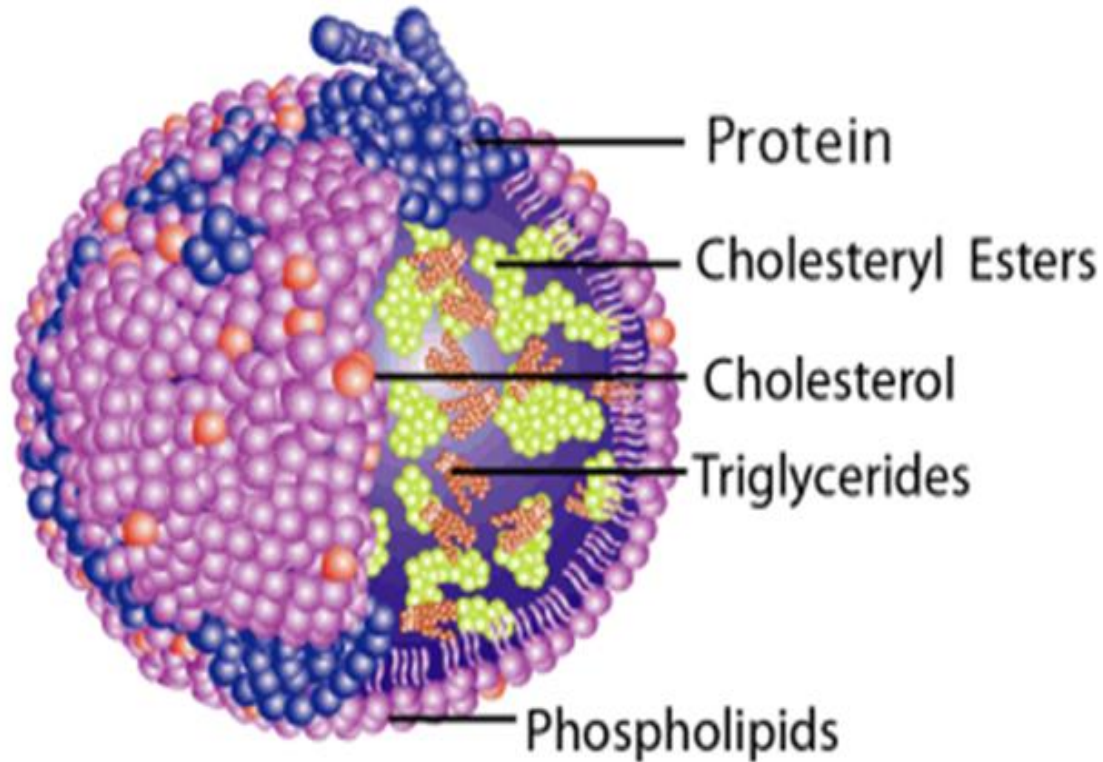


# Lipoproteins Metabolism

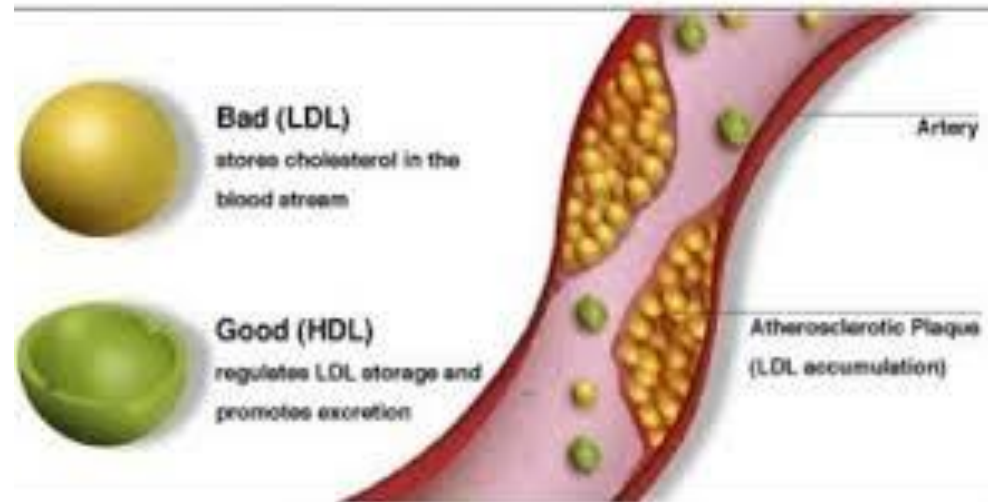


*Dr Sikandar Ali Khan*

# Good & Bad cholesterol

- Metabolism of Chylomicrons
  - Metabolism of VLDL & LDL is “Bad cholesterol” &
  - Metabolism of HDL is “Good cholesterol”
- ❑ Atherosclerosis & Coronary heart diseases
  - ❑ Hyperlipoproteinemias
  - ❑ Fatty liver

Bad vs. Good Cholesterol



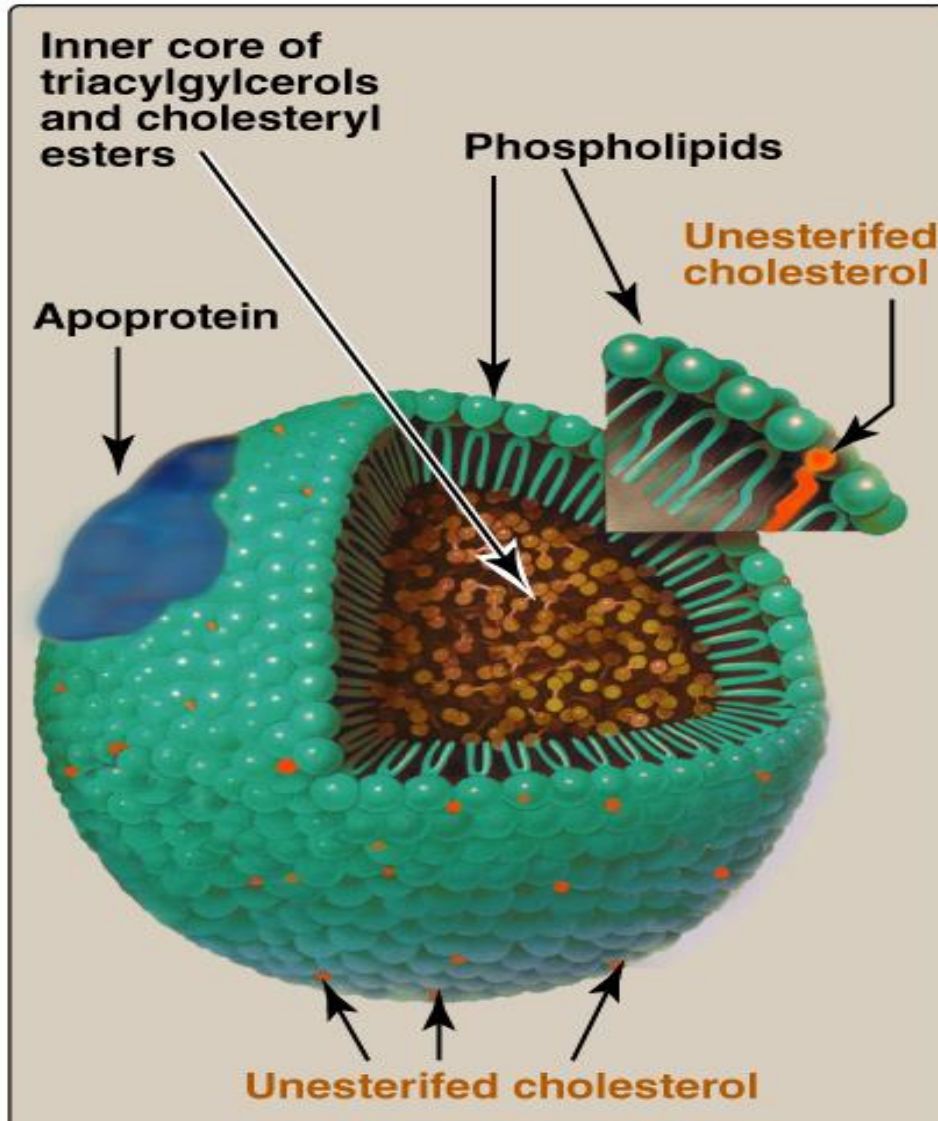
# Lipoprotein Introduction

**Lipid compounds:**

**Relatively water insoluble**

**Therefore, they are transported in plasma (aqueous) as  
Lipoproteins**

# Spherical molecules of lipids and proteins



## Outer coat:

- Apoproteins
- Phospholipids
- Cholesterol (Unesterified)

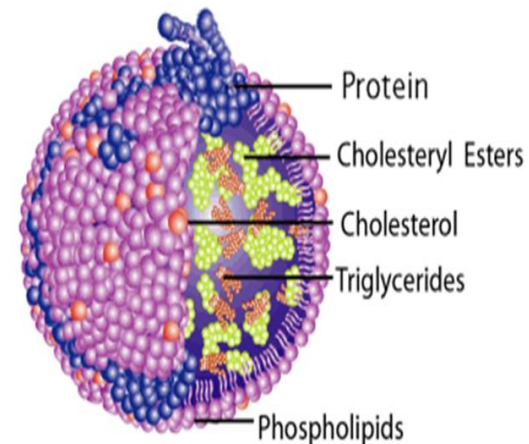
## Inner core:

- TG
- Cholesterol ester (CE)

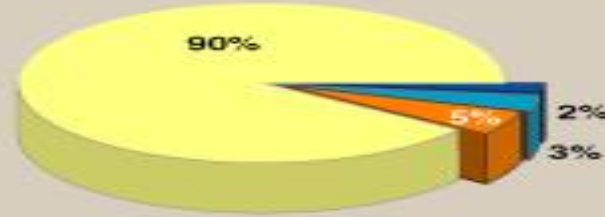
**Lipoprotein Structure**

# Apo proteins

- Five major classes (A-E)
- **Functions**
- Some are required as structural proteins.
- Some are activators.
- Some are recognition sites.



