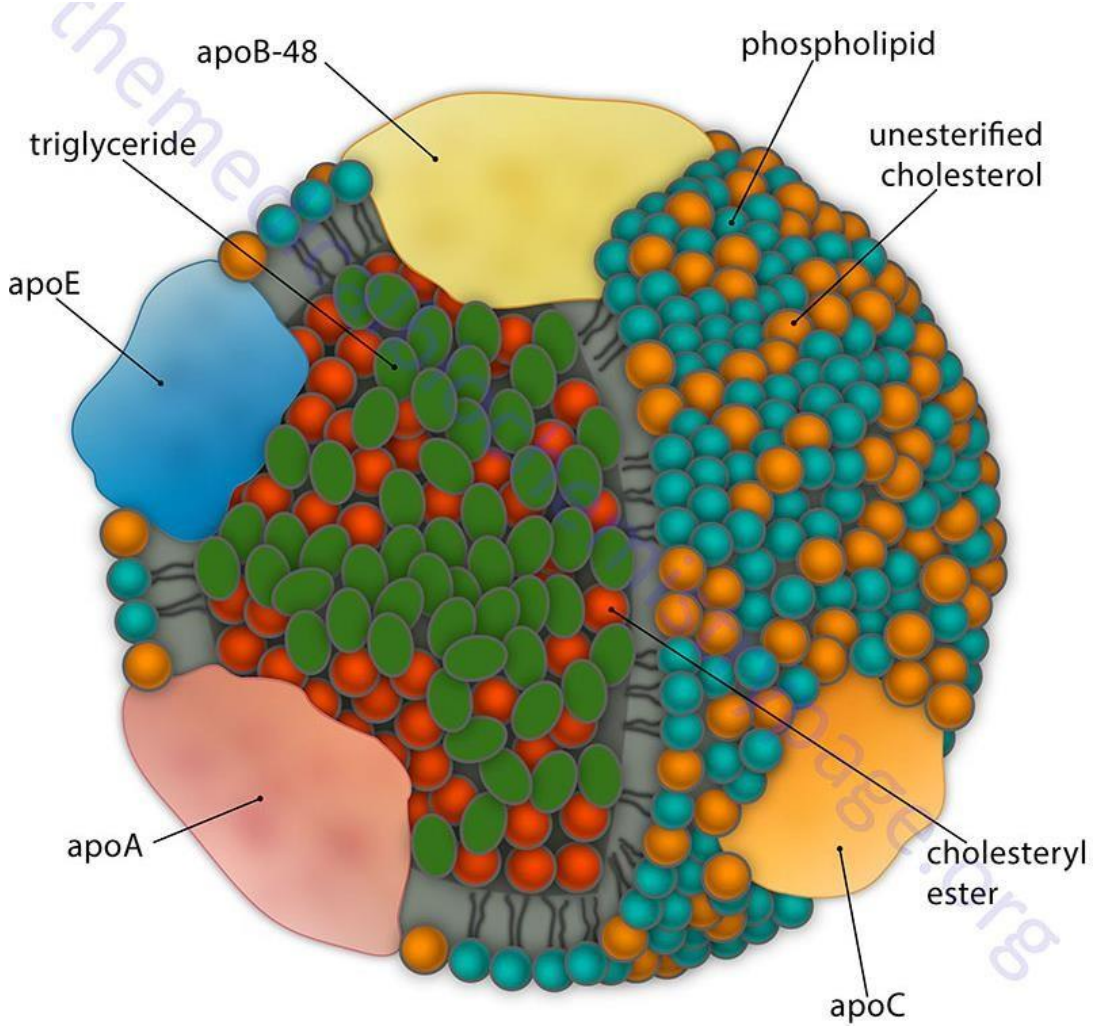
اضغط هنا لشرحٍ أكثر تفصيلًا

Plasma lipoproteins

lipids and proteins.



Lippincott's Biochemistry, Ch. 18

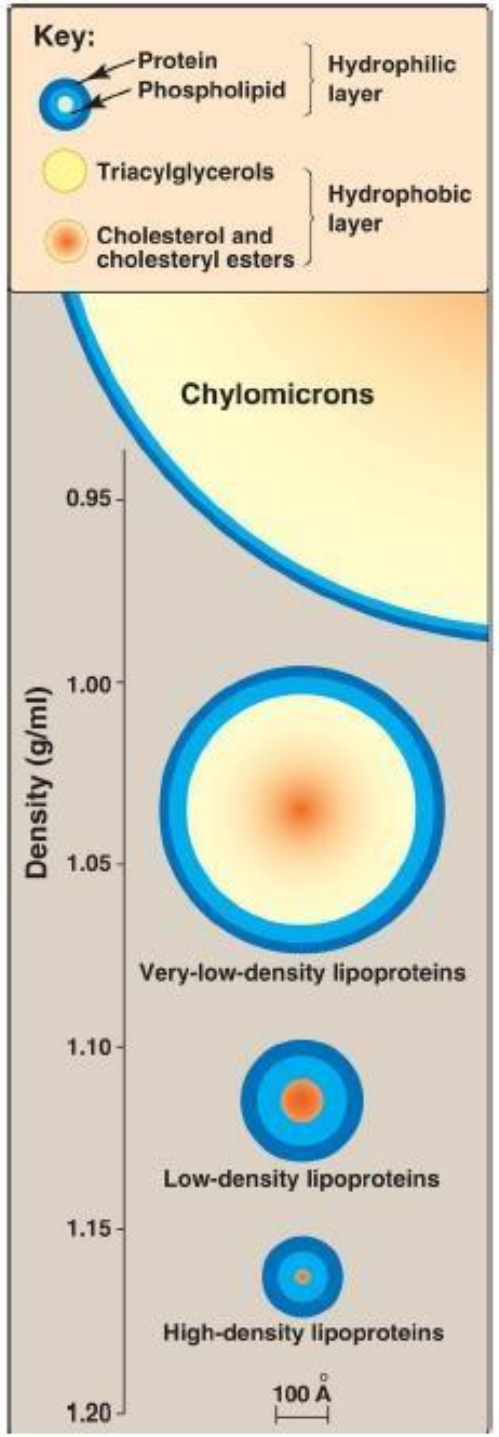
Characteristics of lipoproteins

- Lipoproteins function to
  - Solubilize and carry plasma lipids
  - **Their main role** Transport lipids to (and from) the tissues

- They range in size and density and have variable purposes and lipid and protein composition.

The higher the protein: lipid ratio, the higher the density

More lipids → lower density (bigger size)
More proteins → higher density (smaller size)
if we brought two guys with the same weight one is bigger than the second means he has more lipids than the thinner one, the same here.



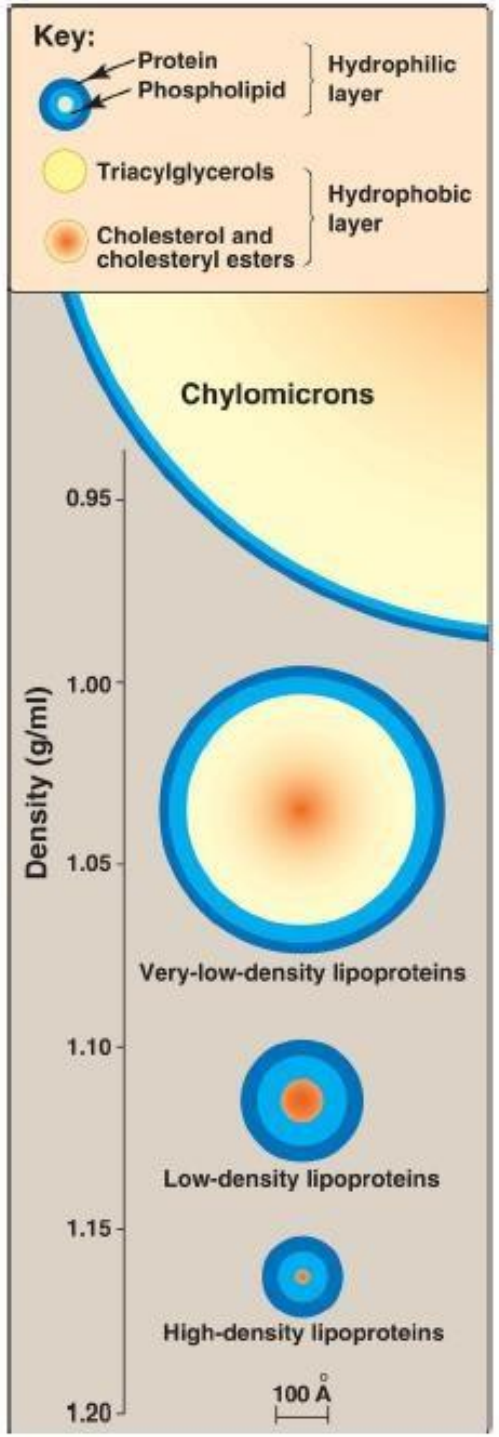
- Lipoproteins are spherical particles composed of an **outer polar layer** and an **inner non-polar core**.

Outer layer:

- Contains phospholipids, free cholesterol, and apolipoproteins.
- These components are polar and interact with plasma.
- Free cholesterol is oriented so that its **OH group faces the surface**.

Inner core:

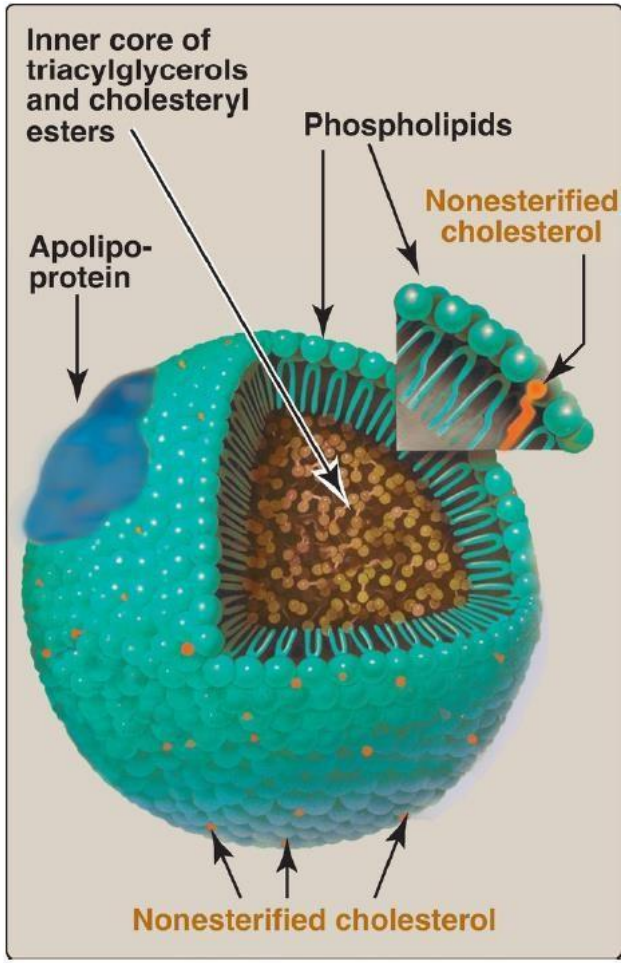
- Contains triacylglycerols (TAGs) and cholesteryl esters.
- TAGs are located deep inside because they are highly hydrophobic.
- Cholesteryl esters are even more deeply packed than free cholesterol



Lipid composition of lipoproteins

- A neutral lipid core (containing TAG and cholesteryl esters) surrounded by a shell of amphipathic apolipoproteins, phospholipid, and non-esterified (free) cholesterol.
  - These amphipathic compounds are oriented such that their polar portions are exposed on the surface of the lipoprotein.
- Sources of the lipid cargo: diet (exogenous source) or de novo synthesis (endogenous source).

