# LIPOPROTEINS

By
Dr. Samta Sharma
S.O.S in Zoology,
Jiwaji University, Gwalior (M.Sc 201-II)

# LIPOPROTEINS

**Definition**:

**A lipoprotein is a biochemical assembly that contains both proteins and lipids ,**

**bound to the proteins , which allow fats to move through the water inside and outside cells.**

- **The proteins serve to emulsify the lipid molecules. Many enzymes, transporters, structural proteins, antigens, and toxins are lipoproteins.**

- **Calssification** : Lipoproteins differ in the ratio of protein to lipids, and in the particular apoproteins and lipids that they contain.

- They are classified based on their density:

1-**LDL** (low density lipoprotein, highest in cholesteryl esters as % of weight)

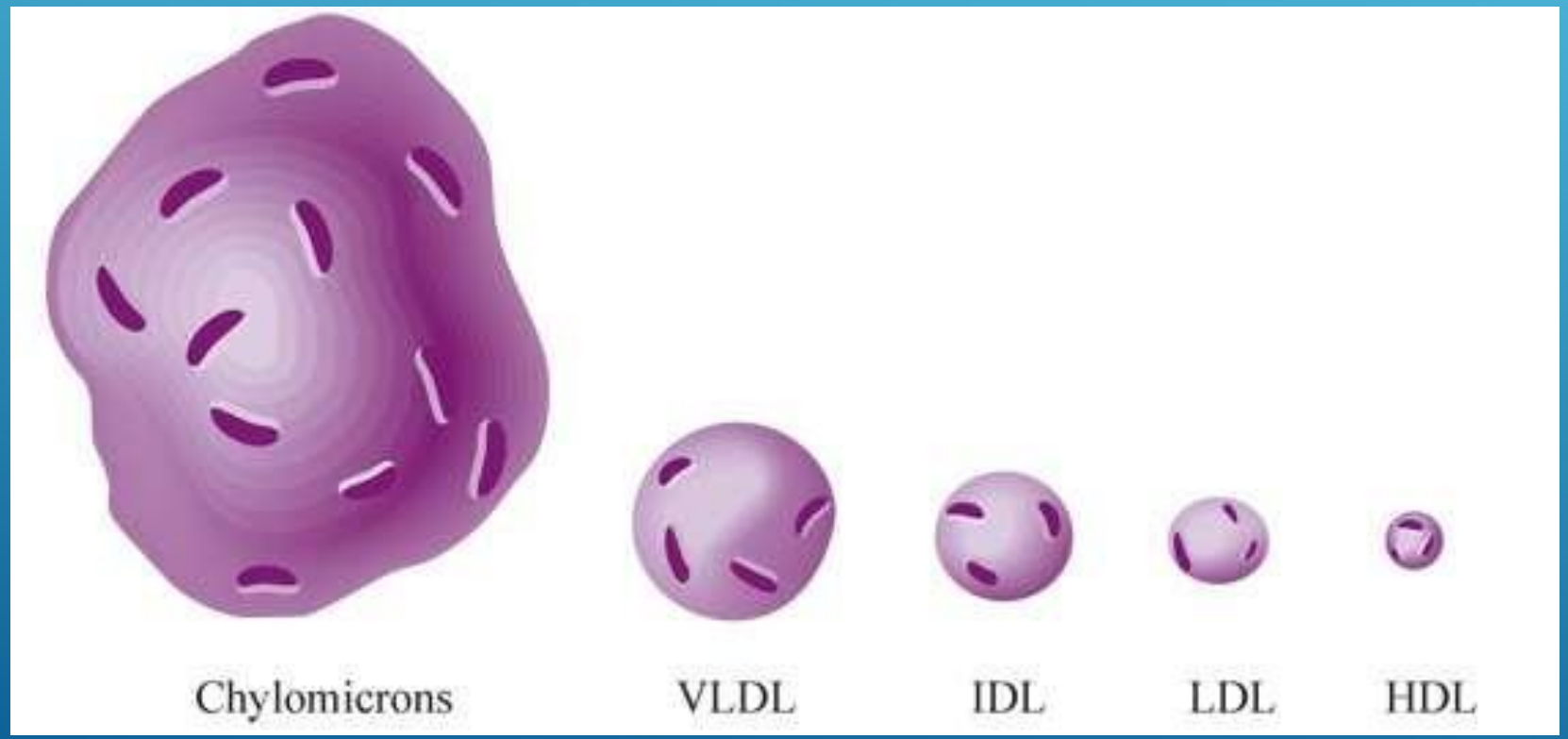
2-**HDL** (high density lipoprotein, highest in density due to high protein/lipid ratio).