# Types and Composition of Lipoproteins



Chylomicron



Very-Low-Density Lipoprotein (VLDL)



Low-Density Lipoprotein (LDL)



High-Density Lipoprotein (HDL)



Chylomicrons

Very low density Lipoprotein (VLDL)

Low density Lipoprotein (LDL)

High density Lipoprotein (HDL)

# Types of Lipoproteins

□ There are various types of lipoproteins:

❖ Chylomicrons

❖ Very low density lipoprotein (VLDL)

❖ Low density lipoproteins (LDL)

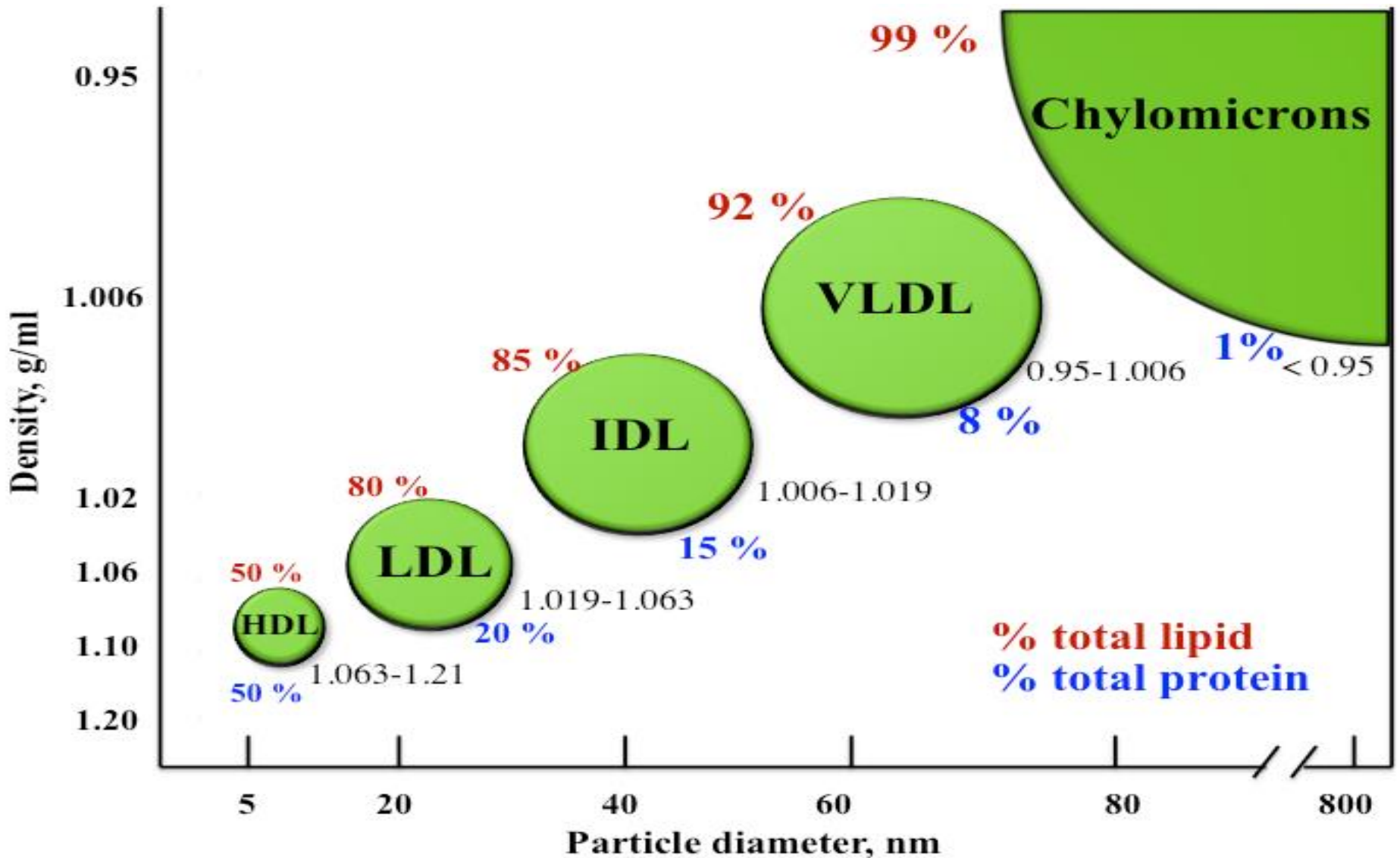
❖ High density lipoproteins (HDL)

# Types of Lipoproteins

- They differ in lipid and protein composition and therefore, they differ in:
  - ❖ Size and density
  - ❖ Electrophoretic mobility



# ❖ Size and density



# Lipoprotein Electrophoresis

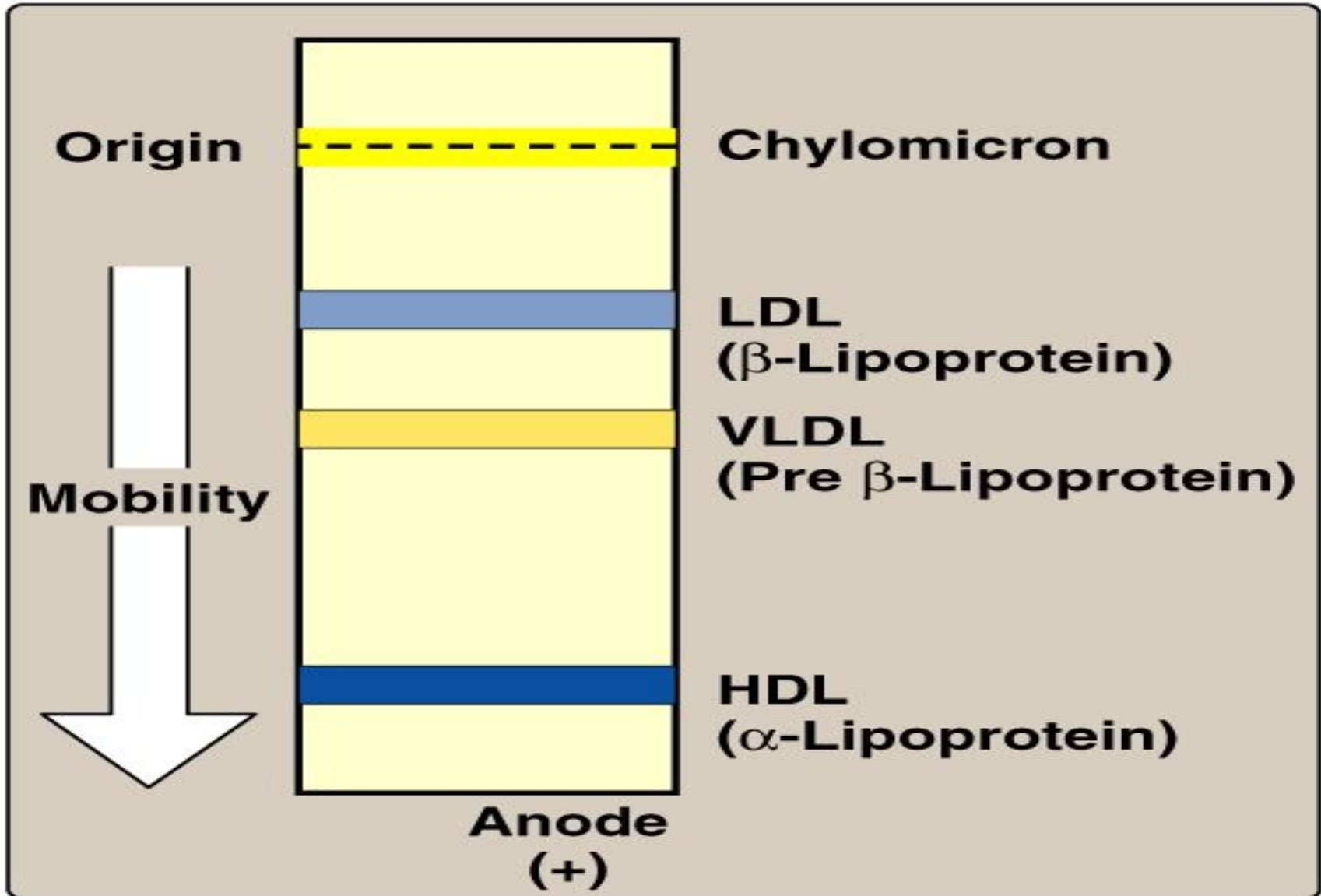


Figure 18-15

**TABLE 14.5 Characteristics of human plasma lipoproteins**

<i>Characteristic</i>	<i>Chylomicrons</i>	<i>VLDL</i>	<i>LDL</i>	<i>HDL</i>
Electrophoretic mobility	Origin	Pre- $\beta$	$\beta$	$\alpha$
Density	<0.96	0.96–1.006	1.006–1.063	1.063–1.21
Diameter (nm)	100–1,000	30–90	20–25	10–20
Apoproteins	AI, AII B <sub>48</sub>	B <sub>100</sub> , CI, CII CIII, E	B <sub>100</sub>	AI, AII, CI, CII, CIII, D, E
<b>Composition</b> (% , approximate)				
Protein	2	10	20	40
Lipid (total)	98	90	80	60
<b>Lipid components</b> (%)				
Triacylglycerol	88	55	12	12
Cholesterol (free and ester)	4	24	59	40
Phospholipids	8	20	28	47
Free fatty acids	—	1	1	1

(VLDL : Very low density lipoproteins; LDL : Low density lipoproteins; HDL : High density lipoproteins).

# Plasma Lipoproteins

For triacylglycerol transport (TG-rich):

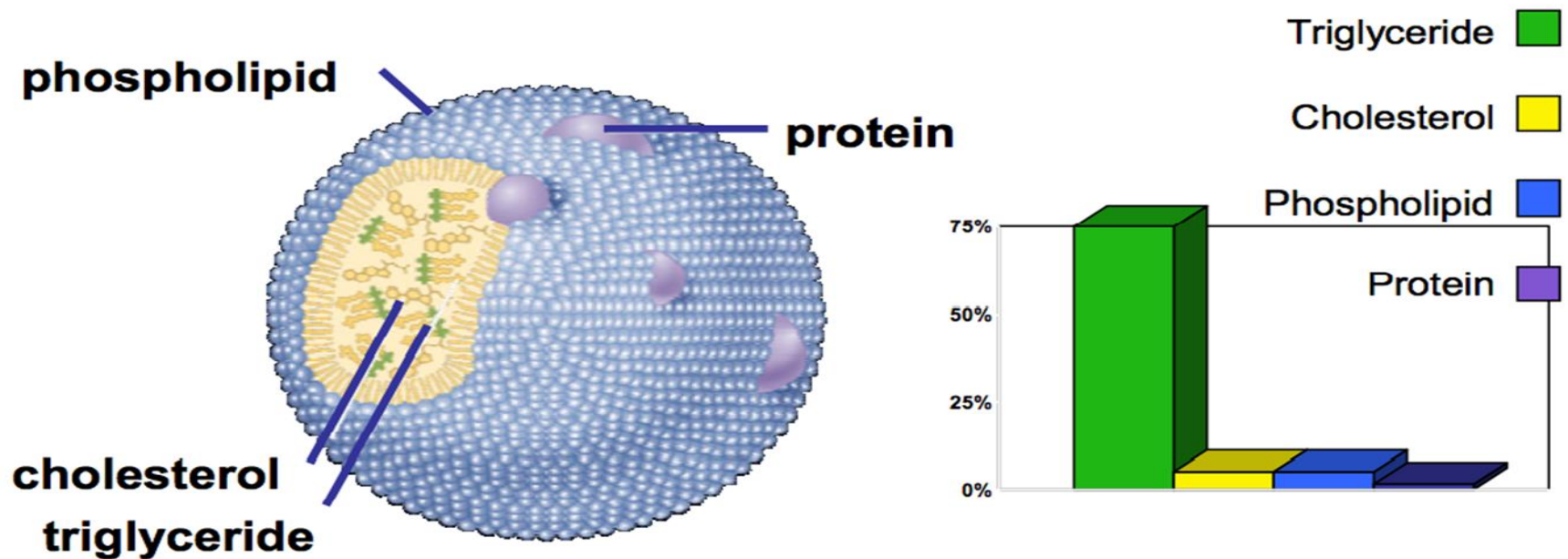
- **Chylomicrons:** TG of dietary origin
- **VLDL:** TG of endogenous (hepatic) synthesis

For cholesterol transport (cholesterol-rich):

**LDL:** Mainly free cholesterol

**HDL:** Mainly esterified cholesterol

# *Metabolism of* Chylomicrons



# Scenario

Patients present with recurrent abdominal pain (pancreatitis), the presence of xanthomas, and hepatosplenomegaly.