- Total cholesterol=LDL-C + HDL-C + VLDL-C
  - VLDL-C is calculated by dividing TAG by 5 because the TAG/cholesterol ratio is 5/1 in VLDL.
    - The goal value for total cholesterol is <200 mg/dl.



Lipid Composition of Lipoproteins

The type and amount of lipid differ between lipoproteins.

Chylomicrons:

- Will move through lymphatic then Venus circulation then liver so it's not connected to the general circulation
- Most of their lipid content is TAG.

VLDL:

- Contain less TAG than chylomicrons and more cholesterol.

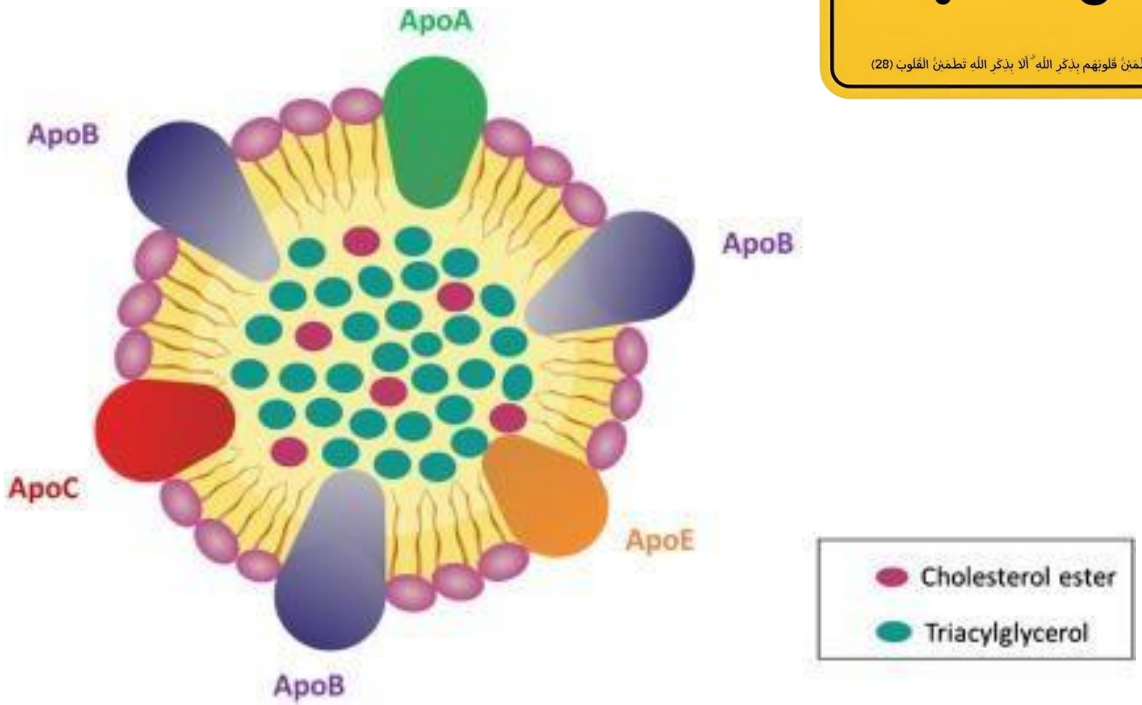
LDL and HDL:

- Most of their lipid content is cholesterol or cholesteryl esters.

Protein composition of lipoproteins

(Apolipoproteins)

- Functions:
  - Structural (cannot be removed).
  - Recognition sites for cell-surface receptors
  - Activators or coenzymes for enzymes involved in lipoprotein metabolism.
- some are exchanged freely among lipoproteins.



Classes of apolipoproteins are denoted by letters (ApoA , ApoB, ApoC, ApoE), and subclasses are designated by Roman numbers.

- Example: apoC-I, apoC-II, and apoC-III.

Apolipoproteins

- **Structural apolipoproteins:**
- Apo B-48 → Chylomicrons only
- Apo B-100 → VLDL, IDL, LDL(only one protein)
- Apo A-I → HDL
- **Exchangeable apolipoproteins:**
- A-I, A-II, C-I, C-II, C-III, E
- **Only chylomicrons:** Apo B-48
- **Only HDL structural:** Apo A-I
- **LDL receptor binding:** Apo B-100
- **Remnant clearance:** Apo E

Apolipo-protein	Molecular Weight	Chylomicron (CM)	VLDL	IDL/CM remnants	LDL	HDL
AI	28,016	Ex	Ex			St
AII	17,414	Ex	Ex			Ex
B100	515,000		St	St	St	
B48	241,000	St*		St*		
CI	6600	Ex	Ex			Ex
CII	8800	Ex	Ex			
CIII	8750	Ex	Ex	Ex		Ex
E	34,100	Ex	Ex	Ex		Ex

*B48 is exclusive to chylomicrons and chylomicrons remnants. St, structural apolipoprotein; Ex, exchangeable apolipoprotein. Other apolipoproteins (AIV, AV, D, F, G, H, J, (a)) are beyond the scope of this review.

They can be classified into:

- **Structural (St)** apolipoproteins
- **Exchangeable (Ex)** apolipoproteins
- Structural apolipoproteins cannot be removed from the lipoprotein particle.
- Exchangeable apolipoproteins can move between different lipoproteins.

Apolipoproteins in LDL and HDL

- **LDL** contains **one apolipoprotein only**, which is **ApoB-100**, and it is a **structural protein**.
- **HDL** contains **more than one apolipoprotein**.
- The main structural protein is **ApoA-I**.
- HDL also contains **ApoA-II, ApoC-I, ApoC-II, ApoC-III, and ApoE**.
- Exchangeable apolipoproteins contribute to the **intermediate density** of HDL compared to purely structural ones.

ApoB-100 and ApoB-48

- **ApoB-100 and ApoB-48 are derived from the same gene**.
- The difference between them is due to **RNA editing (cytidine deamination)**.
- This RNA editing introduces a **stop codon**.
- Translation stops early, producing **ApoB-48**, which is a truncated form of ApoB-100.

Why ApoB-100 Is Not Present in Chylomicrons

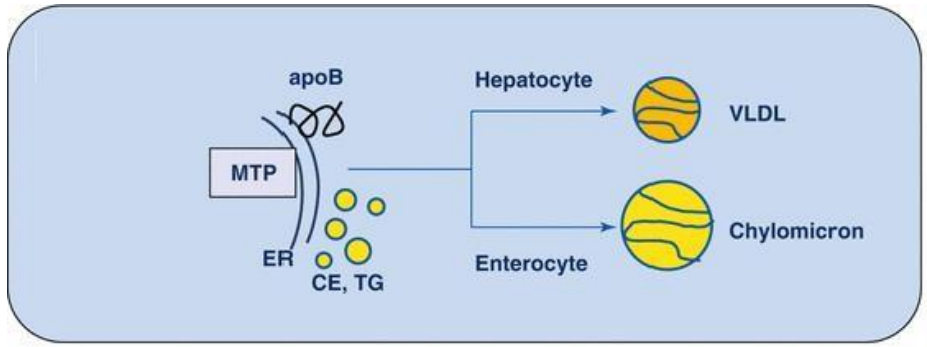
- ApoB-100 is **not present in chylomicrons**.
- Instead, chylomicrons contain **ApoB-48**.
- This is because:
- Chylomicrons are synthesized in **intestinal cells**.
- In intestinal cells, RNA editing occurs, leading to the production of **ApoB-48** instead of ApoB-100.

Site of Synthesis

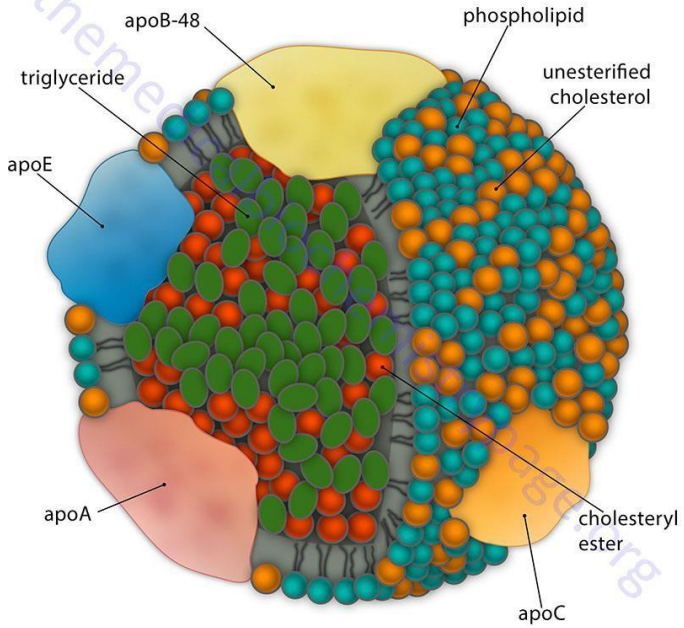
- **Chylomicrons** are synthesized in the **intestinal epithelial cells** and therefore contain **ApoB-48**.
- **VLDL, IDL, and LDL** are synthesized in the **liver** and therefore contain **ApoB-100**.

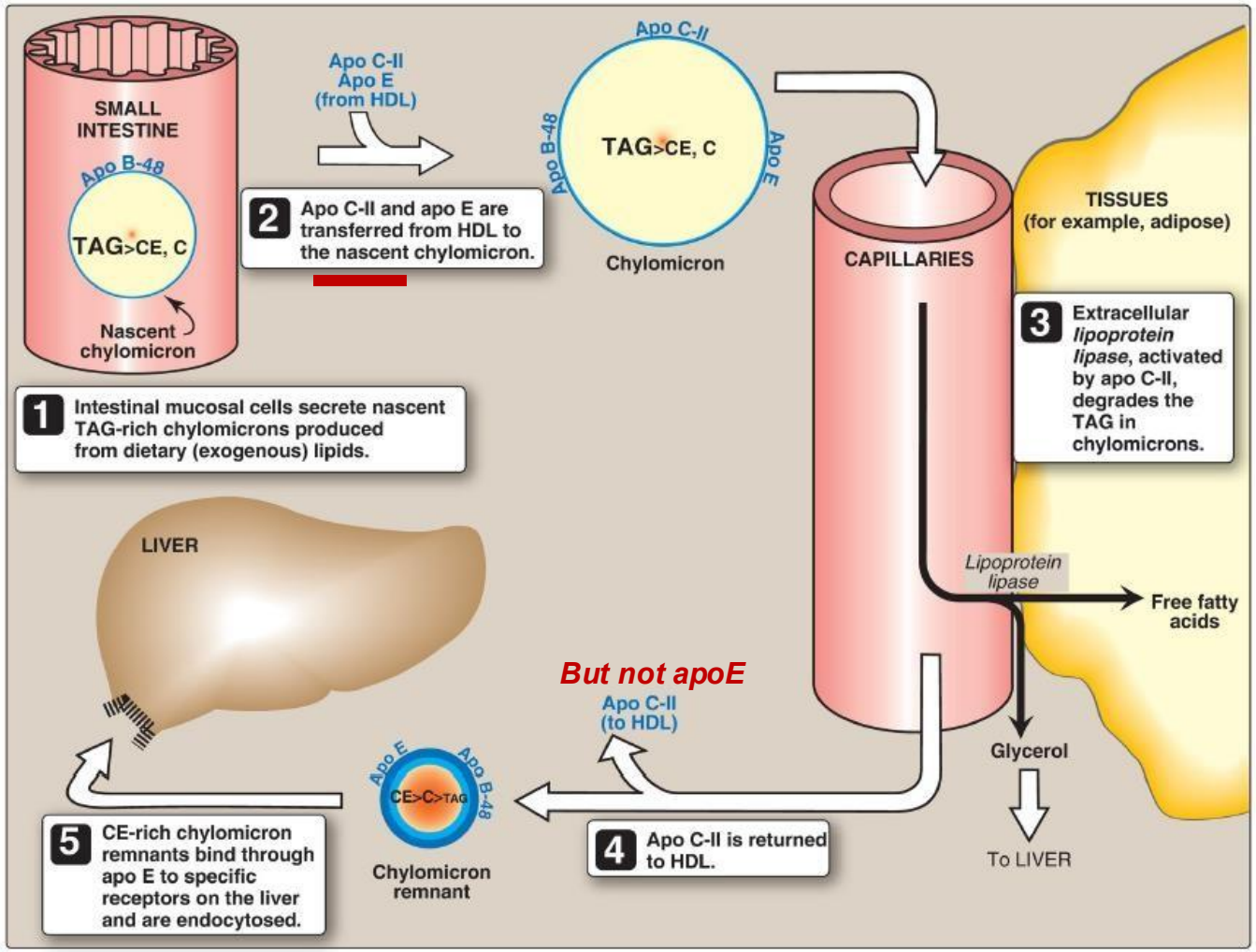
Chylomicrons

Microsomal triglyceride transfer protein (MTP) assembles the apoB protein with the lipids in the ER before transition to the Golgi, where the particles are packaged in secretory vesicles.