3-**Chylomicron** (largest; lowest in density due to high lipid/protein ratio; highest in triacylglycerols as % of weight).

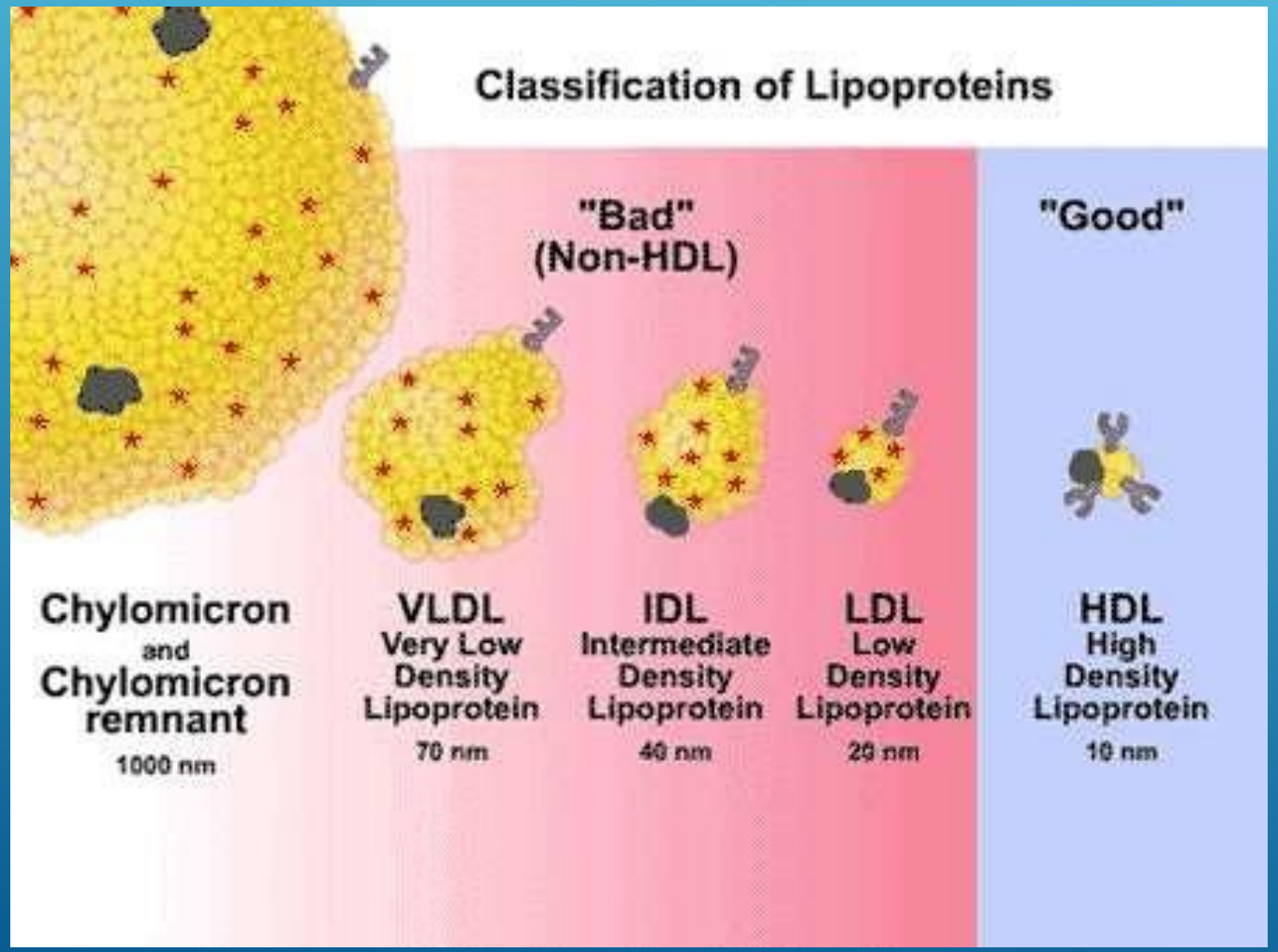
4-**VLDL** (very low density lipoprotein; 2nd highest in triacylglycerols as % of weight).

5-**IDL** (intermediate density lipoprotein).