The treatment consists of reducing fat consumption in the diet to less than 15% of total calories, or about 20 g of fat a day.

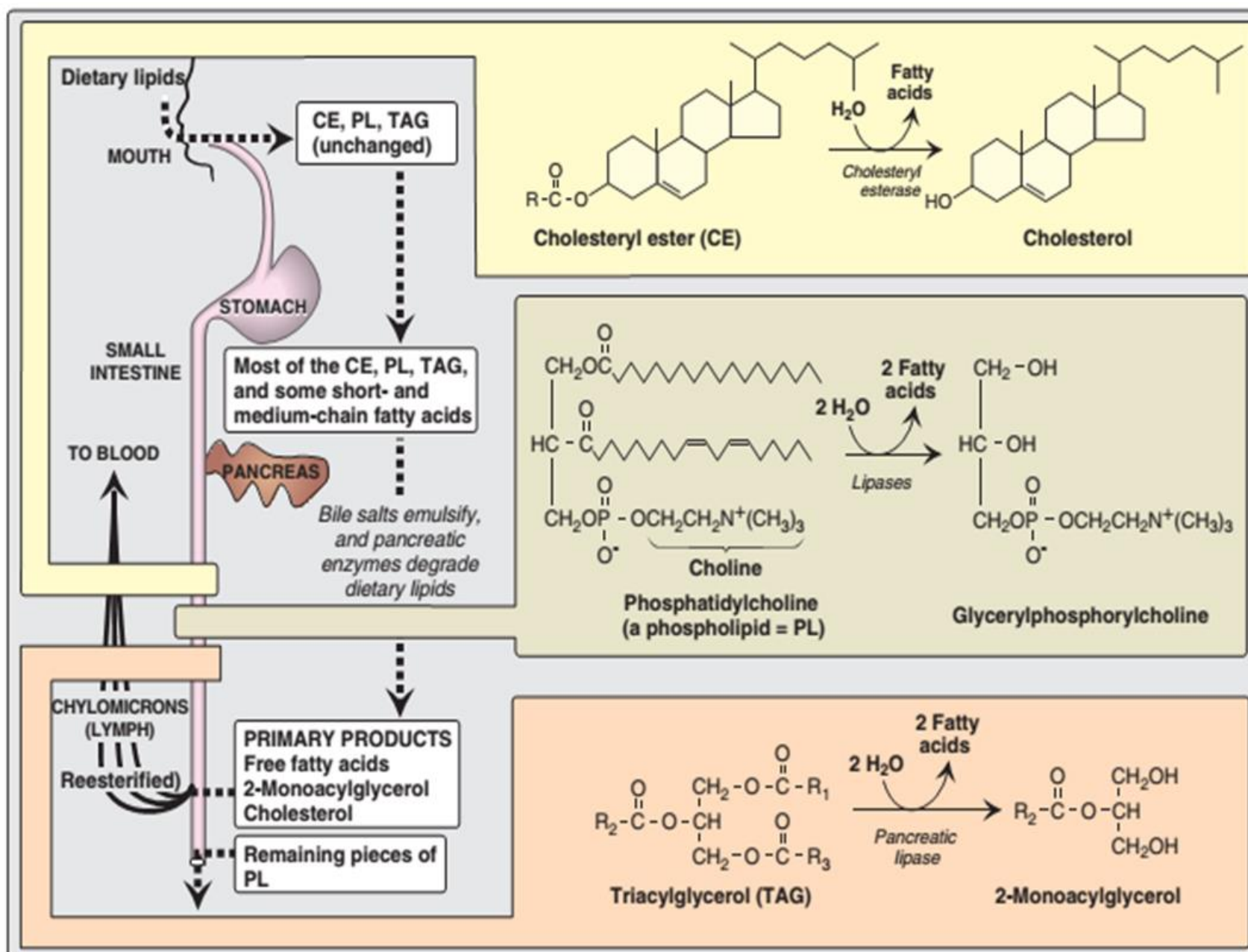
This will greatly reduce chylomicron synthesis, and dramatically reduce the levels of circulating triglycerides.

# Metabolism

- **ABC transporter proteins:**

- are ubiquitous family of proteins
- Characterized by an **A**TP **B**inding **C**assette
- The bound ATP is hydrolysed in a process coupled to transport of their substrate
- One such protein is **cholesterol transporter**  
**ABC-A1**  
**Function:** transfer excess cholesterol to HDL particles

