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Lipoprotein Metabolism

Color Index:

- Original content
- Important
- Extra info, Dr's notes

Objectives:

Slide No. 5	Define and list the types, structure and composition of lipoproteins
Slide No. 5	Understand various functions of lipoprotein particles
Slide No. 8	Compare the functions of lipoprotein particles and their implications in disease
Slide No. 6	Understand the metabolism of chylomicrons, VLDL and LDL particles
Slide No. 7	Discuss the functions of lipoprotein lipase and its role in disease
Slide No. 8	List the diseases due to imbalance in the metabolism of lipoproteins

Overview:

- Lipoprotein types and composition
- Apolipoproteins
- Chylomicrons
- VLDL particles and their metabolism
- Lipoprotein lipase
- VLDL diseases

Lipoproteins

What is a lipoprotein?

Plasma spherical macromolecular complexes of **Lipids** and **Specific proteins** (**apolipoproteins**).

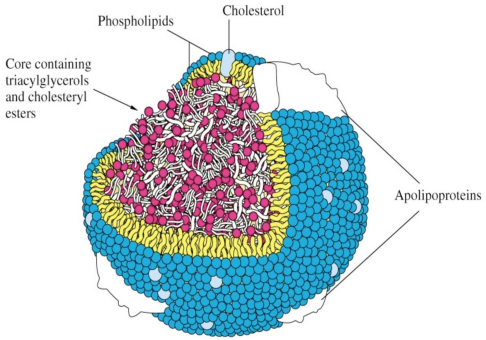
Composition

1. **Neutral lipid core (hydrophobic):**

-Triacylglycerols (TAGs)
-Cholesteryl esters

2. **Hydrophilic shell:**

-Amphipathic apolipoproteins
-Phospholipids
-Free cholesterol



Function

Keep the hydrophobic lipid contents soluble while transporting them to and from the tissues.

Apolipoproteins

★ Types

1 Apo B-48, B-100

☆ **Apolipoprotein B100**: Found in VLDL and LDL it represents the entire protein encoded by the gene for apo B.

☆**ApoB-48**: is so named because it constitutes the N-terminal 48% of the previous protein.

2 Apo C-I, C-II, C-III

mainly associated with HDL. During absorption of dietary fat, the apo C preferentially redistribute to the surface of the triglyceride-rich chylomicrons and VLDL

3 Apo E

☆ **exists in three isoform:**

1- Apo E-2 (binds poorly to the receptors)
2- Apo E-3 "in majority of people"
3- Apo E-4

★ Functions:

1 Provide structure to lipoprotein particles

Some are essential structural components of the particles and cannot be removed whereas others are transferred freely between lipoproteins

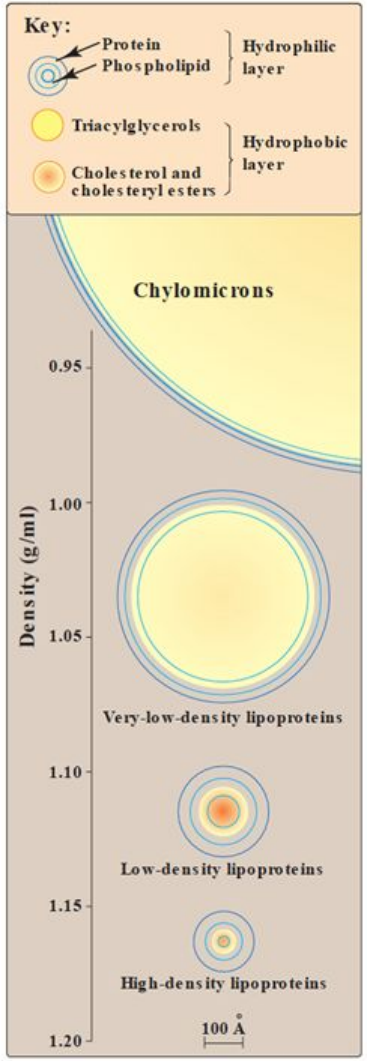
2 Provide recognition sites for cell-surface receptors