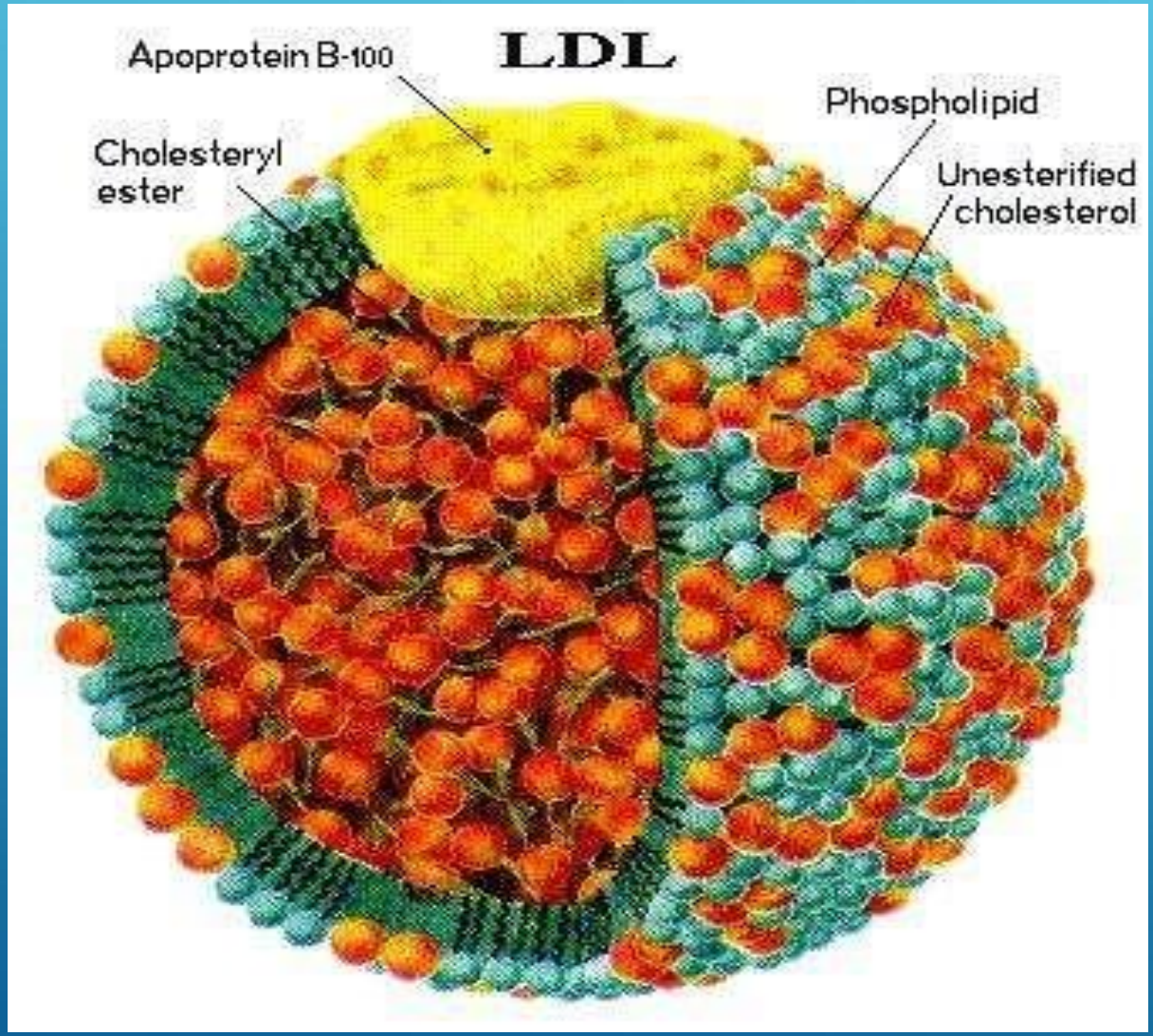
# CLASSIFICATION ACCORDING TO SIZE



# CLASSIFICATION ACCORDING TO BAD AND GOOD LIPOPROTEINS



# LOW DENSITY LIPOPROTEINS (LDLS)



-They are products of VLDL and IDL metabolism, and the most cholesterol-rich of all lipoproteins.

## Function of LDLs :

low density lipoprotein is sometimes called "bad cholesterol" in actuality, however, LDLs:

- Are the principal cholesterol and fat transporter in human blood that carries cholesterol from the liver to the body tissues and cells.
- Despite cholesterol's negative reputation, it's nevertheless an important biomolecule that serves a number of vital purposes in the body.
- Appropriate levels of LDL cholesterol can positively impact health in many ways.
- In metabolism their function is mediating by cellular uptake via receptor-mediated endocytosis followed by lysosomal degradation , and is strongly dependent on the lipid distribution .

- -Apart from their well-established role as lipid transporter,
- LDL particles are intimately involved in the progression of cardiovascular diseases such as atherosclerosis or stroke,
- which are among the most prevalent causes of death.
- Raised plasma levels of LDL are linked to an increased risk for disease.

# Metabolism of LDL :

- About 40 to 60% of all LDL are cleared by the liver in a process mediated by apo B and hepatic LDL receptors.