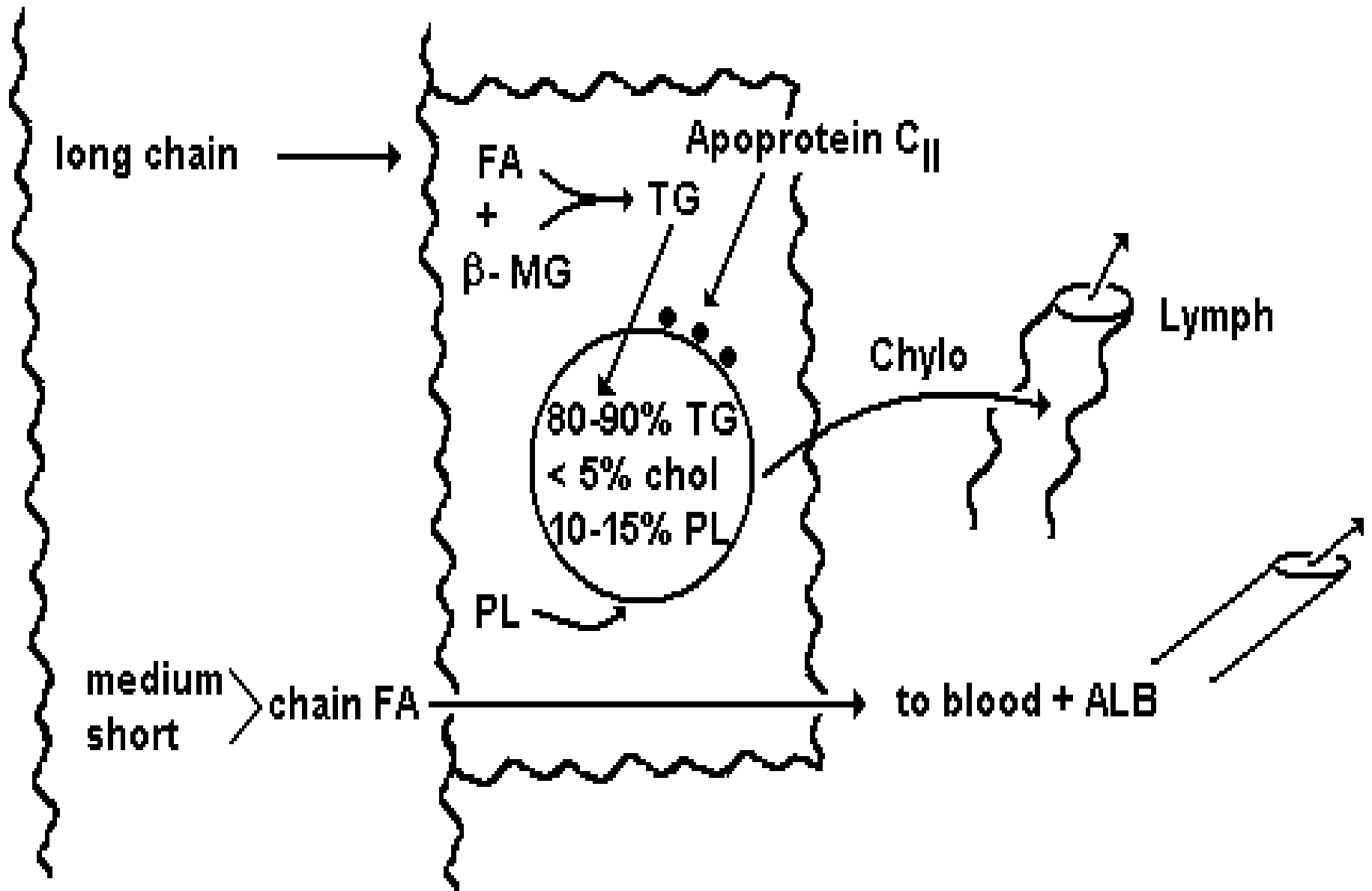


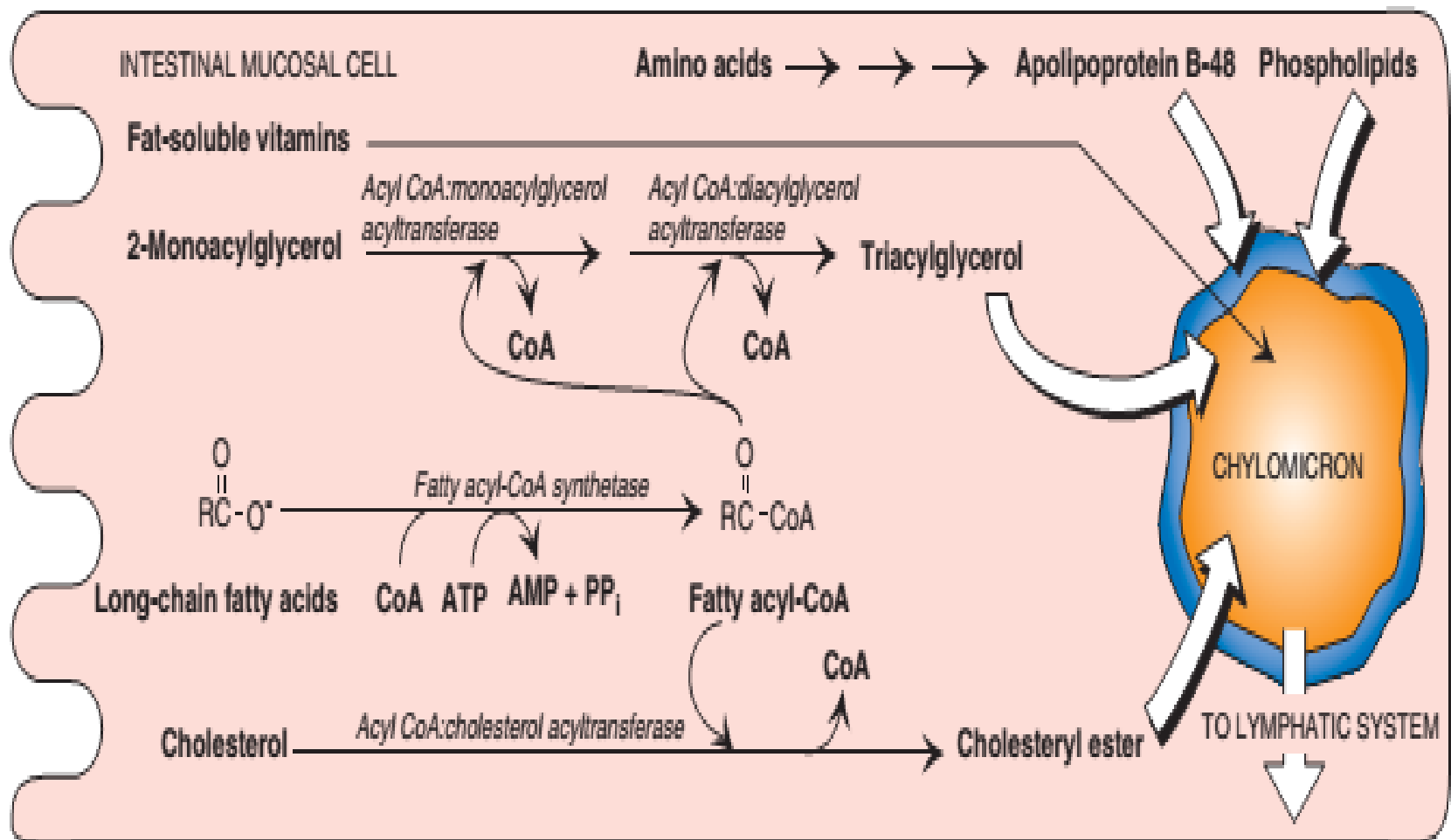


**Figure 15.2**  
Overview of lipid digestion.



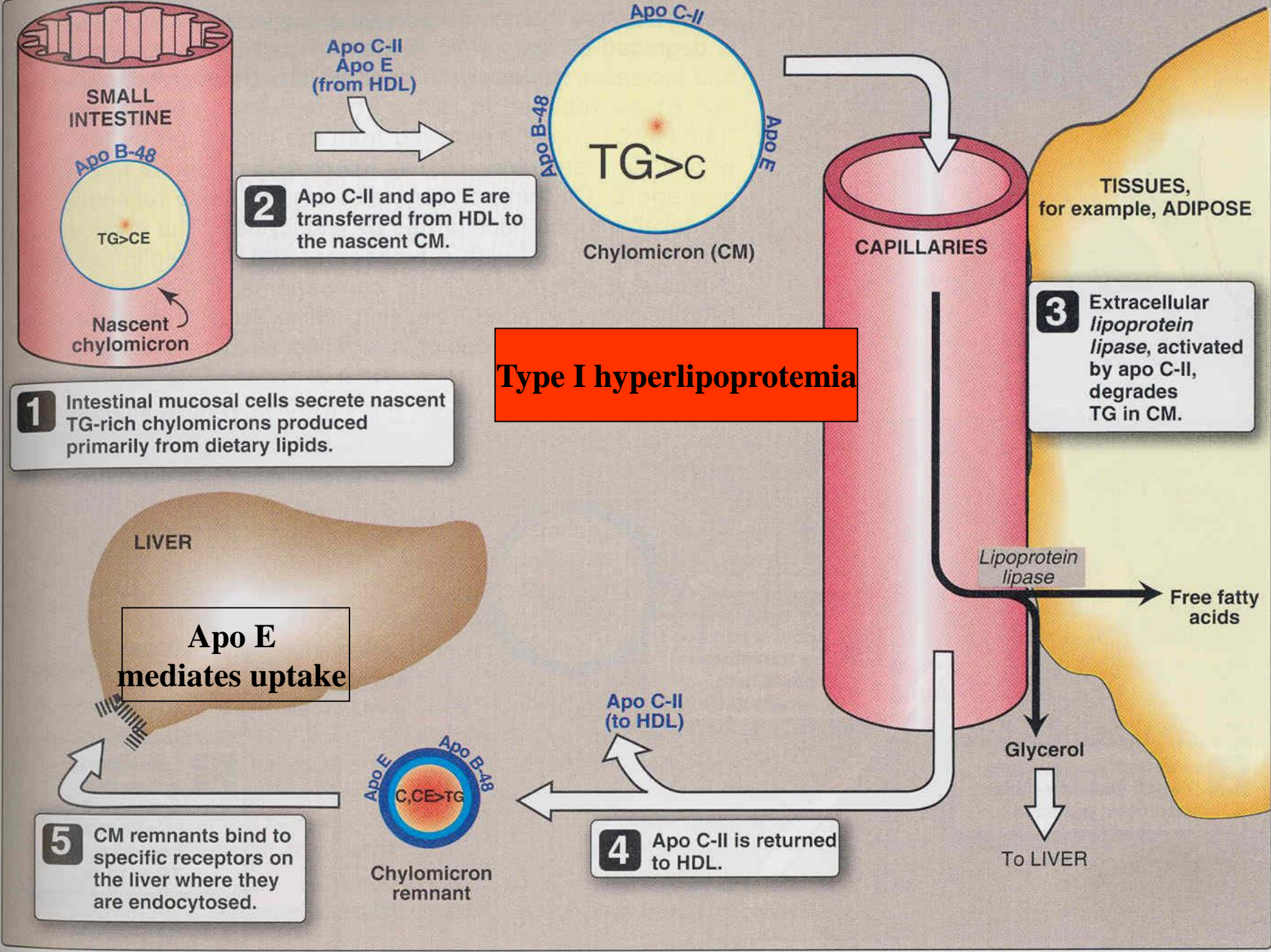
# Formation; Composition





**Figure 15.6**

Assembly and secretion of chylomicrons by intestinal mucosal cells. [Note: Short- and medium-chain length fatty acids do not require incorporation into micelles and directly enter into the blood.]



**Type I hyperlipoproteinemia**

**Apo E mediates uptake**

## **Type 1 Hyperlipoproteinemia :**

- **Lipoprotein lipase deficiency ,**
- **C2 deficiency**

# Chylomicrons

- Assembled in intestinal mucosal cells
- Lowest density
- Largest size
- Highest % of lipids and lowest % proteins
- Highest triacylglycerol (**dietary origin**)
- Carry **dietary** lipids to peripheral tissues
- Responsible for physiological milky appearance of plasma (**up to 2 hours after meal**)

# *Drugs*

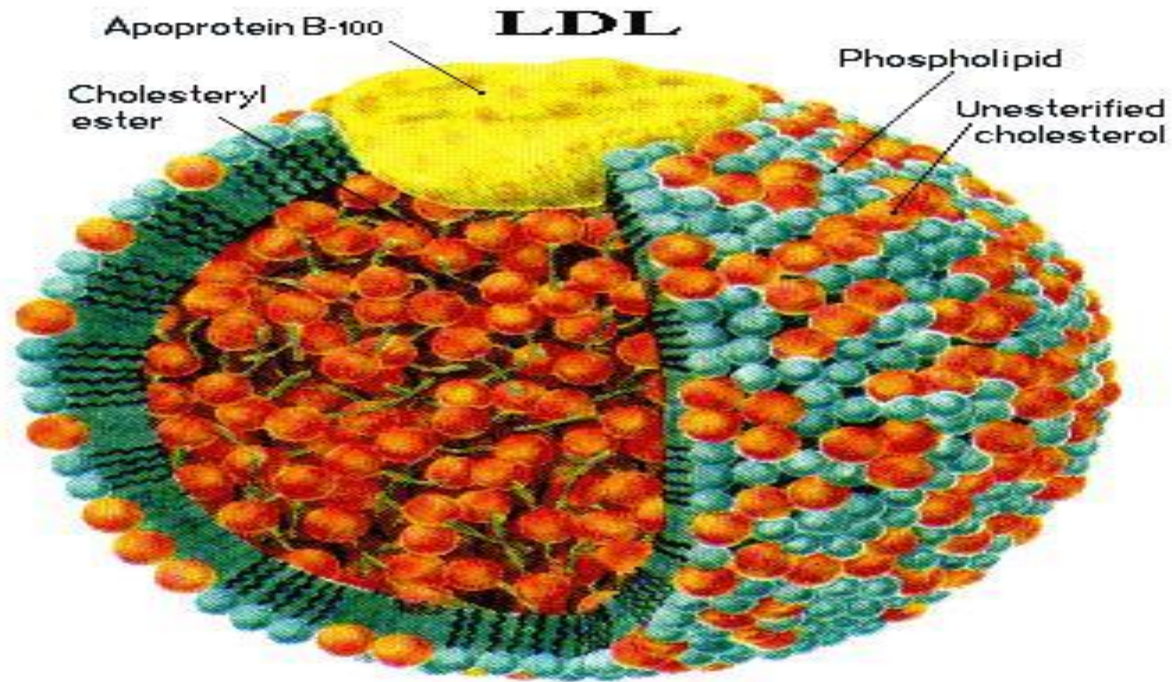
- **Ezetimibe**: new drug which inhibits cholesterol absorption
- **Gemfibrozil (fibrates)**: stimulate LPL



# **Familial lipoprotein lipase (LPL) deficiency**

- **is characterized by very high levels of circulating triglycerides (hypertriglyceridemia), due to the triglycerides in chylomicrons remaining in the circulation as they cannot be digested by the missing LPL activity.**

# *Metabolism of VLDL & LDL*





**1. ApoA1: In HDL(90% total protein),  
Chylomicron (3% total protein)**

- High affinity for cholesterol,
- removes cholesterol from cells
- Activates LCAT

## 2. ApoB48 : In Chylomicrons

- Made in intestine when TAG biosynthesis is active during fat absorption

### **3. ApoB100 :In VLDL (and in IDL & LDL which are derived from VLDL)**

- Made in hepatocytes when TAG & cholesterol biosynthesis is active
- Bind to receptor