3 Activators or coenzymes for the enzymes involved in lipoprotein metabolism

Types Of Lipoproteins

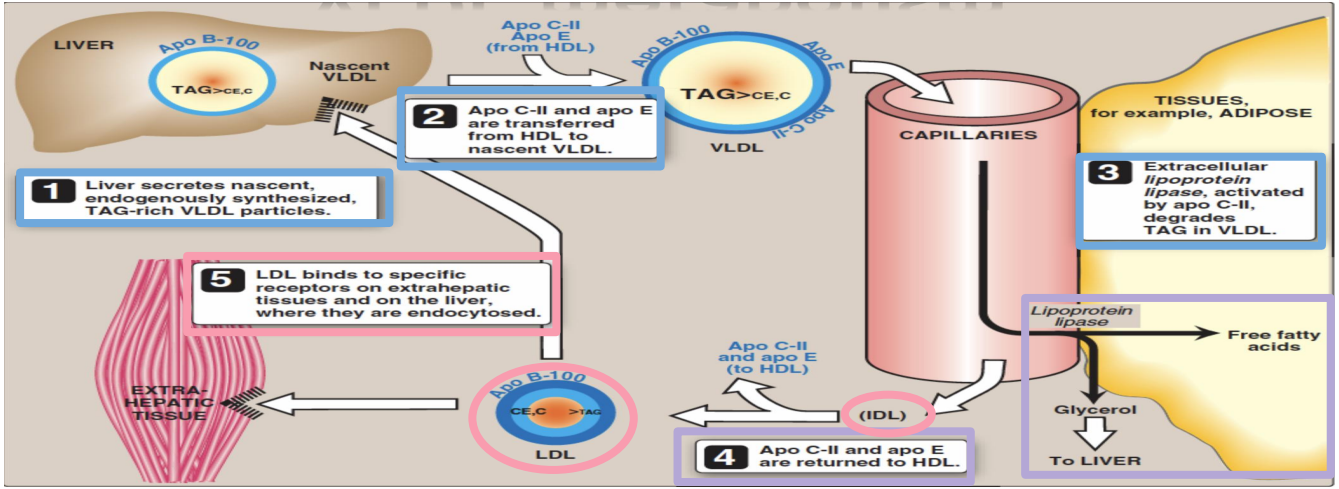
Lipoprotein	Composition	Density	Size	Produced in	Final destination	Notes
Chylomicrons	☆ Dietary TAGs (90%) • Cholesterol • Cholesteryl esters • Fat-soluble vitamins	Lowest	Largest	Intestinal mucosal cells	Peripheral tissue	Responsible for The milky appearance of plasma after a meal 
VLDL (Very low density lipoprotein)	☆ Endogenous TAGs (mainly) Cholesterol (free and esterified)	Low	Large	Liver	Peripheral tissue	
LDL (Low density lipoprotein)	• Cholesterol • cholesteryl esters	High	Small	from VLDL particles (Liver)	Peripheral tissue	binds to cell surface receptors thru Apo B-100 so it act as a recognition molecule by the cell receptors (receptor-mediated endocytosis).
HDL (High density lipoprotein)	☆ cholesterol • cholesteryl esters • Protein • Phospholipids	Highest	Smallest	• Liver • intestine	Peripheral tissues to the liver	contain: • Apo A-1 • Apo C-2 • Apo E

☆ Proteins have higher density than lipids so increase in the protein content will increase the density of lipoprotein and vice versa
☆ Composition is determined by concentration not amount.



☆ **Chylomicrons have similar pathway** but the differences are:
- Apo B-100 → apo B-48
- IDL → chylomicron remnants

VLDL metabolism



1 Release from liver

☆ **Nascent** (immature) particles containing:
1- TAGs and Cholesterol.
2- **Apo B-100.**

* Obtain **apo C-II** and **apo E** from circulating **HDL** particles. (and become mature)
→ **Apo C-II** required for activation of **LPL**

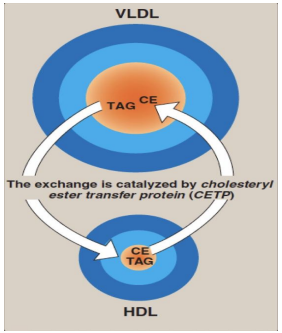
2 Modification in the circulation

☆ TAGS in VLDL are degraded by **lipoprotein lipase** (LPL).