-The rest are taken up by either hepatic LDL or non-hepatic non-LDL (scavenger) receptors.

- Hepatic LDL receptors

are down-regulated by :

- delivery of cholesterol to the liver by chylomicrons.
- and by increased dietary saturated fat.

They can be up-regulated by decreased dietary fat and cholesterol.

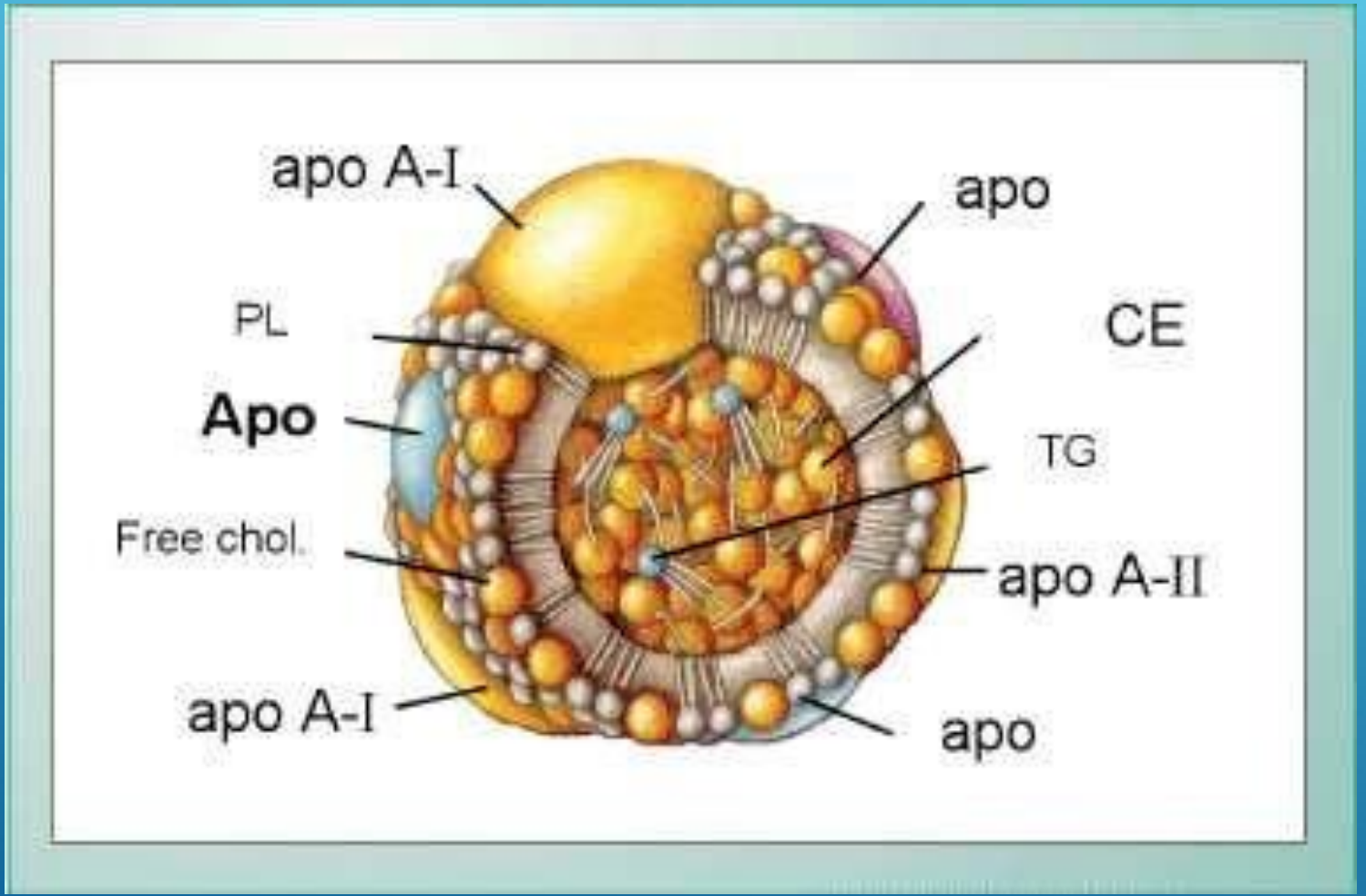
- Non-hepatic scavenger receptors,

- most notably on macrophages.
- take up excess oxidized circulating LDL not processed by hepatic receptors.
- Monocytes rich in oxidized LDL migrate into the sub-endothelial space and become macrophages.
- These macrophages are then take up more oxidized LDL and form foam cells within atherosclerotic plaques .

-The size of LDL particles varies from large and buoyant to small and dense.