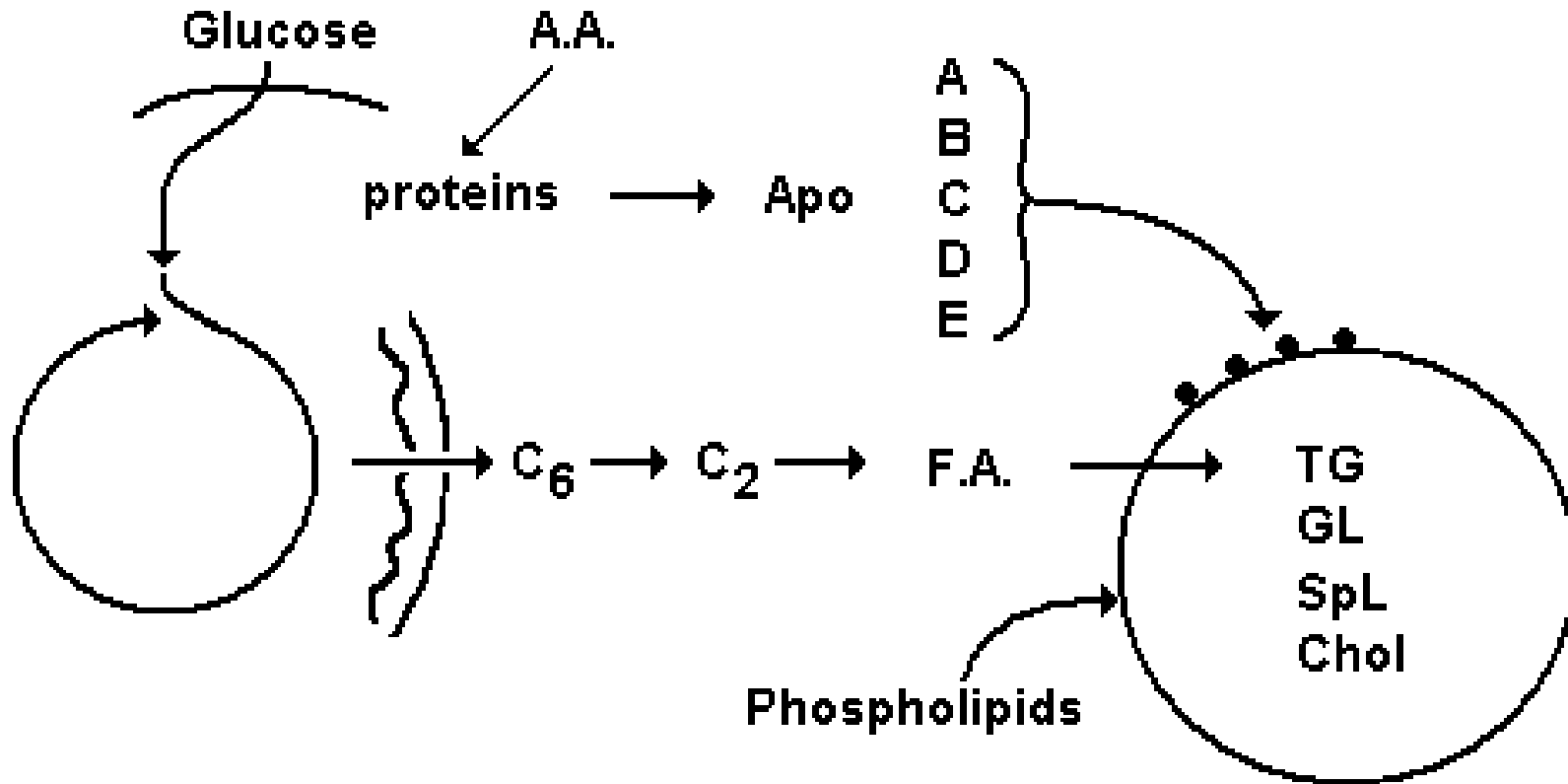
#### **4. ApoC2 : In chylomicrons & VLDL**

- **Activates lipoproteins lipase** when the chylomicrons & VLDL arrive at their tissue

#### **5. ApoE :In chylomicrons, VLDL & HDL**

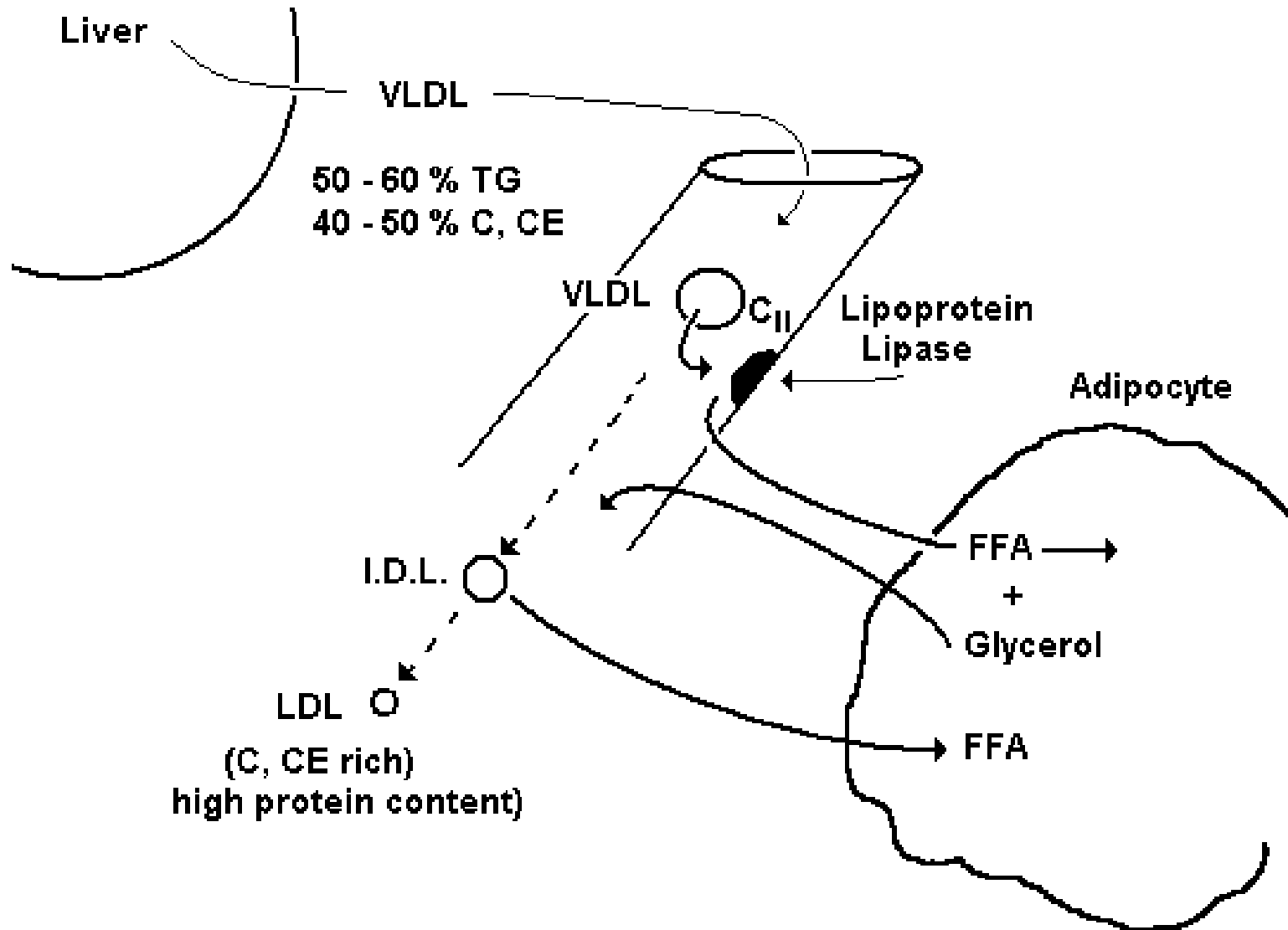
- **Binds to receptor**

# VLDL (Very Low Density Lipoprotein) Synthesis



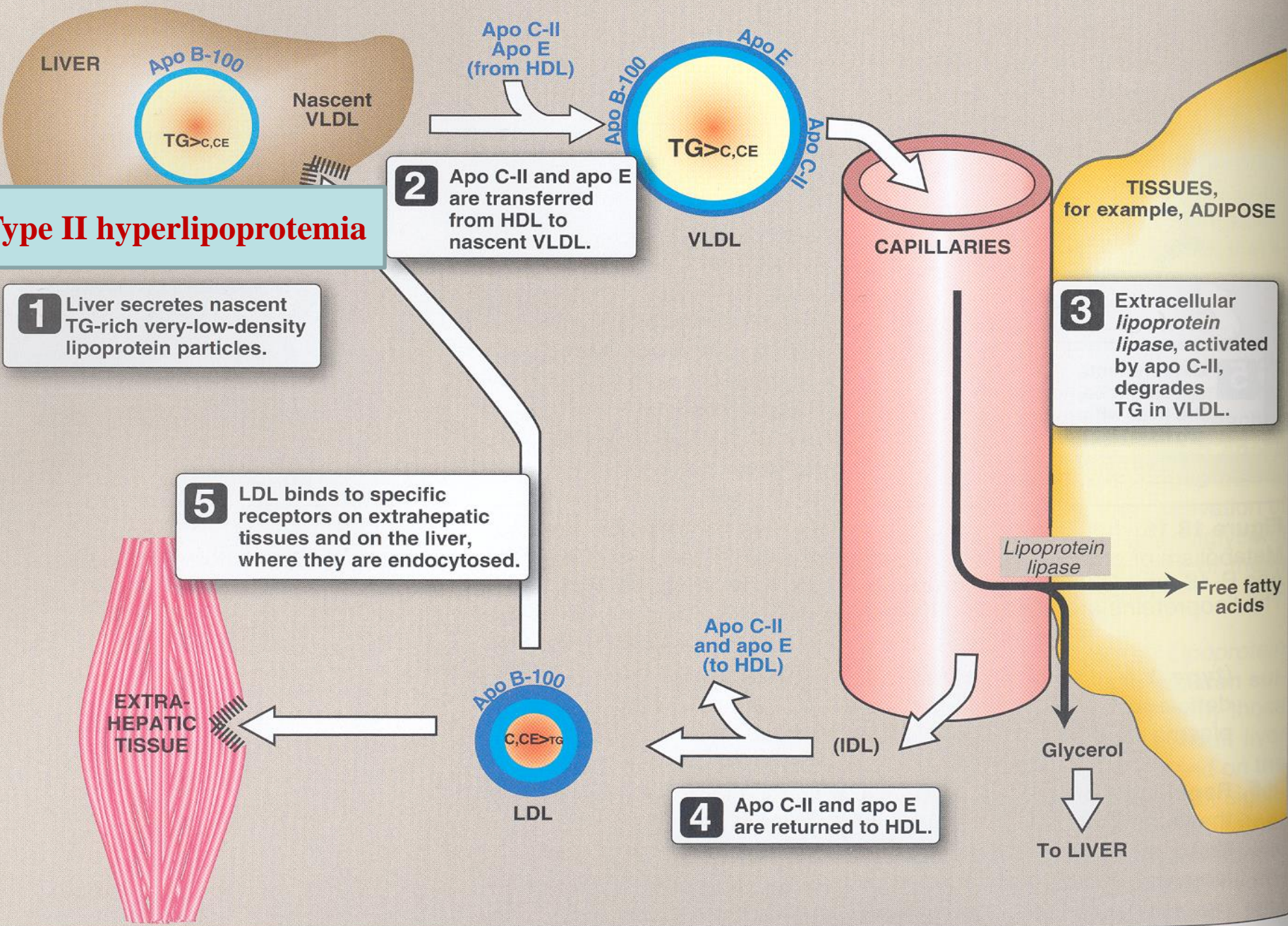
VERY LOW DENSITY LIPOPROTEINS  
(V.L.D.L.)