☆ VLDL becomes smaller and denser **(IDL)**

☆ Surface components (apo C and E , from HDL) are returned to HDL.

☆ VLDL transfers TAGs to HDL in exchange for **cholesteryl esters.**
→ This exchange is catalyzed by **cholesteryl ester transfer protein (CETP).**



3 Conversion to HDL

☆ After modifications, VLDL is converted to:
1- **LDL.**

2- **IDL** it either give up apo C-II and apo E back to the HDL and become LDL, or it can be taken up by liver cells thru apo E

3- **VLDL remnants** "smaller molecule, smaller than VLDL"

Lipoprotein Lipase (LPL)

Extracellular enzyme that degrades lipids

Site:

Anchored (linked) by heparin sulfate to the capillary walls of most tissues.

☆Mainly present in:

- Adipose tissue
- Cardiac muscle
- Skeletal muscle.

Function:

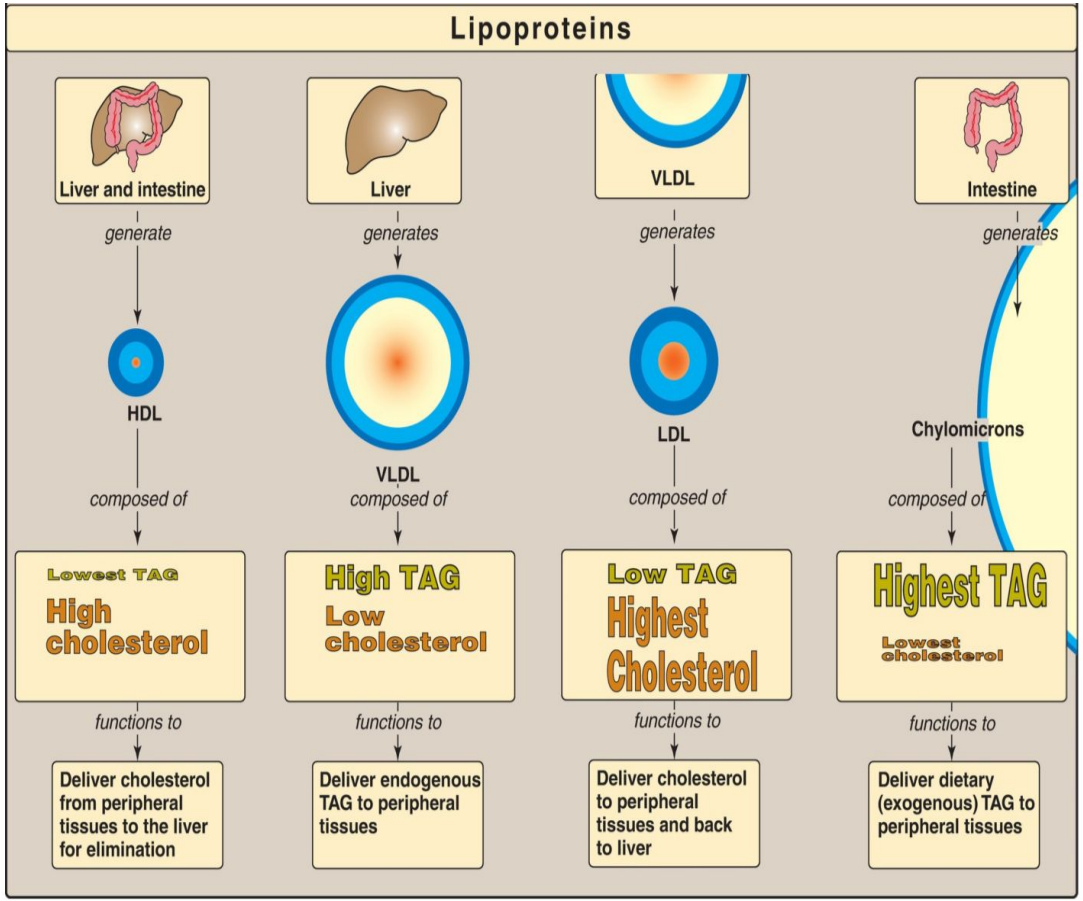
Degrades TAGs into free fatty acids and glycerol.