-Small, dense LDL is especially rich in cholesterol esters,
It is associated with metabolic disturbances such as hypertriglyceridemia and insulin resistance .

# HIGH-DENSITY LIPOPROTEIN (HDL)



- HDL type is the smallest of the lipoprotein particles.
- It is the densest because it contains the highest proportion of protein to lipids.
- Its most abundant apolipoproteins .

# FUNCTION OF HDL :

**High density lipoprotein (HDL)** particles are protective particles that have functions in the body. They :

- **Play a key role in protecting against heart disease via their role in reverse cholesterol transport, or the transport of excess cholesterol out of the body.**

- Are also part of the innate immune system due to their ability to bind a number of toxic substances in the blood.
- Are Reverse Cholesterol Transport .
- Aid Esterification of cholesterol, (through the action of LCAT).
- Are also a reservoir of apoproteins that can be transferred to other lipoproteins.

- Acceptor of unesterified cholesterol (since they are rich in phospholipids, HDL can accept and solubilize cholesterol.

-HDL particles are self-assembling lipid particles that can be synthesized from a variety of combinations of lipids along with different subsets of hdl-associated proteins that confer different functions.

## Metabolism of HDL:

HDLs are synthesized in the **liver** and the **small intestine**. They are the **lipoproteins with the higher protein content** (it can reach around 50 % of the particle total weight). When secreted, they contain little cholesterol and **no** cholesteryl esters.

**-HDL** are formed by different apolipoproteins, including apo A1, apoe and apo C-II. In fact, they act as transporters of apoe and apo C-II from their synthesizing organ (the liver) to the plasma, making available these apoproteins to other lipoproteins.

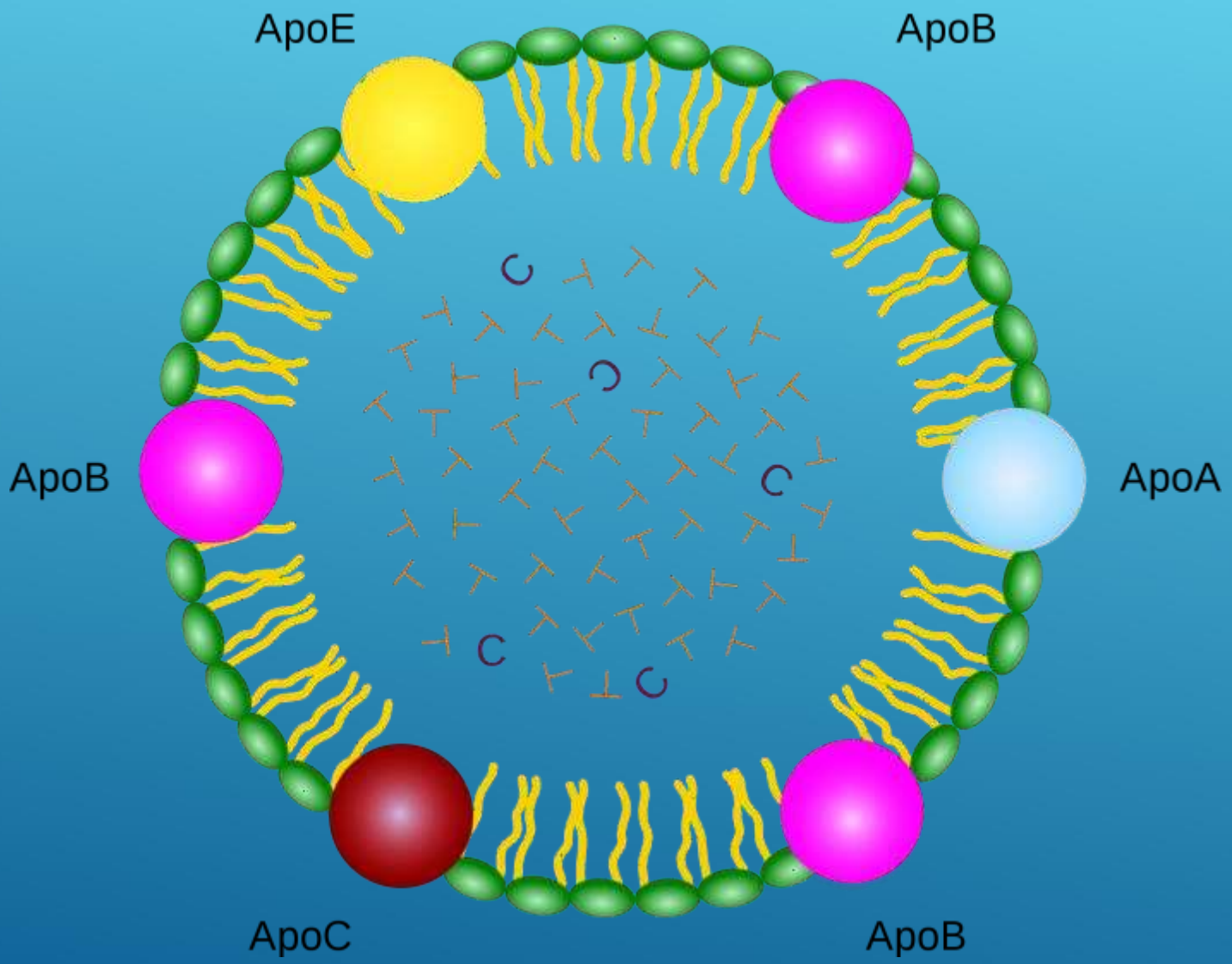
- **Apo A-1** is the main protein in HDL, and activates LCAT, an enzyme associated to HDL.
- **Phospholipids** are the main lipidic content of HDL (35 % of the total weight), and the enzyme Lecithin Cholesterol Acyl Transferase (**LCAT**) catalyze the transfer of acyl groups (fatty acids esterifies to lecithin) from lecithin to cholesterol scavenged from cell membranes of extrahepatic tissues, and from IDL and Chylomicrons remnants, producing cholesterol esters, that are dissolved in the HDL core, so these lipoproteins become the cholesterol rich HDL2 and HDL3.