# VLDL to IDL to LDL





# Type II hyperlipoproteinemia



**1** Liver secretes nascent TG-rich very-low-density lipoprotein particles.

**2** Apo C-II and apo E are transferred from HDL to nascent VLDL.

**3** Extracellular lipoprotein lipase, activated by apo C-II, degrades TG in VLDL.

**5** LDL binds to specific receptors on extrahepatic tissues and on the liver, where they are endocytosed.

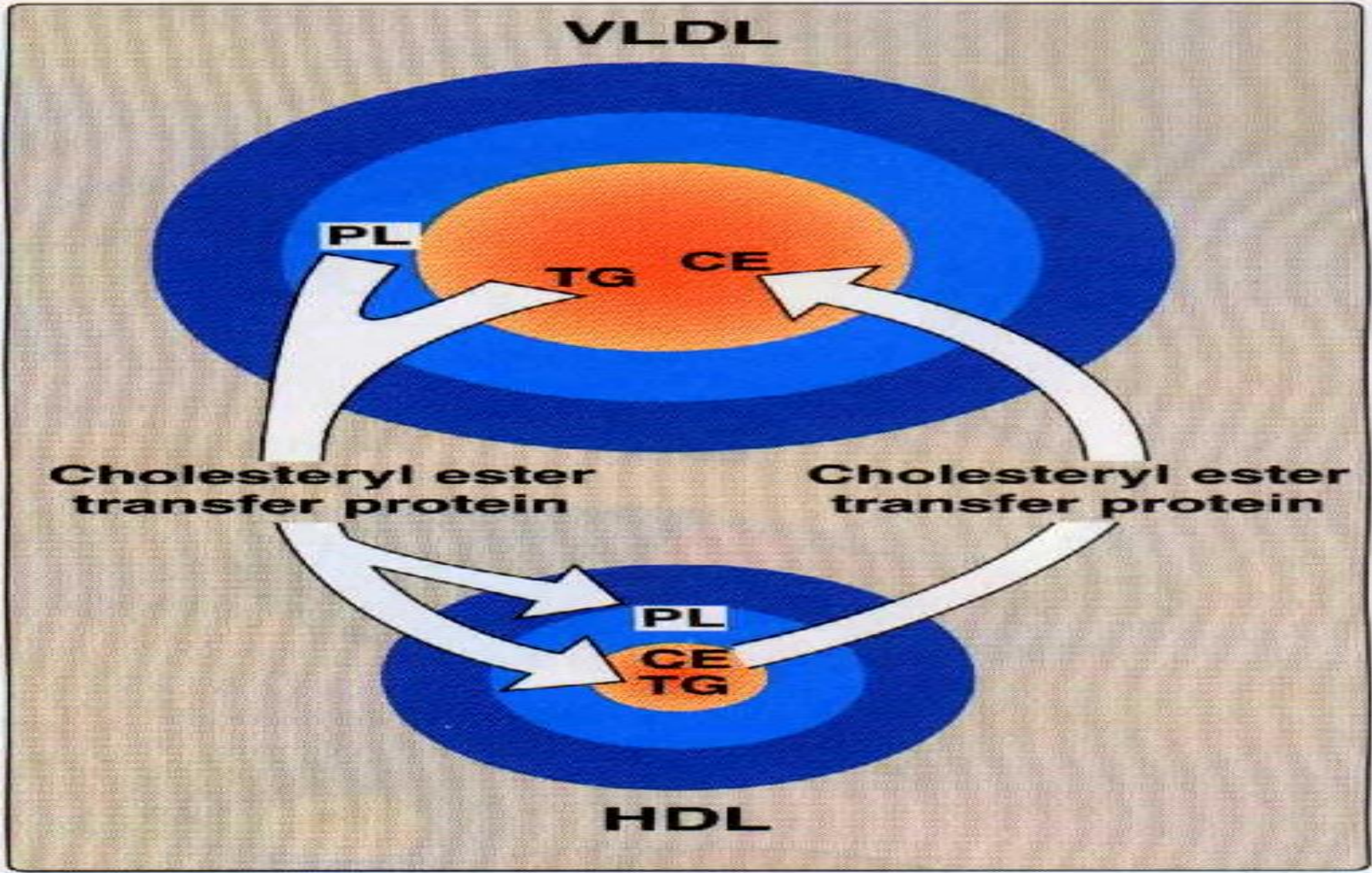
**4** Apo C-II and apo E are returned to HDL.



## Abetalipoproteinemia:

- is a rare **hypolipoproteinemia** caused by a defect in ***microsomal triacylglycerol transfer protein*** (MTP)
- leading to an inability to load apo B with lipid





Transfer of cholesteryl esters (CE) from HDL to VLDL in exchange for triacylglycerol (TG) or phospholipids (PL).

# Low Density Lipoproteins (LDL)

Produced in the circulation as the end product of **VLDLs**

Compared to VLDLs:

**It contains only apo B-100**

**Smaller size and more dense**

**Less TG**

**More cholesterol & cholesterol ester**

Transport cholesterol from liver to peripheral tissues

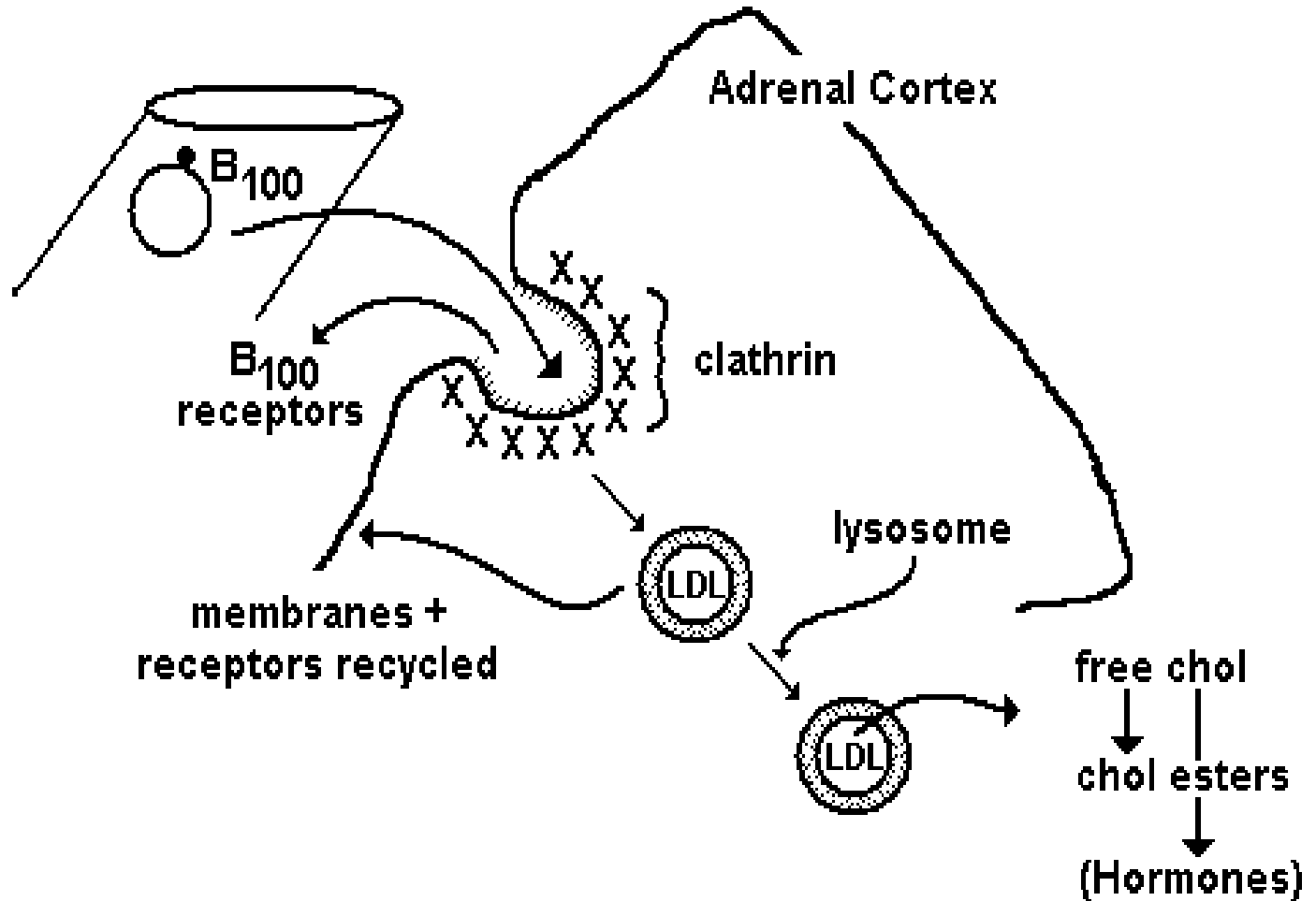
Uptake of LDL at tissue level by

**LDL receptor-mediated endocytosis**

**Recognized by apo B-100**

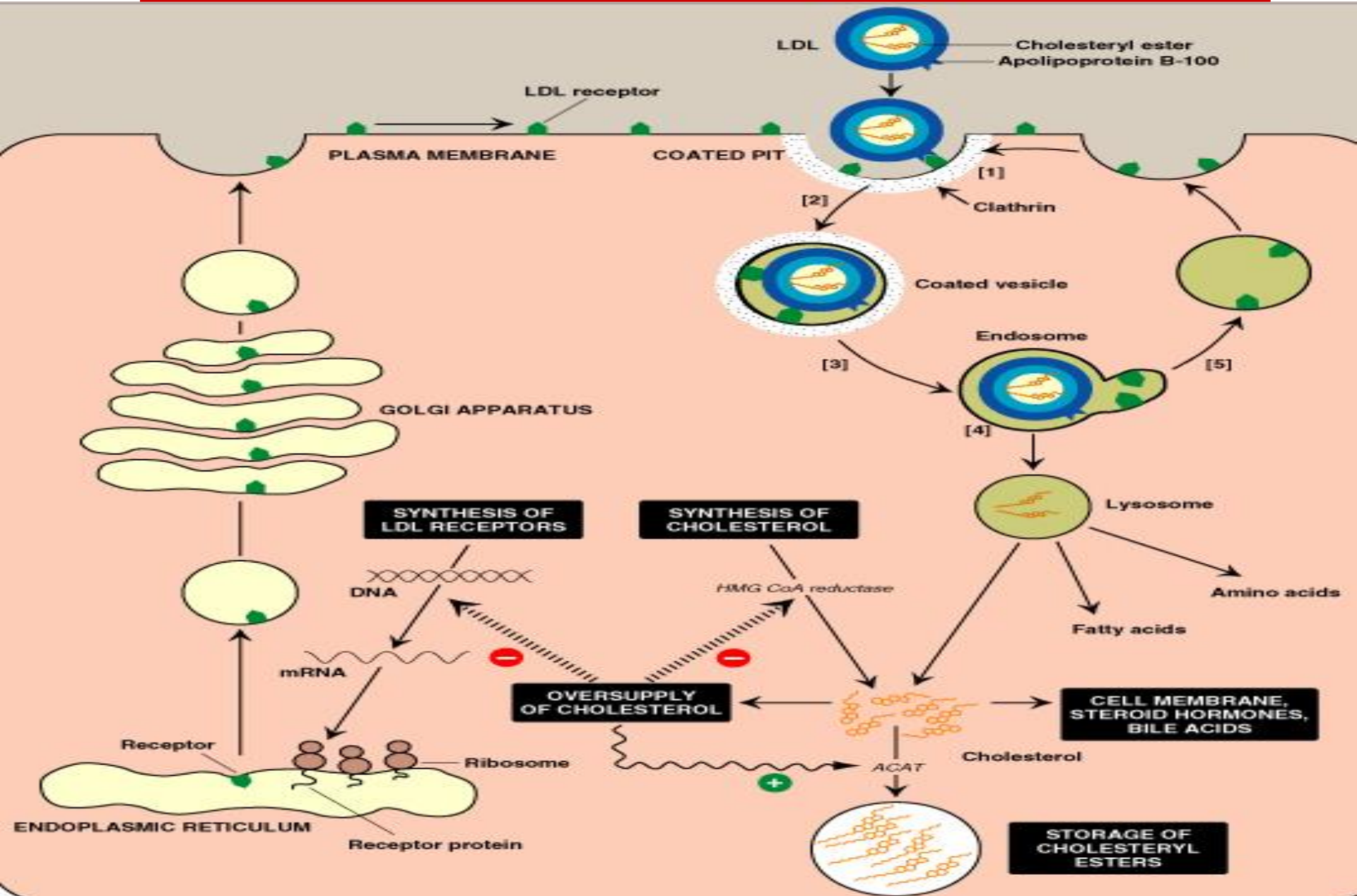
# LDL Metabolism

LDL = C, CE  
= Apo A, D, B100



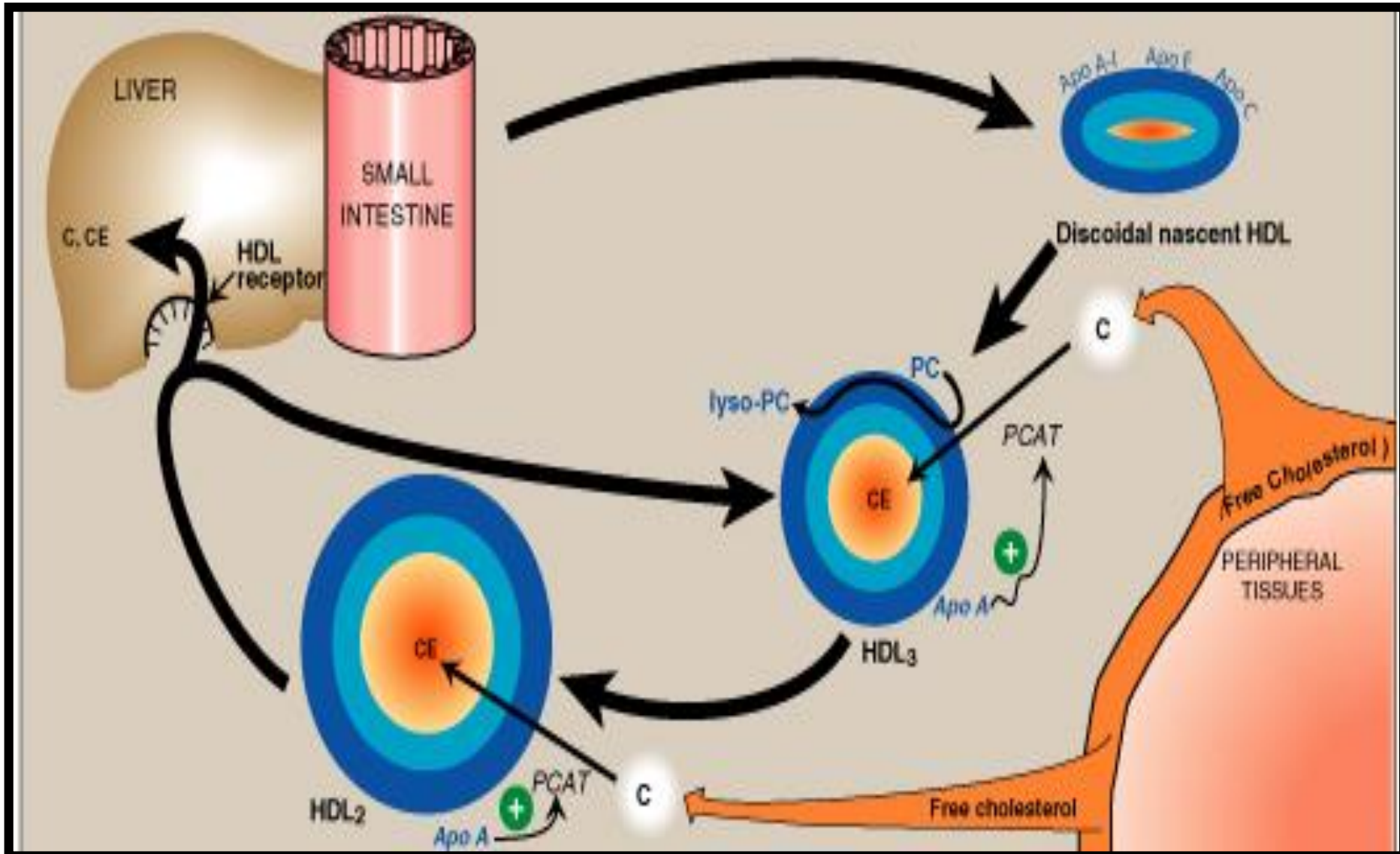


# LDL: Receptor-Mediated Endocytosis





# HDL Metabolism



**PC = Phosphatidylcholine/Lecithin**

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Phosphatidylcholine

Cholesterol

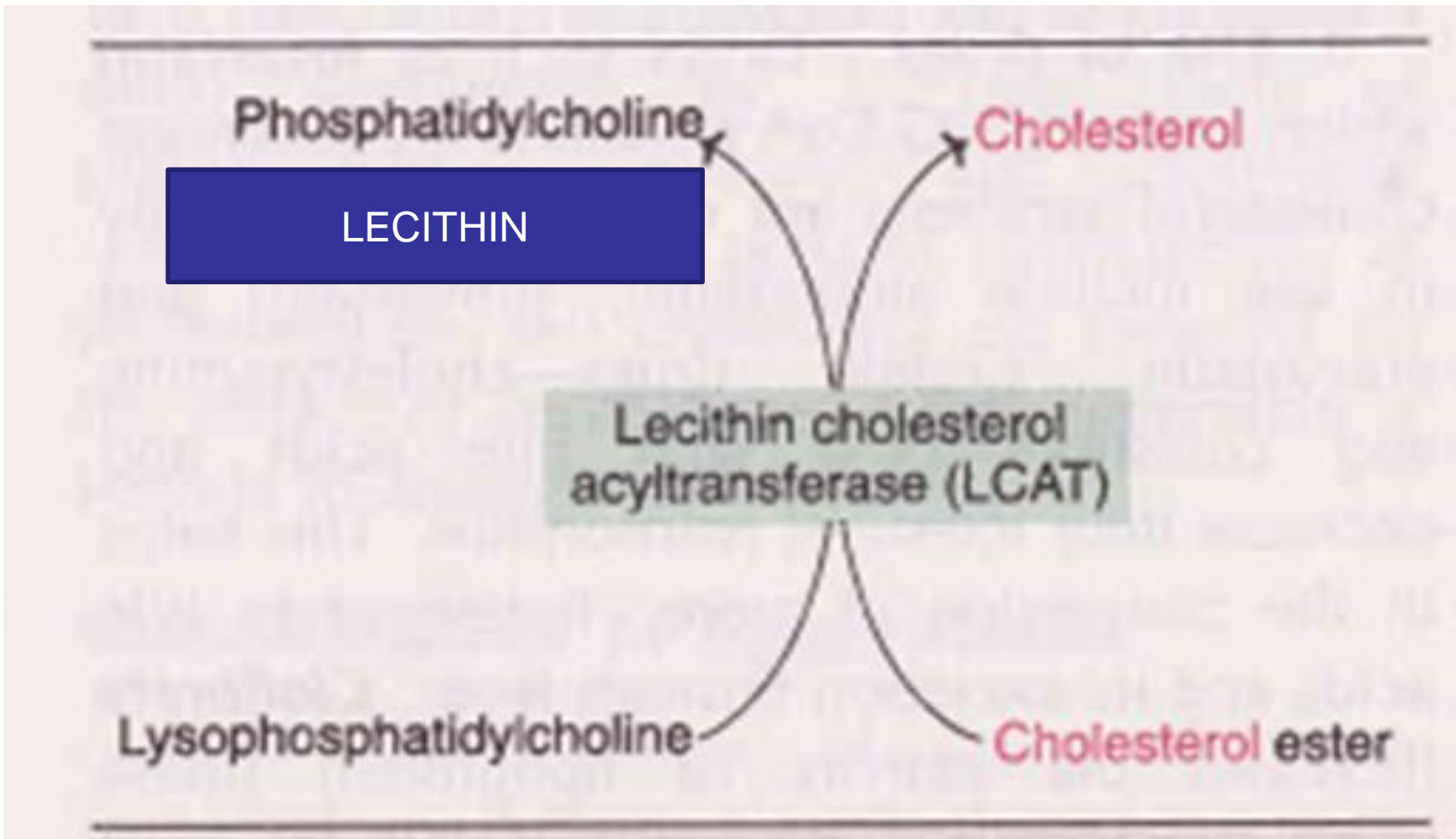
LECITHIN

Lecithin cholesterol  
acyltransferase (LCAT)