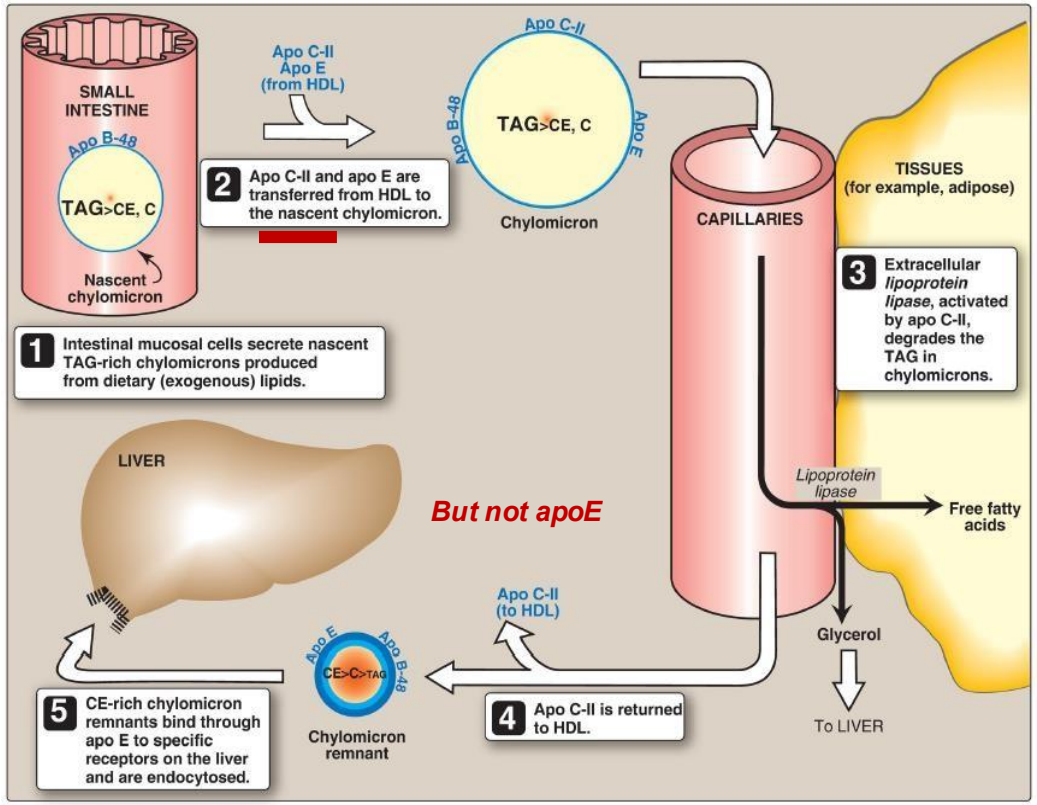


Chylomicron





Chylomicrons

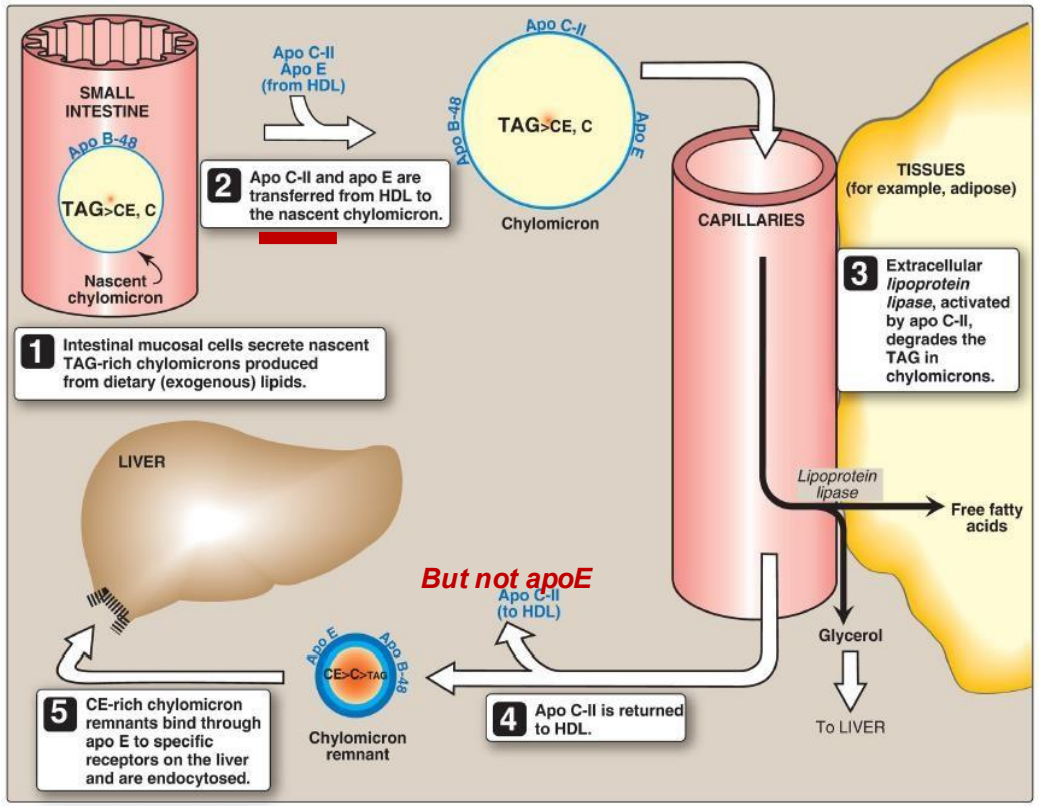


- Chylomicrons are synthesized in **intestinal epithelial cells**.
- They are secreted as **nascent (immature) chylomicrons**.
- Maturation does not occur in intestinal cells; it occurs in the bloodstream.
- The major lipid component of chylomicrons is **TAG**.
- The structural apolipoprotein of chylomicrons is **ApoB-48**

Maturation of Chylomicrons

- Once nascent chylomicrons enter the blood, they acquire apolipoproteins from HDL.
- These apolipoproteins are:
- ApoC-II
- ApoE
- After acquiring these apolipoproteins, the chylomicron becomes a **mature chylomicron**.

Chylomicrons



·**Action of Chylomicrons in Capillaries**

·Mature chylomicrons pass through capillaries of adipose tissue and muscle.

·They interact with **lipoprotein lipase (LPL)**, an enzyme attached to endothelial cells.

·ApoC-II activates lipoprotein lipase.

·LPL hydrolyzes TAG into:

·Free fatty acids

·Glycerol

·Fatty acids are taken up by adipose tissue or muscle.

·Glycerol is transported to the liver.

·**Formation of Chylomicron Remnants**

·After most TAGs are removed, the chylomicron becomes smaller.

·ApoC-II is returned to HDL because its function is completed.

·ApoE remains on the particle.

·ApoE is essential because it acts as a **recognition signal** for the liver.

·**Fate of Chylomicron Remnants**

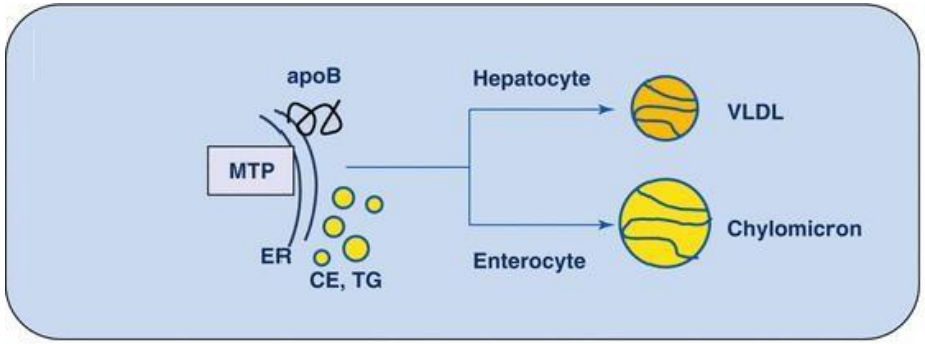
·Chylomicron remnants are recognized by ApoE receptors on hepatocytes.

·They are taken up by the liver via receptor-mediated endocytosis.

·Inside the liver, they are degraded.

·Their components are reused for synthesis of **VLDL**.

Chylomicrons

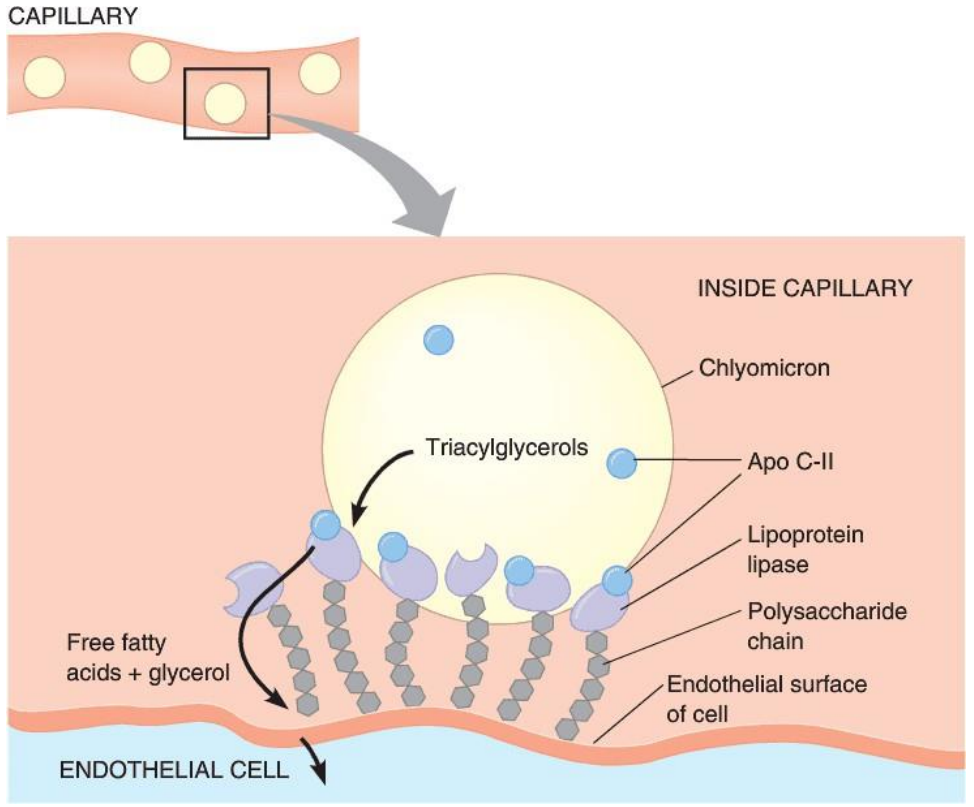


Role of MTP (Microsomal Triglyceride Transfer Protein)

- MTP is essential for the assembly of lipoproteins.
- It transfers lipid components to apolipoproteins during particle formation.
- MTP is found in:
- Intestinal cells → assembly of chylomicrons with ApoB-48
- Hepatocytes → assembly of VLDL with ApoB-100

Function of apo CII

- ApoCII interacts with the lipoprotein lipase, which exists on the cell surface of endothelial cells, activating it.
- Lipoprotein lipase degrades TAG releasing fatty acids and glycerol, which enter the tissues.
- When TAGs are removed, chylomicron remnants are formed, which contain cholesteryl esters, phospholipids, apolipoproteins, fat-soluble vitamins, and a small amount of TAGs.