- Lecithin + Cholesterol → Lysolecithin + Cholesterol ester

Since hepatocytes have receptors for apo A1 – the main protein of HDL- these rich-in- cholesterol lipoproteins are taken up by the hepatocytes. Consequently, the net effect is the transportation of cholesterol from the peripheral tissues to the liver (reverse cholesterol transport).

# CHYLOMICRON

- **Chylomicron** (from the Greek chylø, meaning *juice* or *milky fluid*, and micron, meaning *small particle*) are **lipoprotein** particles that consist of
- **Triglycerides** (85–92%),
- **Phospholipids** (6–12%),
- **Cholesterol** (1–3%),
- **Proteins** (1–2%).


ApoE
ApoB
ApoB
ApoA
ApoC
ApoB

# Function of chylomicron

- Chylomicrons transport lipids absorbed from the intestine to
  - adipose ,
  - cardiac,
  - and skeletal muscle tissue,
- where their triglyceride components are hydrolyzed by the activity of lipoprotein lipase
- and the released free fatty acids are absorbed by the tissue.

- When a large portion of the triacylglycerol core have been hydrolyzed, chylomicron remnants are formed and are taken up by the liver, hereby transferring dietary fat also to the liver.
- It transports dietary fats and cholesterol from intestines to tissues.

# Metabolism of chylomicron

- The enzyme **lipoprotein lipase, with apolipoprotein (apo)C-II as a co-factor**, hydrolyzes chylomicron triglyceride allowing the delivery of free fatty acids to muscle and adipose tissue.

- As a result, a new particle called a chylomicron remnant is formed. This particle is enriched in cholesteryl ester and fat-soluble vitamins and contains apoB-48 and apoE.
- It is rapidly removed from the circulation by the liver. ApoE is the moiety required for rapid hepatic removal.
- Its activity is inhibited by C apolipoproteins, especially apoC-I.
- Hepatic removal appears to be accomplished by several overlapping mechanisms.

- The particle must first achieve a size that allows it to be "sieved" through the endothelial fenestre
- **Here, it may**
- 1) be removed directly by LDL receptors.