Lysophosphatidylcholine

Cholesterol ester

---



# High Density Lipoproteins (HDL)

- **Produced by intestine and liver**
- **Nascent HDL:**
  - Disk-shaped**
  - Contains apo A-I, C-II and E**
  - Contains primarily phospholipid (PC)**
- **Mature HDL (HDL<sub>2</sub>):**
  - First, the HDL<sub>3</sub> collects cholesterol (C)**
  - Then, C is converted to CE (C- ester)**



# Functions of HDL

## ❑ Reservoir of apoproteins

e.g., Apo C-II and E to VLDL

## ❑ Uptake of cholesterol:

From other lipoproteins & cell membranes

## ❑ Reverse cholesterol transport

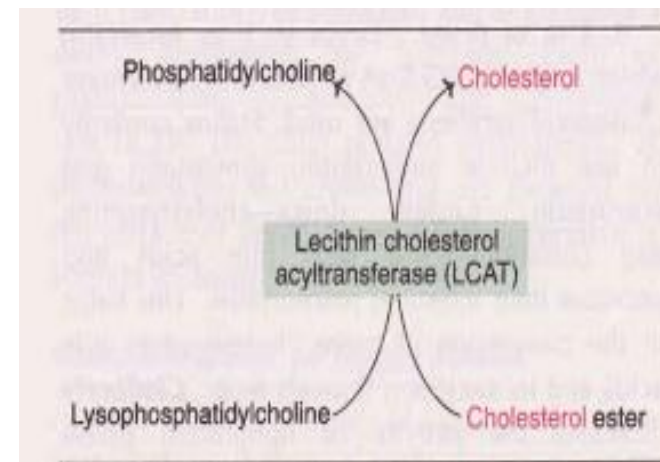
## ❑ Esterification of cholesterol:

Enzyme: **PCAT/LCAT**

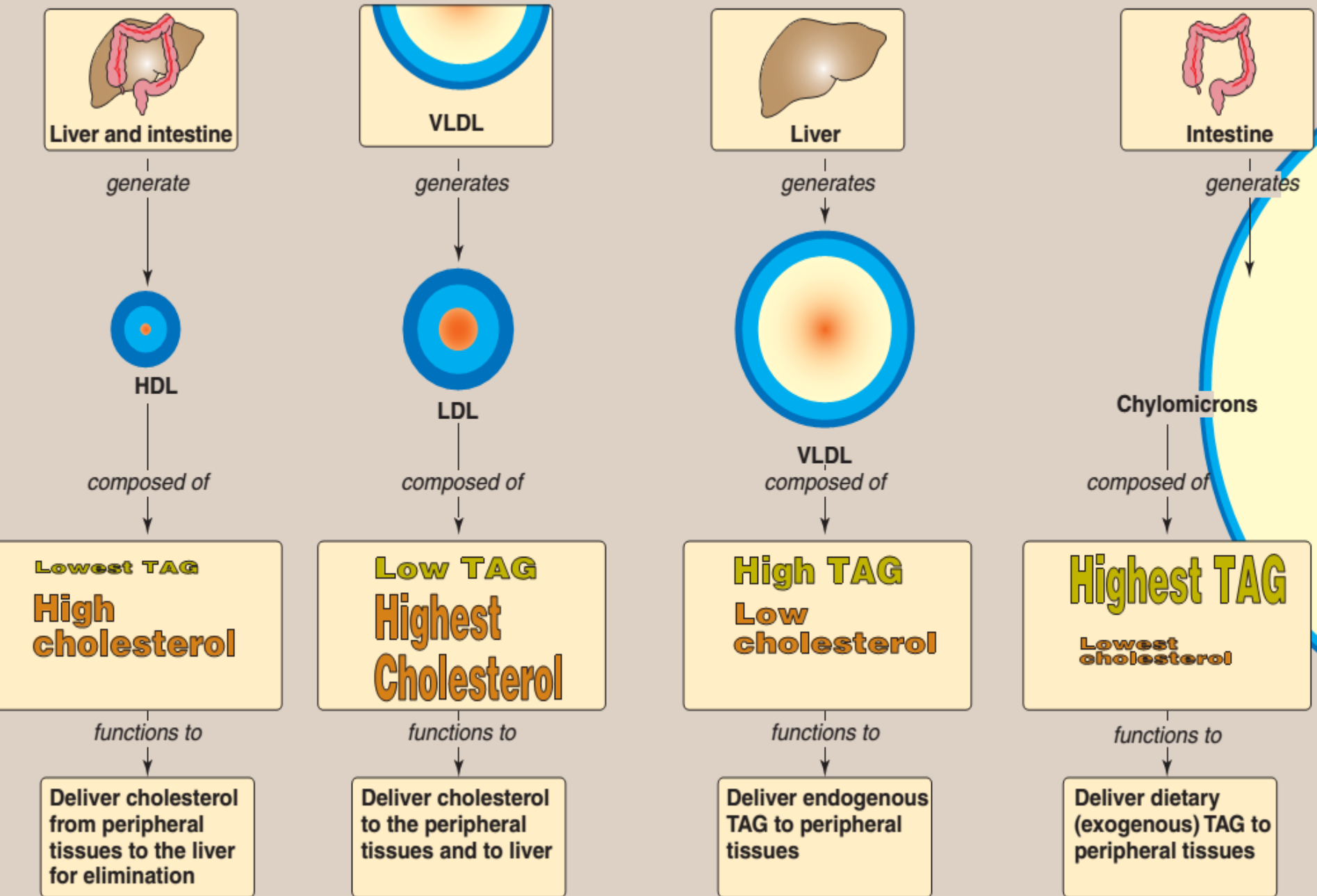
Activator: **Apo A-I**

Substrate: **Cholesterol**, Co-substrate: **PC**

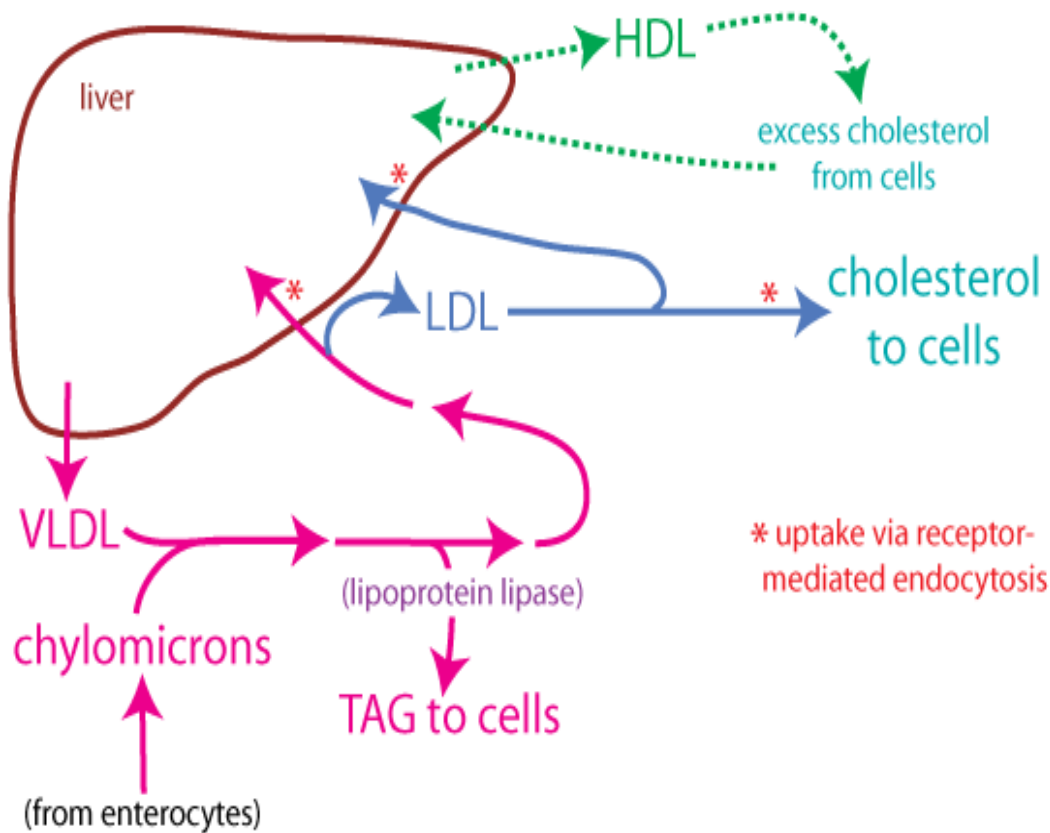
Product: **Cholesterol ester (& Lyso-PC)**



# Lipoproteins



# Summary of formation and fate of lipoproteins



- Chylomicrons is a transporter of dietary lipids whereas VLDL is a transporter of endogenous lipids (mainly TGs).
- LDL transports cholesterol to peripheral cells while HDL transports cholesterol from peripheral cells back to liver.

# Abnormalities in lipoprotein metabolism

**Type I hyperlipoproteinemia = F.lipoprotein lipase deficiency**

**Due deficiency of lipoprotein lipase or apo C-II**

-> accumulate of triacylglycerol –rich lipoproteins in plasma

**Type II hyperlipidemia = F.hypercholesterolemia**

**deficiency of functional LDL receptors**

-> elevation of plasma cholesterol but plasma TG remains normal

**There is premature atherosclerosis**

**Type III hyperlipoproteinemia = broad B disease**

**Deficiency of apo E**

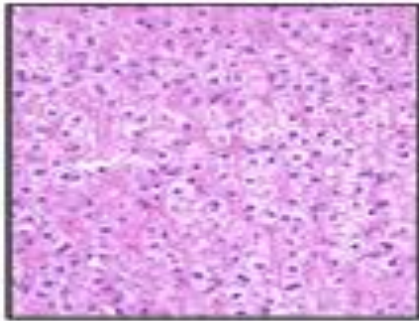
-> accumulation of chylomicron remnants in plasma .

**There's hypercholesterolemia with premature atherosclerosis**

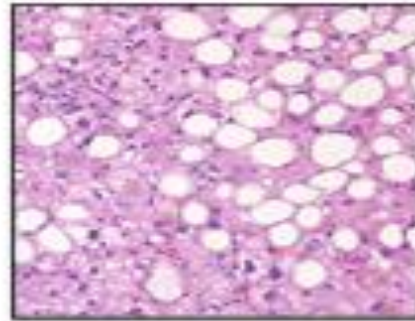
## Fatty liver :

There's imbalance between hepatic TG synthesis & secretion of VLDL

Normal  
liver



Fatty  
liver



# TREATMENT

## Fatty Liver Treatment Focus Points

Lose weight

Exercise regularly

Eat healthy food

Avoid carbonated drinks

Avoid eating fried and high fat food

Consider nutritional supplements

Fatty Liver



Healthy Liver