Characteristics:

- Requires apo C-II for activation
- Insulin stimulates it's synthesis

VLDL diseases

Disease	About	Cause	Lead to
Hypolipoproteinemia	-	Abetalipoproteinemia (inability to load apo B with lipids)	• Few VLDLs and chylomicrons • TAGs accumulation in liver and intestine
Steatohepatitis	(Fatty liver disease)	Imbalance between: • TAG synthesis in the liver • Secretion of VLDL from the liver	1- accumulation of TAGs in the liver 2-Obesity 3-Type 2 diabetes mellitus
Type I hyperlipoproteinemia	• Rare, autosomal recessive. • High fasting plasma TAGs are observed in these patients	familial deficiency of • LPL • or its coenzyme (apo C-II)	excessive accumulation of chylomicrons in plasma (≥1000 mg/dl) (hyperchylomicronemia)
Type III hyperlipoproteinemia	Other names: • familial dysbetalipoproteinemia • broad beta disease	Individuals homozygous for apo E-2 → deficient in clearing: • Chylomicron remnants and • IDL from the circulation	• Hypercholesterolemia • Premature atherosclerosis



Take home message

- 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

Quiz

MCQs

Q1: Imbalance between TAG synthesis in the liver and Secretion from the liver?
a) Hypolipoproteinemia **b)** Steatohepatitis
c) Type I hyperlipoproteinemia **d)** Type III hyperlipoproteinemia

Q2: LPL Requires which of the following for activation?
a) Heparin **b)** TAGs **c)** Apo C-II **d)** Insulin

Q3: TAGs are mainly transported by?
a) LDL **b)** HDL **c)** Chylomicron **d)** IDL

Q4: Which of the following is the function of apolipoproteins?
a) Provide recognition sites for cell-surface receptors
b) Mainly present in adipose tissue, cardiac and skeletal muscle.
c) Degrades TAGs into free fatty acids and glycerol.
d) inhibitors of the enzymes involved in lipoprotein metabolism

Q5: What is the major apoprotein in LDL?
a) Apo A **b)** Apo B-100 **c)** Apo D **d)** Apo C

Q6: What is the smaller form of VLDL?
a) VLDL remnants **b)** LDL **c)** HDL **d)** IDL

Q7: patients with type III hyperlipoproteinemia & homozygous apo E-2 are deficient in clearing?
a) Chylomicron remnants **b)** IDL **c)** HDL **d)** Both a & b

Q8: What is the cause of fatty liver?
a) ↑ TAG synthesis in the liver **b)** ↓ Secretion of VLDL from the liver
c) Obesity **d)** Both a & b

SAQs

Q1: list the types of lipoproteins

Q2: list the functions of Apolipoproteins?

☆ For Questions 3 and 4, use the following scenario:
A young girl with a history of severe abdominal pain was taken to her local hospital at 5 a.m. in severe distress. Blood was drawn, and the plasma appeared milky, with the triacylglycerol level >2,000 mg/dl (normal = 4–150 mg/dl). The patient was placed on a diet extremely limited in fat but supplemented with medium-chain triglycerides.

Q3: which lipoprotein particles are most likely responsible for the appearance of the patient's plasma?

Q4: Which protein is most likely to be deficient in this patient?

★ MCQs Answer key:

1) B 2) C 3) C 4) A 5) B 6) D 7)D 8) D

★ SAQs Answer key:

1) Chylomicrons (lowest density, largest), VLDL (very low density lipoproteins), LDL (low density lipoproteins) And HDL (high density lipoproteins).

2) Provide structure to lipoprotein particles, Provide recognition sites for cell-surface receptors, Activators or coenzymes for the enzymes involved in lipoprotein metabolism

3) Chylomicrons

4) Apolipoprotein C-I

Team members

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- Alkaseem binobaid
- Fares Aldokhayel
- Naif Alsolais
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