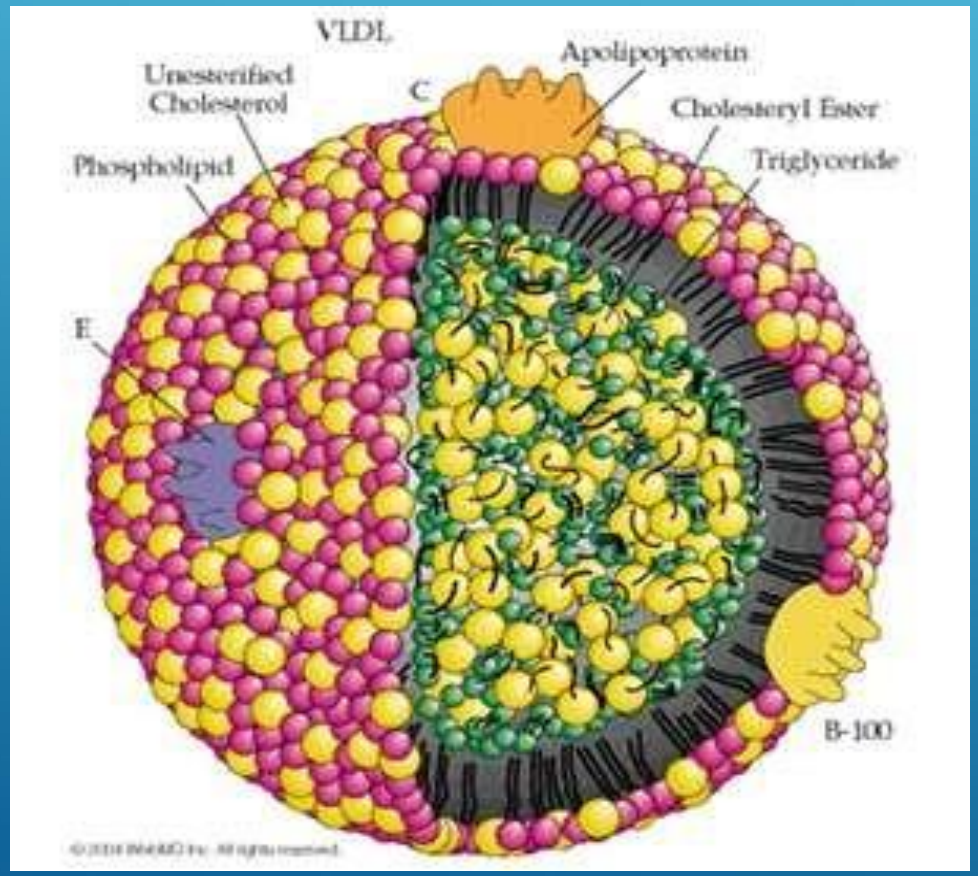
- 2) acquire additional apoE that is secreted free into the space, and then be removed directly by the LDL receptor-related protein (LRP);

- 3) it may be sequestered in the space. Sequestration occurs by binding of apoE to heparan sulfate proteoglycans and/or binding of apoB to hepatic lipase.

- -Sequestered particles may be further metabolized allowing apoE, and lysophospholipid enrichment, followed by transfer to one of the above receptors for hepatic uptake.
- The above formulation is based upon animal studies. In humans, delayed removal of chylomicron remnants has been documented in diabetes, renal failure, and familial combined hyperlipemia and is the abnormality resulting in type III hyperlipidemia. Case control studies have identified delayed remnant removal as an independent risk factor for atherosclerotic cardiovascular disease.

# VERY-LOW-DENSITY LIPOPROTEIN (VLDL)

- -It is a type of lipoprotein made by the liver.



# FUNCTION OF VLDL

- VLDL transports endogenous triglycerides , phospholipids, cholesterol, and cholesteryl esters.
- It functions as the body's internal transport mechanism for lipids.
- In addition it serves for long-range transport of hydrophobic intercellular messengers, like the morphogen.