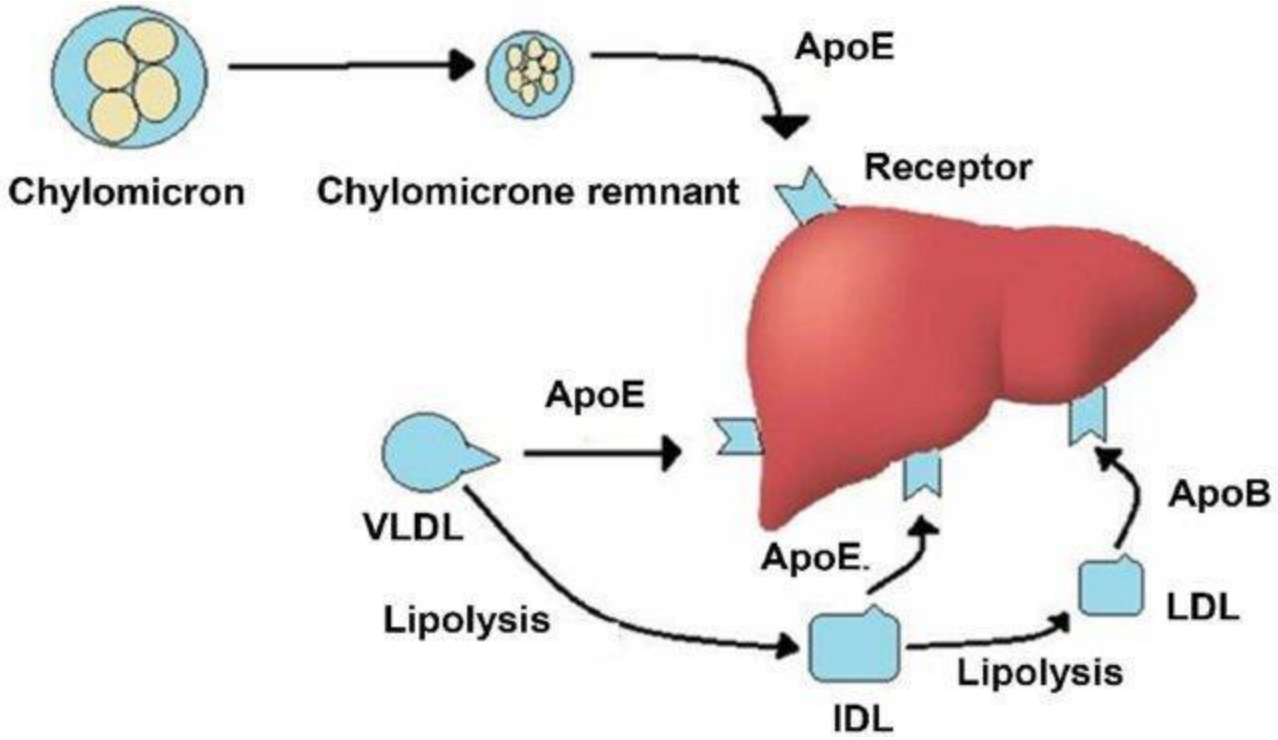


- **Type I hyperlipoproteinemia, familial chylomicronemia, hypertriacylglycerolemia: Deficiency of LPL or apo C-II leading to the accumulation of chylomicron-TAG in the Plasma.**

Fate of chylomicron remnant

- Chylomicron remnants bind to apoE receptors on the cell surface of hepatocytes and are taken into the by receptor-mediated endocytosis.
- The intracellular remnants are hydrolyzed to their component parts.

The chylomicron remnants are degraded in the liver, and their lipid components can contribute to hepatic TAG synthesis, which may later be used for de novo VLDL assembly and secretion



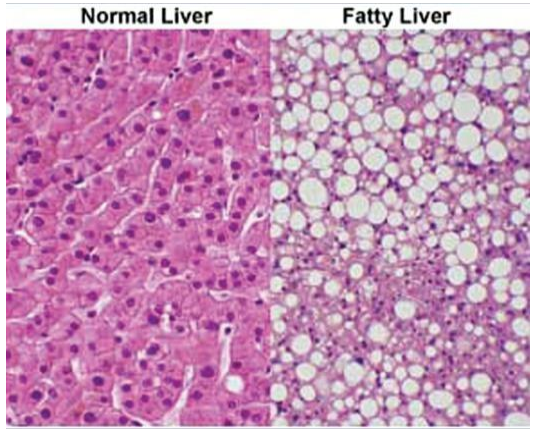
Type III hyperlipoproteinemia: mutations in apoE gene leading to decreased clearance of chylomicron remnants.

Very-low-density lipoprotein (VLDL)

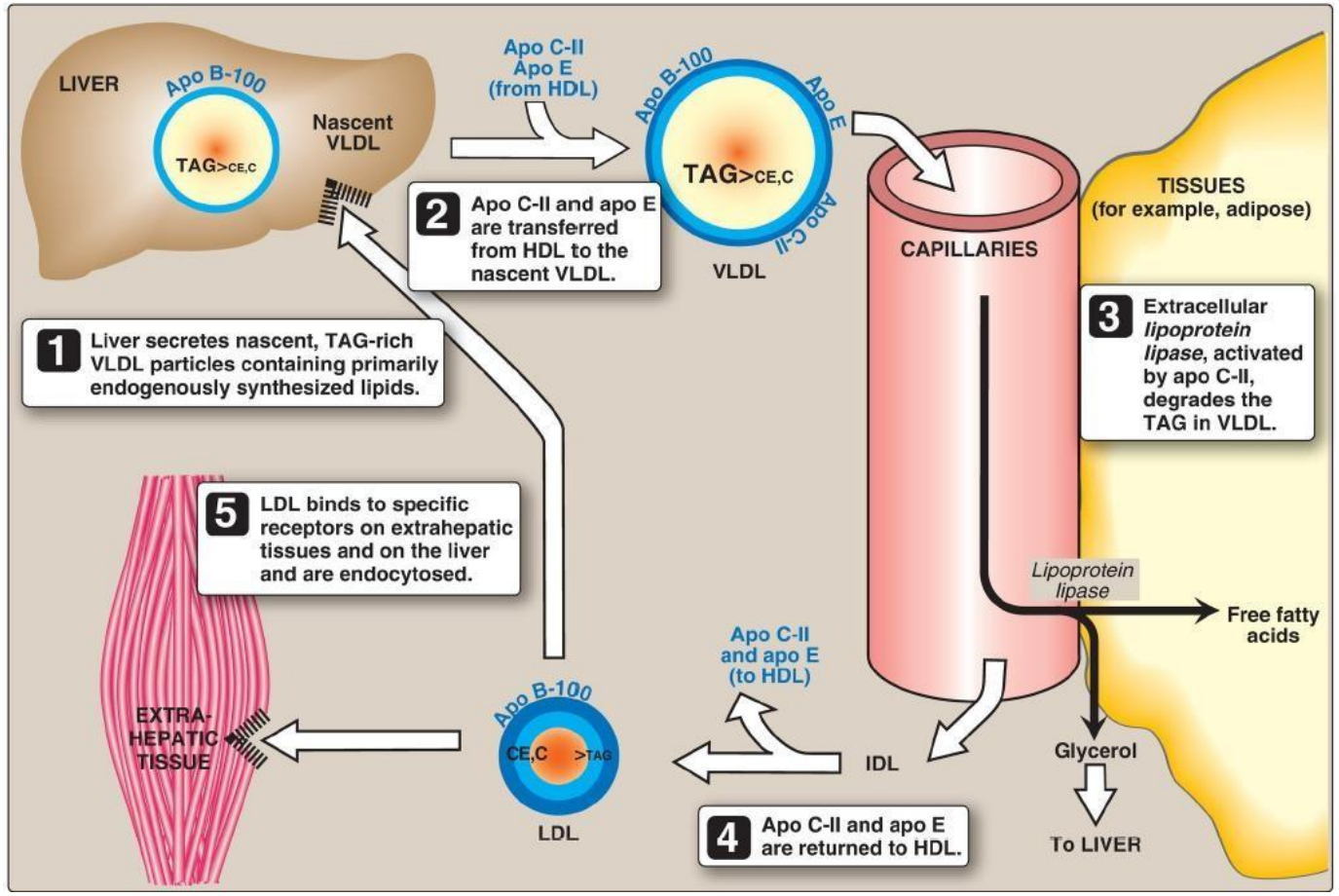
- Nonalcoholic fatty liver (hepatic steatosis):

<u>hepatic TAG synthesis >> VLDL release</u>

  - Examples: obesity and type 2 DM



- **Abetalipoproteinemia**: a rare hypolipoproteinemia caused by <u>defective</u> <u>MTP</u>, leading to low VLDL or chylomicrons and TAG accumulates in the liver and intestine(toxic effect).
  - Deficient fat-soluble vitamins why? Because when the chylomicron are packaged it also package lipid soluble vitamins, cannot be absorbed even from diet

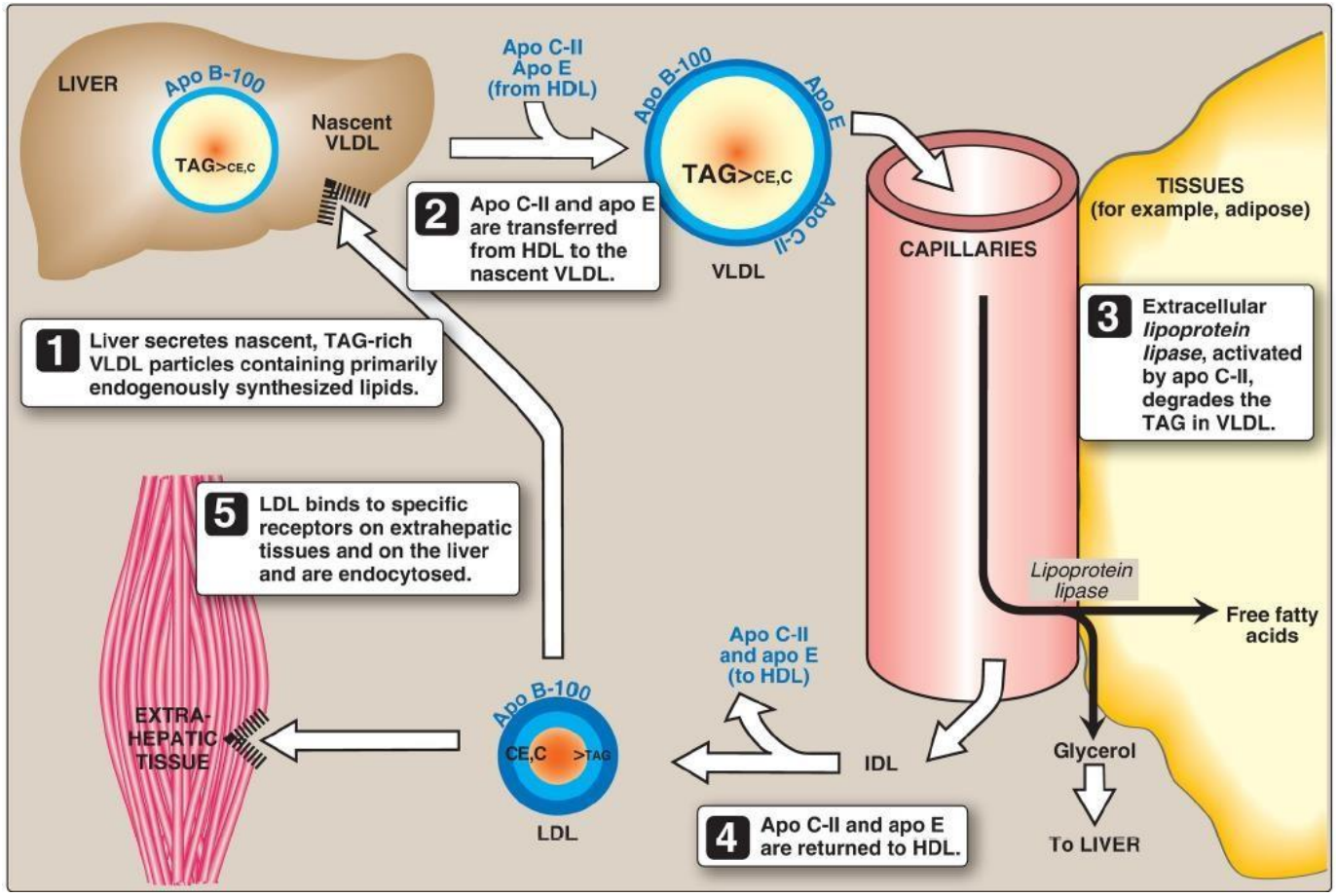


Very-low-density lipoprotein (VLDL)