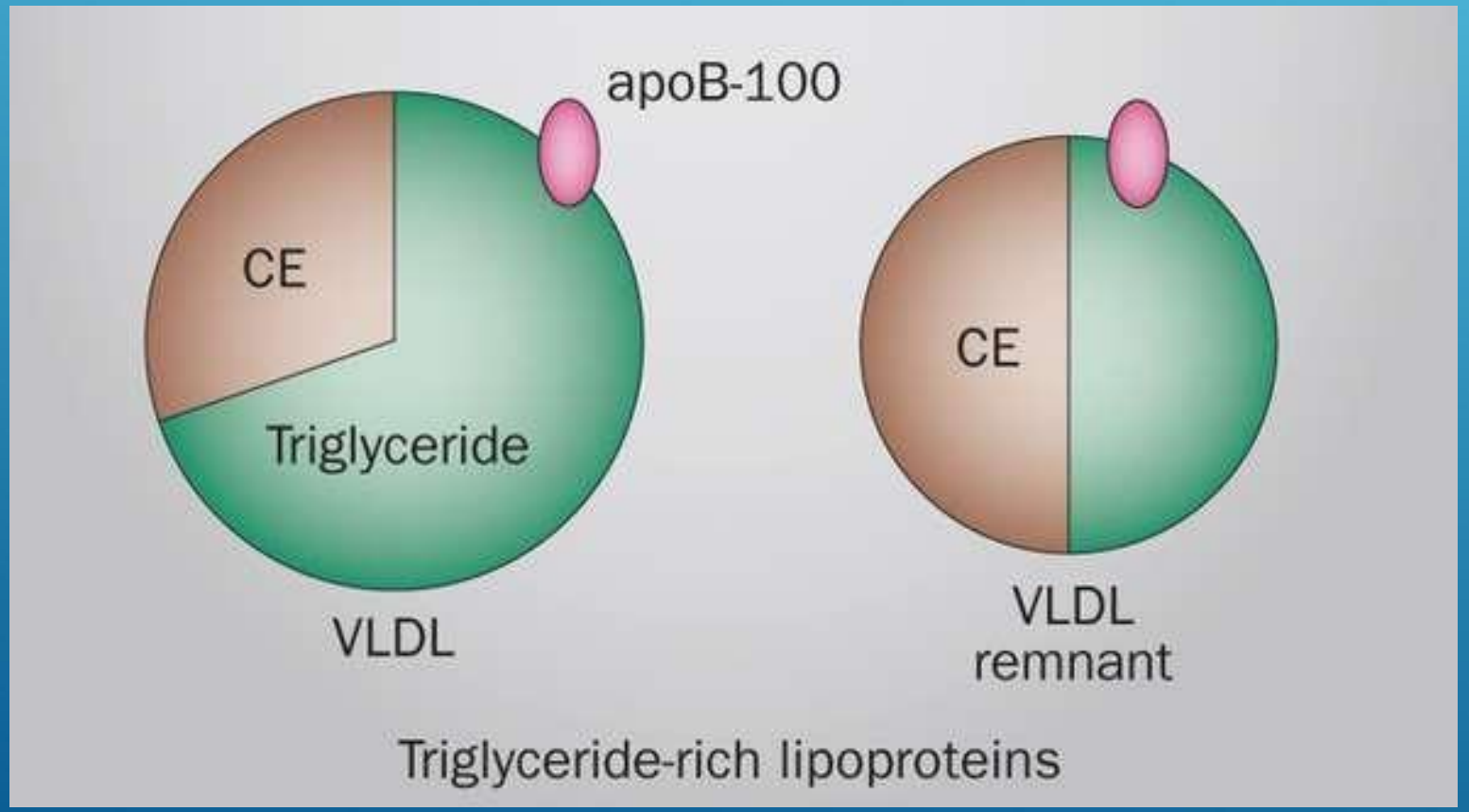
# METABOLISM OF VLDL

- **VLDL** metabolism is very similar to Chylomicrons metabolism. the main lipid found in VLDL is also **triacylglycerol**, but in this case **triacylglycerols** come from excess fatty acids on diet or an increase in the hepatic synthesis of fatty acids as a consequence of excess carbohydrates in diet. Fats coming from the hepatocytes uptake of Chylomicrons remnants are also a source of triacylglycerols for VLDL.

- Additionally to triacylglycerols, VLDL contains around **35 % of free and esterified cholesterol**, **35 % of phospholipids**, and **various apoproteins**, including **ApoB-100.**

- **VLDL**, in the same way than Chylomicrons, acquires in the blood stream Apo C-II and Apo E. The functions of these apoproteins in VLDL are similar to their functions in Chylomicrons: Apo C-II activates Lipoprotein Lipase and as a consequence, VLDL triacylglycerols are hydrolyzed, so the proportion of cholesterol increases.

- The VLDL remnant is called IDL, or Intermediate Density Lipoprotein.



# IDL (INTERMEDIATE DENSITY LIPOPROTEIN)

- **-**It's formed from the degradation of **very low-density lipoproteins.** Their size is, in general, 25 to 35 nm in diameter, and they contain primarily a range of **triacylglycerols** and **cholesterol esters.**

# FUNCTION OF IDL

- It enables fats and cholesterol to move within the water-based solution of the bloodstream.

- Each native IDL particle consists of protein that encircles various fatty acids, enabling, as a water-soluble particle, these fatty acids to travel in the aqueous blood environment as part of the fat transport system within the body.

- In general, IDL, somewhat similar to low-density lipoprotein (LDL), transports a variety of triglyceride fats and cholesterol and, like LDL, can also promote the growth of atheroma.

# METABOLISM OF ILDL

- VLDL is a large, triglyceride-rich lipoprotein secreted by the liver that transports triglyceride to adipose tissue and muscle.

- The triglycerides in VLDL are removed in capillaries by the enzyme lipoprotein lipase, and the VLDL returns to the circulation as a smaller particle with a new name, intermediate-density lipoprotein (IDL).

- The IDL particles have lost most of their triglyceride, but they retain cholesteryl esters.
- Some of the IDL particles are rapidly taken up by the liver; others remain in circulation, where they undergo further triglyceride hydrolysis and are converted to LDL.
- A distinguishing feature of the IDL particle is their content of multiple copies of the receptor ligand ApoE in addition to a single copy of ApoB-100.

- The multiple copies of ApoE allow IDL to bind to the LDL receptor with a very high affinity.
- When IDL is converted to LDL, the ApoE leaves the particle and only the ApoB-100 remains.
- Thereafter, the affinity for the LDL receptor is much reduced.

# Thank you