- VLDL is synthesized in the liver.
- Its major lipid component is TAG.
- Its structural apolipoprotein is **ApoB-100**.
- VLDL is secreted as a nascent particle.
- It receives ApoC-II and ApoE from HDL to become mature.

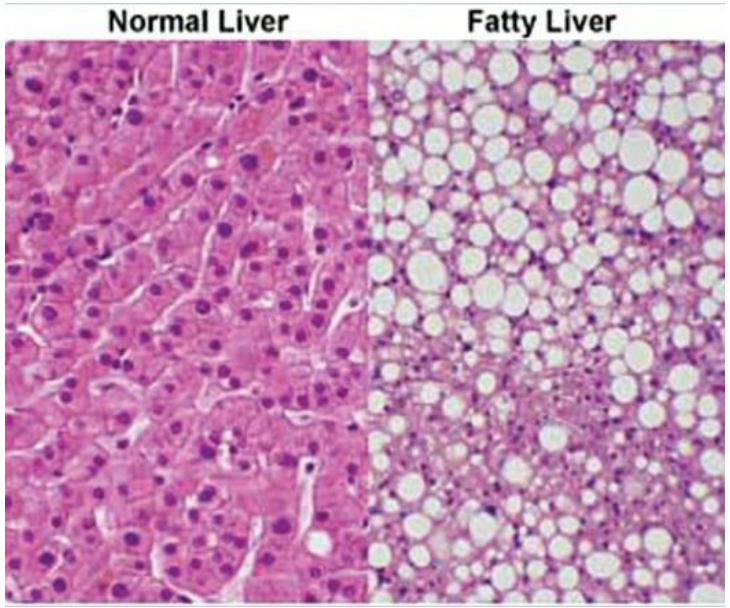
- **Metabolism of VLDL**
- ApoC-II activates lipoprotein lipase.
- TAGs are hydrolyzed into fatty acids and glycerol.
- As TAG content decreases, VLDL becomes **IDL (intermediate density lipoprotein)**
- **Fate of IDL**
- Two possibilities:

1. Taken up by liver via ApoE
2. Further TAG loss → becomes **LDL**
3. During this process:
   - ApoC-II and ApoE are returned to HDL



The lower TAG the higher CE, C

Very-low-density lipoprotein (VLDL)



- Nonalcoholic fatty liver (hepatic steatosis):

hepatic TAG synthesis >> VLDL release

- Examples: obesity and type 2 DM

•increased Hepatic TAG Synthesis and Fatty Liver
•High sugar intake increases hepatic TAG synthesis.
•Excess glucose enters multiple pathways:
-Glycolysis -Pentose phosphate pathway (PPP) -Glycogen synthesis
•Glycolytic intermediates such as:
-Glyceraldehyde-3-phosphate -Dihydroxyacetone phosphate
are converted into **glycerol-3-phosphate**.
•Glycerol-3-phosphate combines with fatty acids to form **TAG**.
•Increased TAG synthesis leads to increased VLDL production.
•If VLDL release is insufficient, TAG accumulates in the liver.
•This leads to **fatty liver**, which may be:
•Non-alcoholic fatty liver disease (SUCH AS IN THIS CASE) كرش مرتفع من اسفل القلب Alcoholic fatty liver disease
•If fatty liver persists, it damages hepatocytes.
•This can progress to **liver cirrhosis** and eventually **liver failure**.

Low density lipoprotein (LDL) bad cholesterol

- Primary lipoprotein is B-100.
- Plasma cholesterol, ~70% of LDL content, is taken to peripheral tissues.
- Receptor-mediated endocytosis
- Type IIa hyperlipidemia (familial hypercholesterolemia [FH]): reduced synthesis of functional LDL receptor leading to premature atherosclerosis.
- Defective apo B-100: autosomal dominant hypercholesterolemia with reduced binding to LDL receptor.

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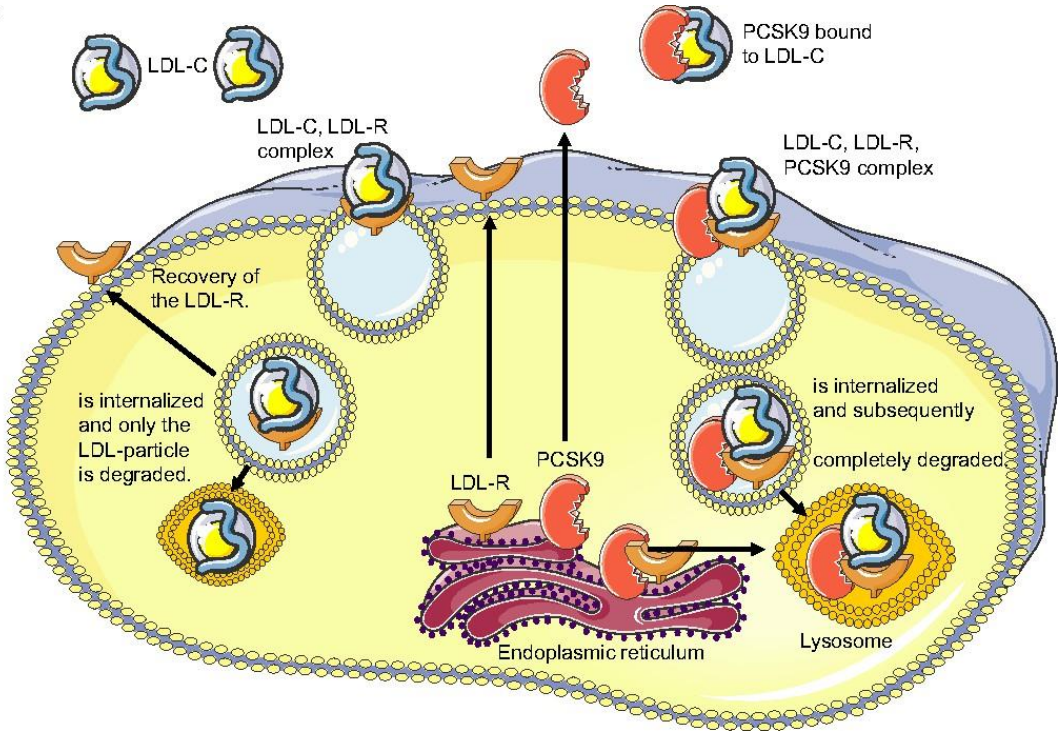
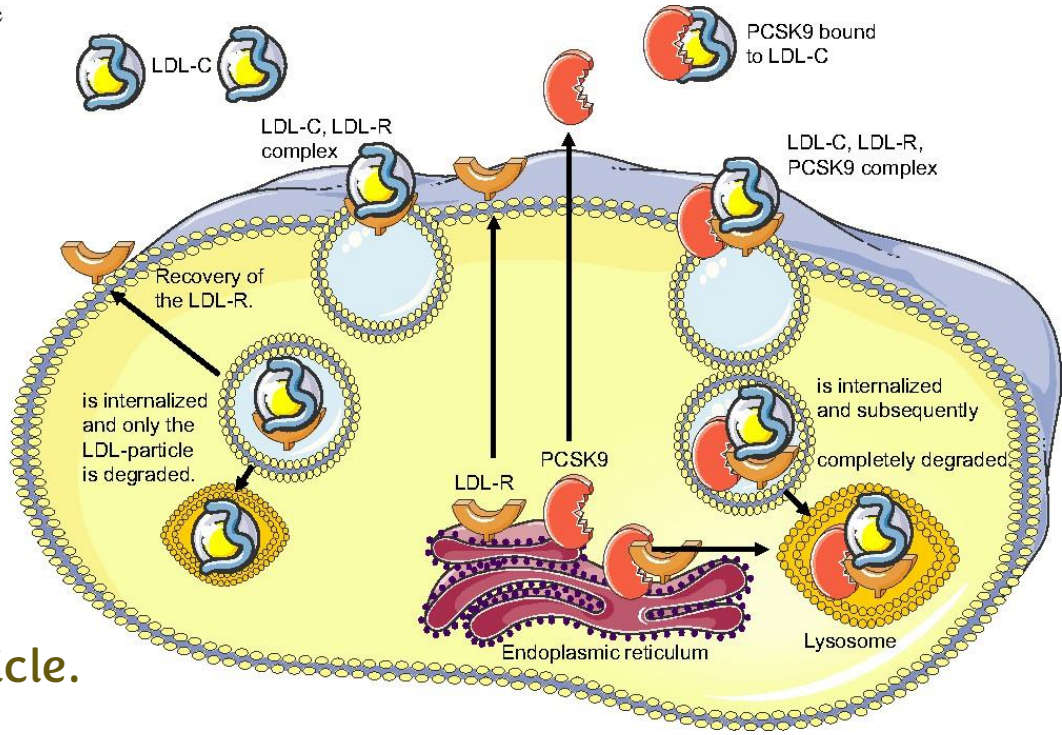


- Proprotein convertase subtilisin/kexin type 9 (PCSK9) promotes internalization and lysosomal degradation of the receptor.
  - PCSK9 inhibitors are now available for the treatment of hypercholesterolemia.

Low density lipoprotein (LDL)

- LDL is synthesized from VLDL after progressive loss of TAGs.
- LDL contains:
- Cholesterol and cholesteryl esters
- Only one apolipoprotein: **ApoB-100**
- LDL has its own specific receptors on cell surfaces.



LDL Receptor-Mediated Endocytosis

- LDL binds to the LDL receptor via ApoB-100.
- A complex is formed and internalized into the cell inside a vesicle.
- The vesicle fuses with lysosomes.
- LDL is degraded, releasing cholesterol inside the cell.
- The LDL receptor is normally recycled back to the cell surface.

Role of PCSK9

- PCSK9 promotes internalization of LDL receptors and prevents their recycling.
- When PCSK9 activity is high, LDL receptors are degraded.
- This reduces the number of LDL receptors on the cell surface.
- As a result, LDL uptake decreases and blood cholesterol increases.

Low density lipoprotein (LDL)

·**Effects of Increased Intracellular Cholesterol**

•High intracellular cholesterol causes:

•Inhibition of **HMG-CoA reductase** (↓ cholesterol synthesis)

•Down-regulation of LDL receptor synthesis

•Activation of **ACAT**

•**ACAT (acyl-CoA cholesterol acyltransferase)** converts cholesterol into cholesteryl esters for storage.

•Stored cholesterol esters accumulate inside the cell.

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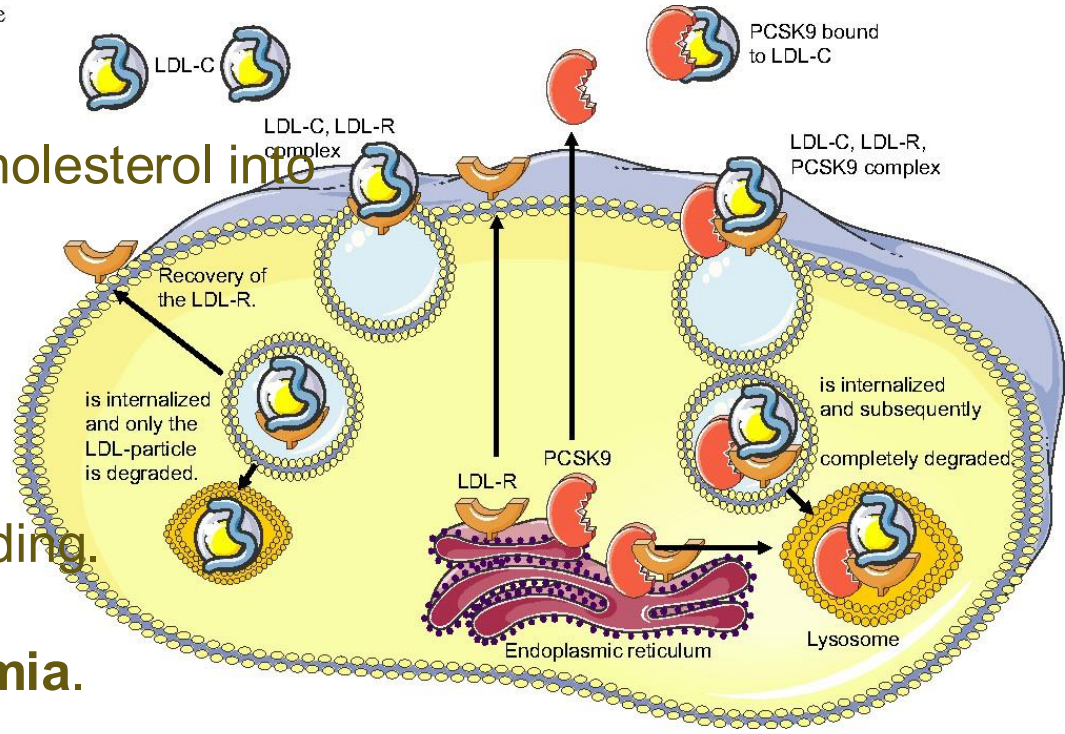


·**LDL Receptor Deficiency and Hypercholesterolemia**

•Mutation in ApoB-100 or LDL receptor causes defective binding.

•LDL cannot be recognized or internalized properly.

•LDL accumulates in the blood, causing **hypercholesterolemia**.

•LDL particles are rigid and hydrophobic.

•They aggregate on blood vessel walls.

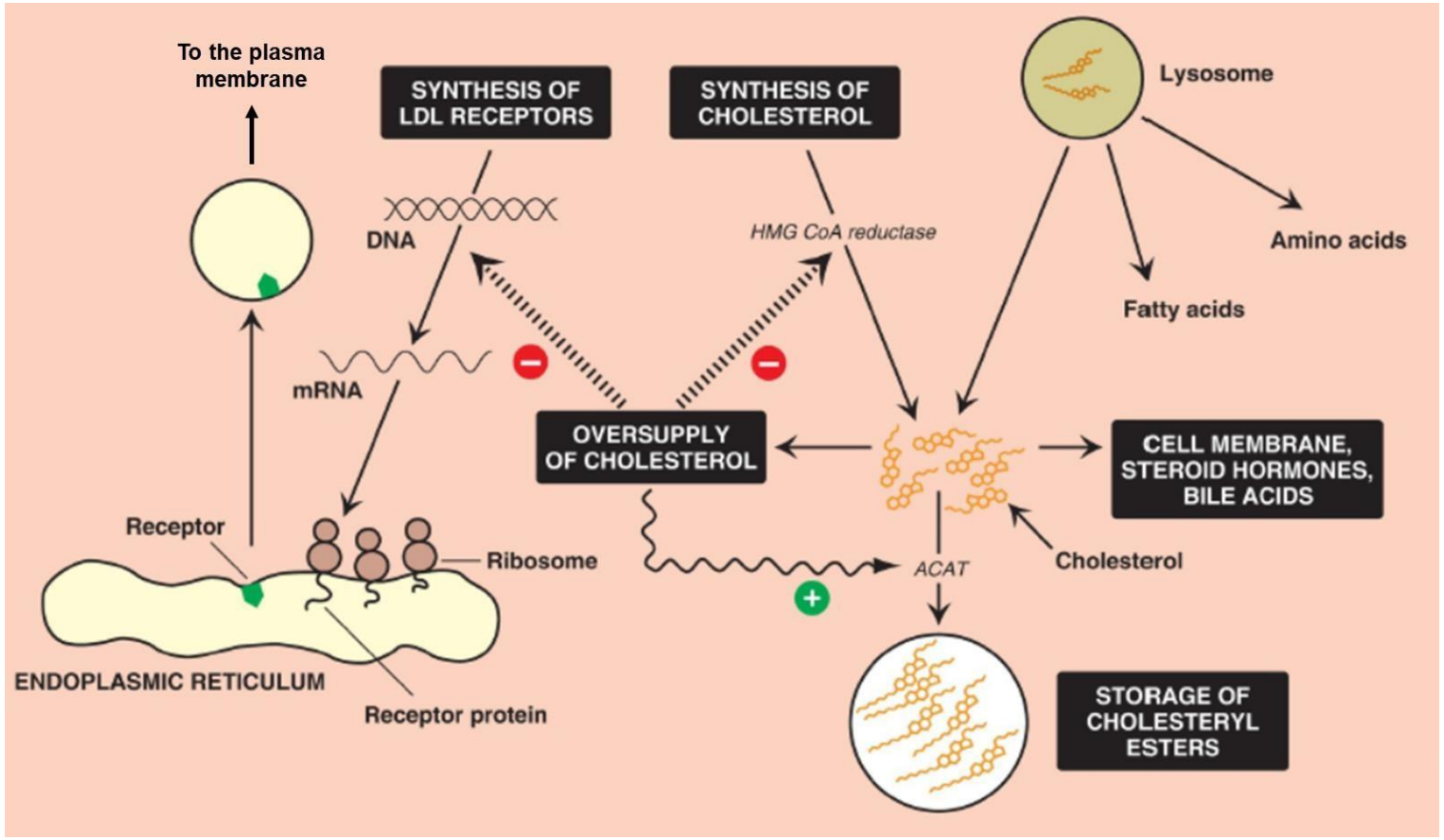
•This causes narrowing of the vessel lumen and rigidity of smooth muscle.

•The vessels lose their ability to contract and relax normally.

•This leads to **atherosclerosis**, often at an early age.

Fate and effects of cholesterol

- High intracellular cholesterol levels
  - inhibit de novo cholesterol synthesis
  - induce the degradation of HMG CoA reductase.
  - decrease the synthesis of LDL receptor through the negative regulation of SREBP-2.
- Excess cholesterol is esterified by *acyl CoA:cholesterol acyltransferase* (*ACAT)* and stored in the cells.
  - The activity of ACAT is enhanced by the increased intracellular cholesterol.



- Regardless of the source, cholesterol enters the cell mainly through **LDL particles**, which are rich in cholesterol and cholesteryl esters.
- LDL enters the cell by **receptor-mediated endocytosis** through the LDL receptor.
- After internalization, the LDL–receptor complex is delivered to endosomes.
- The receptor is usually recycled back to the cell surface, while LDL is transferred to lysosomes.
- In the lysosome, LDL is degraded by lysosomal enzymes, releasing **free cholesterol** inside the cell.
- This leads to an **increase in intracellular cholesterol levels**, which represents an oversupply of cholesterol to the cell

Regulatory Effects of Increased Intracellular Cholesterol

- High intracellular cholesterol causes **inhibition of cholesterol synthesis** inside the cell.
- This occurs by **inhibition and increased degradation of HMG-CoA reductase**, the rate-limiting enzyme in cholesterol synthesis.
- Increased intracellular cholesterol also causes **downregulation of LDL receptor synthesis**.
- As a result, fewer LDL receptors are produced, leading to decreased uptake of additional LDL from the blood.
- This mechanism protects the cell from excessive cholesterol accumulation.

Role of ACAT in Cholesterol Storage

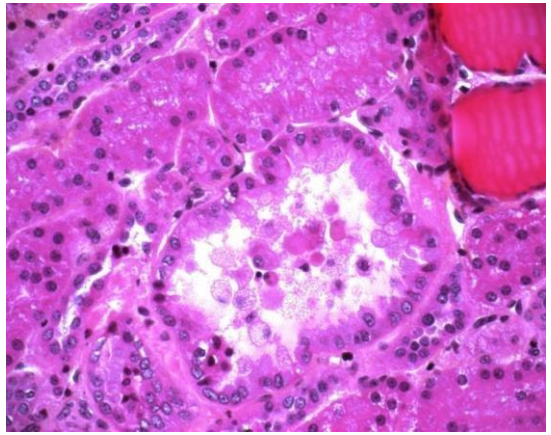
- When cholesterol levels inside the cell become high, **ACAT (acyl-CoA:cholesterol acyltransferase)** becomes activated.
- ACAT catalyzes the **esterification of free cholesterol** by adding a fatty acyl group from acyl-CoA.
- This reaction forms **cholesteryl esters**, which are less toxic and more suitable for storage.
- Cholesteryl esters are stored inside the cell, mainly in lipid droplets.
- When present in very large amounts, they accumulate significantly inside cells.

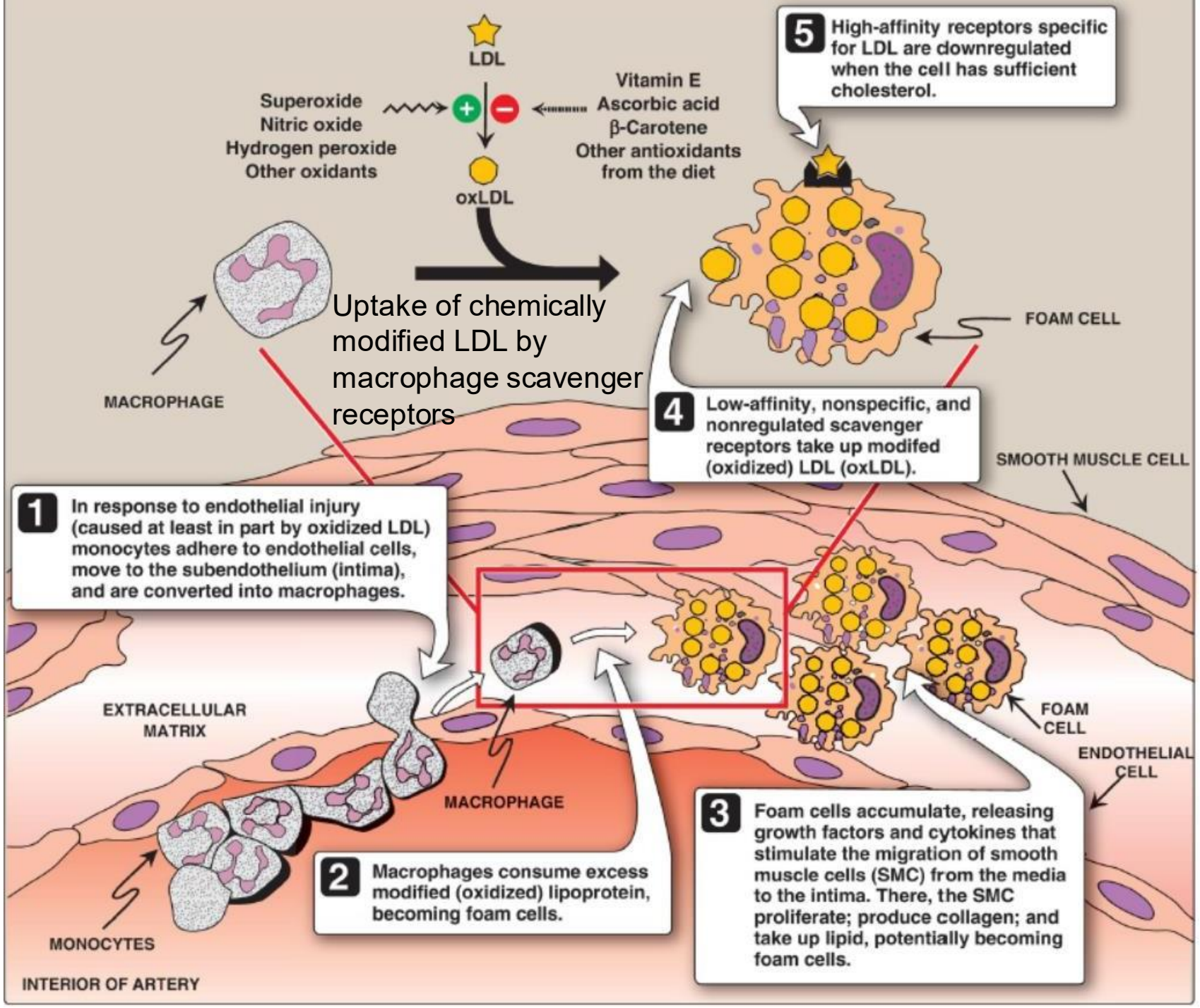
Utilization of Cholesterol by Different Cells

- If the cell is a **liver cell**, cholesterol can be used to synthesize:
- Bile acids
- Vitamin D
- If the cell is involved in **steroid hormone synthesis**, cholesterol is used as a precursor:
- In adrenal cortex cells → synthesis of aldosterone and cortisol
- In gonadal cells → synthesis of sex hormones
- Cholesterol is also an essential structural component of:
- Plasma membranes
- Organelle membranes
- It contributes to membrane stability, fluidity, and proper cellular function.

Foam cells

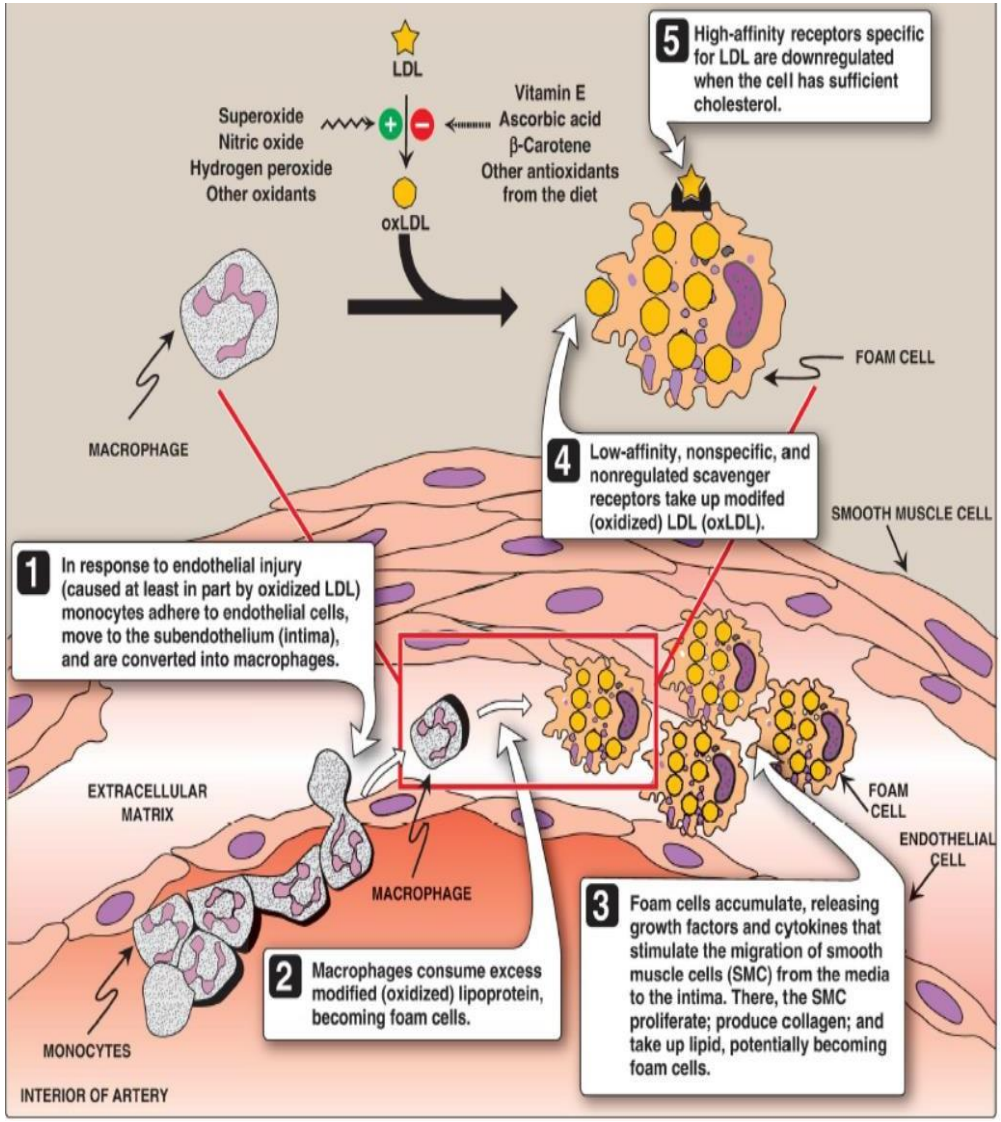
- Macrophages possess high levels of unregulated scavenger receptor class A (SR-A) that can bind and endocytose LDL particles carrying oxidized lipids.
- Unlike the LDL receptor, the scavenger receptor is not down-regulated in response to increased intracellular cholesterol.
- Cholesteryl esters accumulate in macrophages, which transform into “foam” cells that form atherosclerotic plaque.
- LDL-Cholesterol is the primary cause of atherosclerosis.





(Explanation)

- LDL particles can become **oxidized** when they remain for a long time in the circulation or penetrate the arterial wall.
- Oxidized LDL is **not recognized by the normal LDL receptor**. Instead, it is taken up by macrophages via **scavenger receptors (SR-A)**.
- Scavenger receptors are **not regulated by intracellular cholesterol levels**, unlike LDL receptors.
- Therefore, macrophages continue to take up oxidized LDL **without feedback inhibition**.
- As cholesteryl esters accumulate inside macrophages, they transform into **foam cells**.
- Foam cells are lipid-loaded macrophages and represent the **earliest cellular event in atherosclerosis**.
- Foam cells aggregate within the arterial intima forming **fatty streaks**, which later progress into **atherosclerotic plaques**.
- These plaques narrow the vessel lumen, impair blood flow, and increase the risk of **ischemia and cardiovascular disease**.



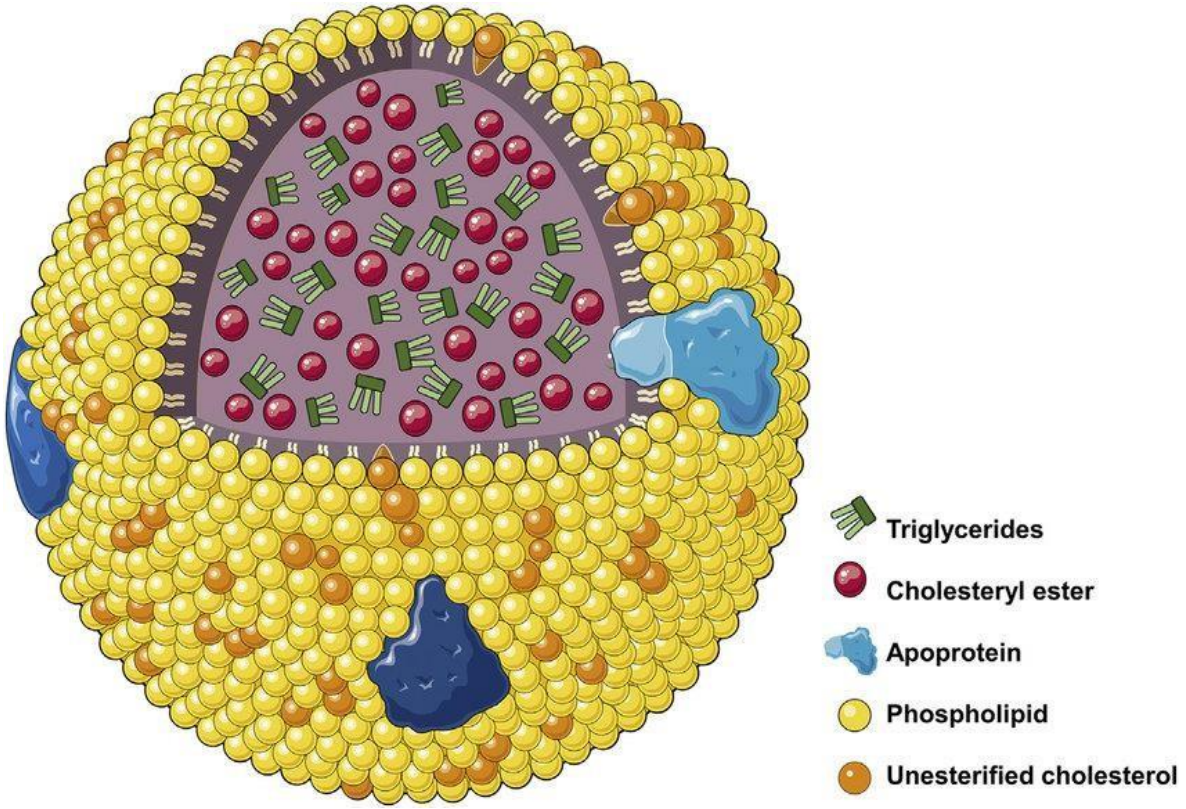
High-density lipoprotein (HDL)

- HDL particles are formed by the addition of lipid to apo A-1 (~70% of lipoproteins in HDL), which is synthesized by the liver and intestine.
- Functions:

1. HDL is a reservoir of apolipoproteins: HDL particles serve as a circulating reservoir of apo C-II (transferred to VLDL and chylomicrons, and is an activator of lipoprotein lipase), and apo E (required for the receptor-mediated endocytosis of IDLs and chylomicron remnants).

2. HDL uptake of unesterified cholesterol: Nascent HDL are disk-shaped particles containing primarily phospholipid (PC) and apo-A, C, and E. They take up cholesterol from non-hepatic (peripheral) tissues and return it to the liver as cholesteryl esters

3. Esterification of cholesterol by LCAT (in the blood stream)



•HDL is called **high-density lipoprotein** because it contains a **high proportion of protein relative to lipids**, which gives it the highest density among lipoproteins. Unlike other lipoproteins, HDL does not have a well-defined storage function; instead, it primarily acts as a **transport and exchange particle**.
•HDL contains different types of apolipoproteins, mainly **Apo A-I**, which is the most important **structural and functional apolipoprotein** and is essential for HDL formation, maturation, and activity. HDL carries cholesterol and cholesteryl esters in a **protective manner**, which is why it is referred to as **"good cholesterol."** Compared to triglycerides (TAGs), HDL has a **higher proportion of cholesteryl esters**.
•Clinically, **higher levels of HDL in the blood are associated with a lower risk of cardiovascular disease**, due to its role in removing excess cholesterol from peripheral tissues.

•Synthesis of HDL

•HDL is synthesized in the **liver** and the **small intestine**. The newly formed particle is known as **nascent HDL**. Nascent HDL is rich in **phospholipids and proteins**, with only a small amount of cholesterol. These components give HDL its **amphipathic nature**, allowing it to interact efficiently with plasma and peripheral tissues and enabling its role in cholesterol transport.

Transport of cholesterol by HDL

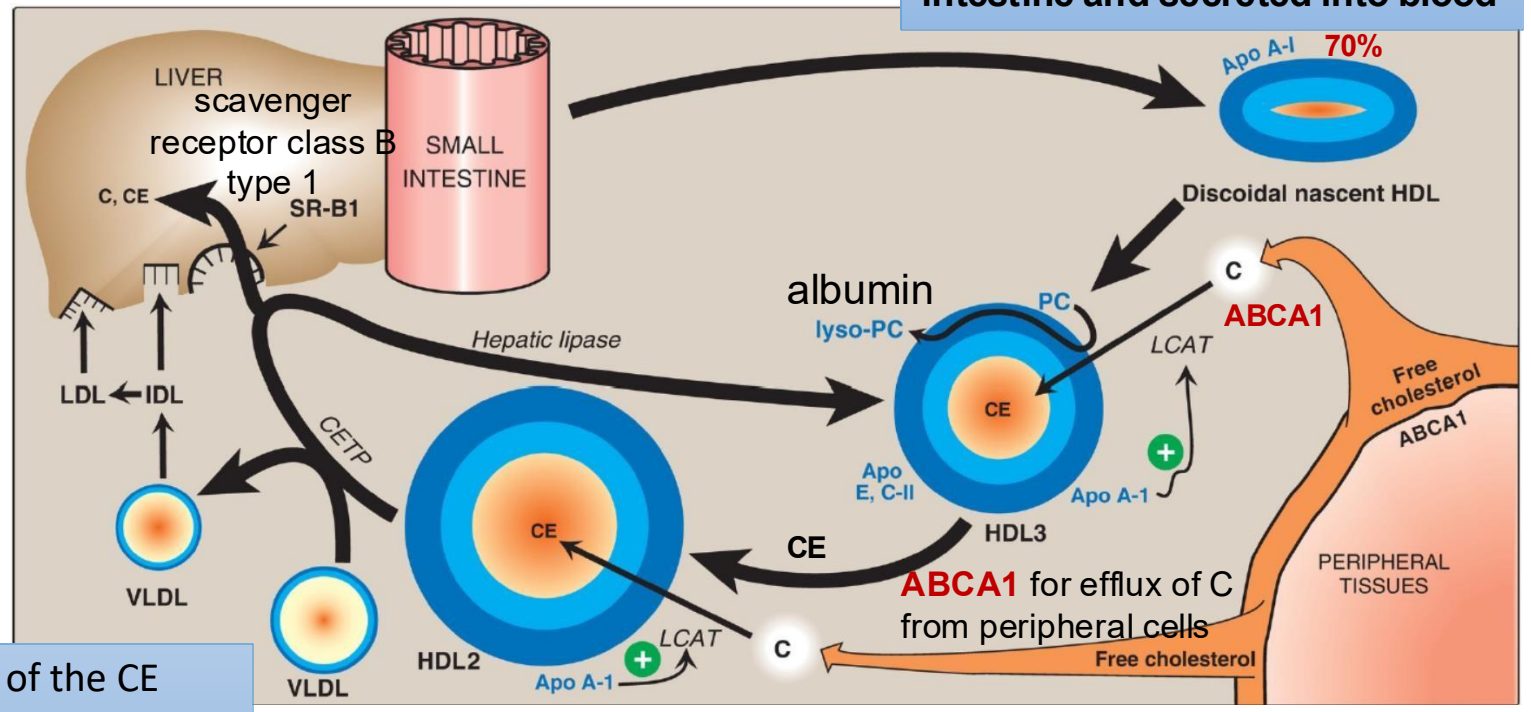
- HDL comprise a heterogeneous family of lipoproteins with a complex metabolism that is not completely understood.
- The liver-synthesized, nascent, HDL-bound plasma enzyme lecithin: cholesterol acyltransferase (LCAT or PCAT) esterifies the HDL-carried cholesterol by transferring the FA of carbon 2 of PC and the CE is sequestered in the HDL core.

✓ When C is taken up by HDL, it is immediately esterified by the plasma enzyme LCAT. LCAT binds to nascent HDL, and is activated by apo A-I but inhibited by CE. LCAT transfers the FA from C2 of PC to cholesterol producing CE, which is sequestered in the core of the HDL, and lyso-PC, which binds to albumin becoming spherical.

➢ Hepatic lipase, which degrades TAG and phospholipids, helps in the conversion of HDL2 to HDL3.

Lecithin = phosphatidylcholine (PC)

Apo A-1 is made by the liver and intestine and secreted into blood



CETP moves some of the CE from HDL to VLDL in exchange for TAGs, relieving product inhibition of LCAT

HDL2 is CE-rich and carries CE to the liver

Tangier disease: no ABCA1, no HDL particles, degradation of apo A-1.

Further explanation

Transport of cholesterol by HDL

HDL is synthesized in both the liver and the small intestine, and its main protein component is ApoA-I. The newly formed nascent HDL is rich in phospholipids and proteins with only a small amount of cholesterol, which gives it an amphipathic nature that allows it to circulate efficiently in plasma. During its movement in the bloodstream, HDL becomes activated, and ApoA-I activates the enzyme lecithin-cholesterol acyltransferase (LCAT). LCAT transfers a fatty acid from lecithin to free cholesterol, converting it into cholesteryl ester. This cholesteryl ester then migrates into the core of the HDL particle. At the same time, cholesterol is removed from peripheral tissues and transferred to HDL via the ABCA1 transporter, contributing to reverse cholesterol transport.

After cholesteryl ester is synthesized, HDL packages it into its core, which causes the particle to become more spherical and well-circulated, forming HDL_3. As HDL_3 circulates in the blood, it gradually increases in size due to the accumulation of more lipids. The higher the content of cholesteryl ester, the more ApoA-I continues to activate LCAT. LCAT keeps converting free cholesterol into cholesteryl ester using phosphatidylcholine, leading to further enrichment of the HDL particle with cholesterol. With ongoing esterification, HDL_3 transforms into HDL_2. HDL_2 is larger in size and contains a higher amount of cholesteryl ester, making it the richest HDL subtype in cholesterol. At this stage, HDL_2 is ready to deliver cholesterol to the liver and to other tissues that consume cholesterol, including sites where sex hormones are synthesized.

Changes during transport to the liver

While HDL is traveling toward the liver, additional modifications may occur. Cholesteryl ester transfer protein (CETP) transfers some of the cholesteryl ester from HDL to VLDL in exchange for triglycerides. As a result, VLDL undergoes triglyceride degradation while gaining cholesteryl ester, and HDL becomes smaller in size. After this exchange, HDL continues through its metabolic cycle as previously described.

Hepatic uptake of HDL

The remaining HDL particle binds to a specific hepatic receptor called SR-B1. This receptor recognizes HDL2 and selectively internalizes its lipid components rather than the entire particle. The internalized cholesterol is then utilized by hepatocytes for several essential processes, including bile acid and bile salt synthesis, plasma membrane formation, vitamin D synthesis, and other metabolic functions.

Conversion of HDL_2 to HDL_3

Hepatocytes also secrete an enzyme known as hepatic lipase. This enzyme converts HDL_2 back into HDL_3 by reducing the amount of cholesteryl ester within the particle. This process explains the continuous remodeling and recycling of HDL particles during circulation.

ABCA1 deficiency

In ABCA1 deficiency, HDL remains in its discoidal nascent form and fails to mature properly. Cholesterol cannot be efficiently transferred from cells to HDL, leading to the accumulation of cholesterol inside cells. This intracellular accumulation of cholesterol is considered hazardous and contributes to cellular dysfunction.

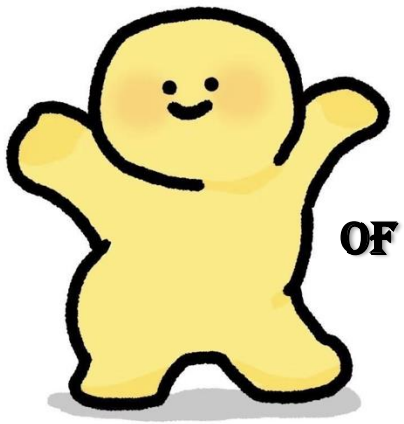
Lipoprotein	Main Lipid Content	Main Apolipoprotein(s)	Site of Synthesis	Main Function
Chylomicron	TAG (very high)	ApoB-48 (structural), ApoC-II, ApoE	Intestine	Transport dietary TAG to tissues
VLDL	TAG (high)	ApoB-100, ApoC-II, ApoE	Liver	Transport endogenous TAG
IDL	TAG ↓, CE ↑	ApoB-100, ApoE	Circulation	Intermediate between VLDL and LDL
LDL	Cholesterol & CE	ApoB-100 only	From VLDL	Deliver cholesterol to cells
HDL	Cholesterol & CE	ApoA-I (main), ApoC-II, ApoE	Liver & intestine	Reverse cholesterol transport

Step	Outcome
LDL oxidation	Forms oxidized LDL
Macrophage uptake	Via scavenger receptors
Foam cell formation	Lipid-loaded macrophages
Fatty streaks	Early plaque
Atherosclerosis	Narrowed vessels & ischemia

Pathogenesis of Atherosclerosis

Fatty Liver Mechanism

Cause	Effect
High sugar intake	↑ Hepatic TAG synthesis
Glycolysis intermediates	↑ Glycerol-3-P
TAG accumulation	↓ VLDL export
Result	Fatty liver
Chronic damage	Cirrhosis → liver failure



THE END

OF LIPIDS METABOLISM

HDL vs LDL

Feature	HDL	LDL
Density	High	Low
Main lipid	CE	CE
Main protein	ApoA-I	ApoB-100
Function	Cholesterol removal	Cholesterol delivery
Clinical role	Protective	Atherogenic

Additional Resources:

Reference Used:
(numbered in order as cited in the text)

1. Lippincott's Biochemistry, Ch. 18

Extra References for the Reader to Use:

1. https://youtu.be/h5eiV_x-qeQ?si=tzz7AOB-mlTlgzor

رسالة من الفريق العلمي:

من فوائد الحوقلة:

يقول ابن القيم: «وأمّا تأثيرُ (لا حولَ ولا قوّةَ إلّا باللهِ) في دفعِ هذا الدّاءِ -يعني الهمَّ والغمَّ- فلما فيها من كمالِ التّفويضِ، والتّبرّي منَ الحولِ والقوّةِ إلّا بهِ وتسليم الأمرِ كلّهِ لهُ، وعدمِ منازعتهِ في شيءٍ منهُ، وعموم ذلكَ لكلِّ تحوّلٍ من حالٍ إلى حالٍ في العالمِ العلويِّ والسّفليِّ، والقوّة على ذلكَ التّحوّلِ، وأنَّ ذلكَ كلّهُ باللهِ وحدهُ؛ فلا يقومُ لهذهِ الكلمةِ شيءٌ. وفي بعضِ الآثارِ: إنّهُ ما ينزلُ ملكٌ منَ السّماءِ، ولا يصعدُ إليها إلّا بـ«لا حولَ ولا قوّةَ إلّا باللهِ»، ولها تأثيرٌ عجيبٌ في طردِ الشّيطانِ»[1].

كتاب: معاني الأذكار.

X: @K_TheRebel

For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			