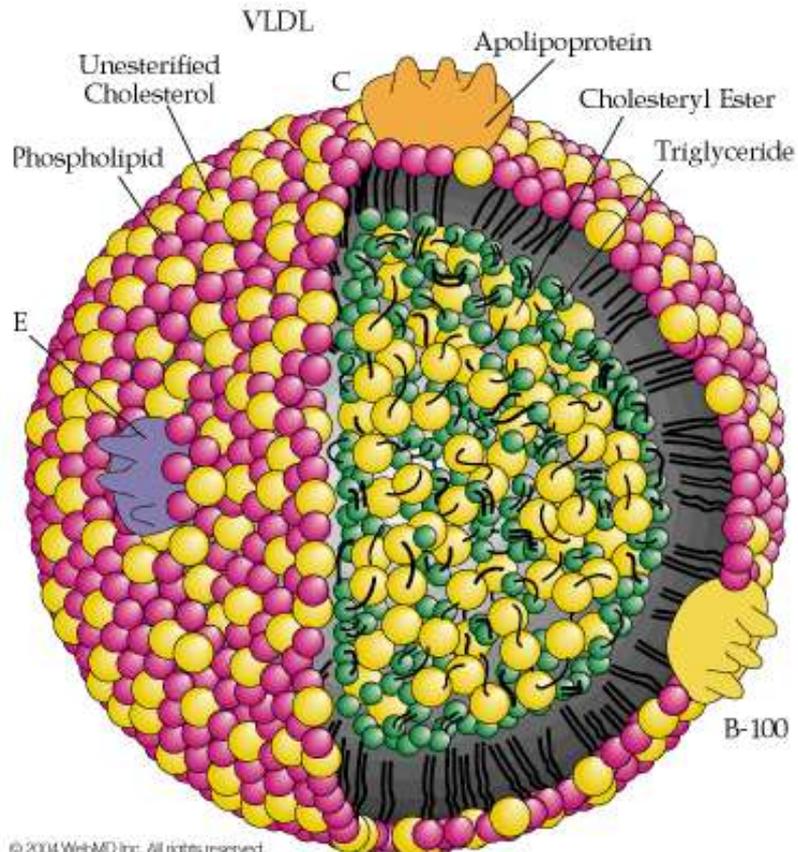


LIPOPROTEIN METABOLISM



BY;
MOHAMMAD SHAHRUKH
M.Sc. Medical Biochemistry
(Ph.D. Scholar)

Lipoproteins?

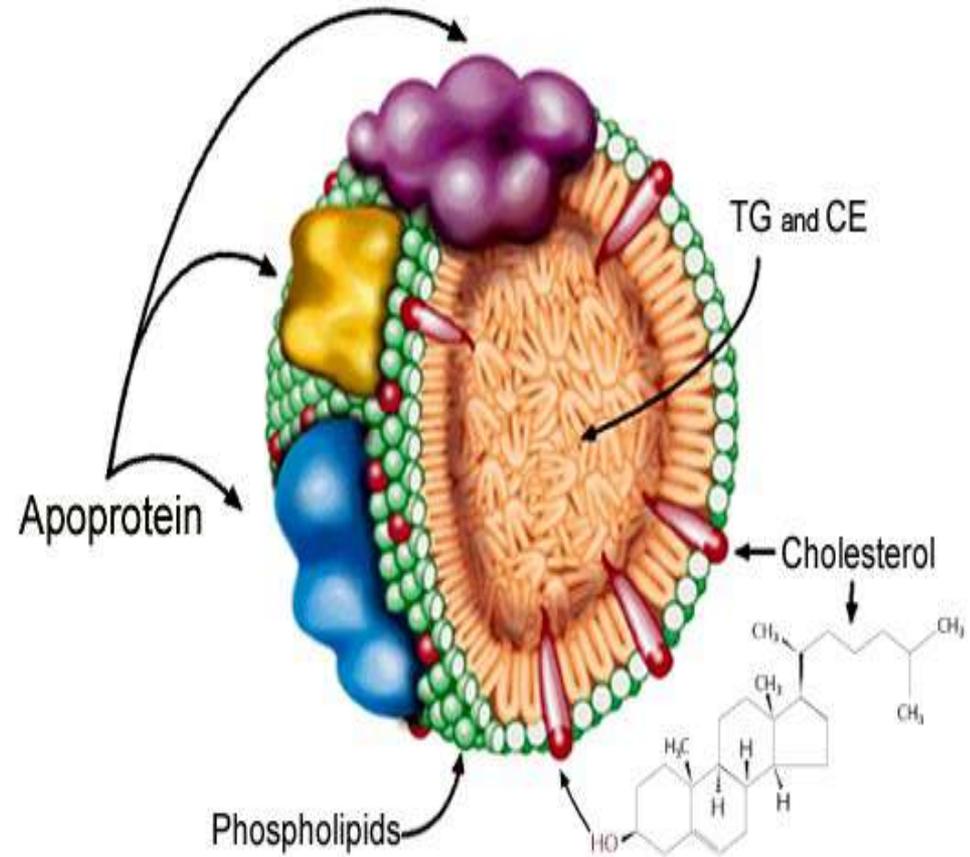
- ❖ Lipoproteins are spherical, macromolecular complexes of lipids and specific protein called Apo-protein.

Functions?

- ❖ They keep water insoluble lipids in solution of aqueous plasma.
- ❖ Provide mechanism for transporting their lipid components to and from the tissue.

Composition of plasma lipoproteins?

- They contain neutral lipid core made of TG , Cholesteryl esters and shell of amphipathic phospholipids, Unesterified cholesterol and apoprotein.

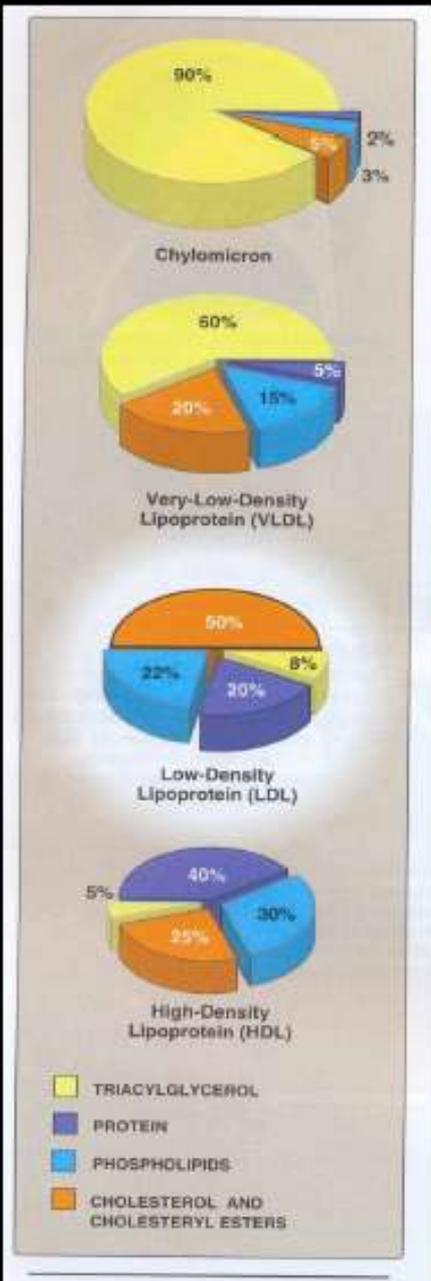


Classes of lipoproteins?

- ❖ Chylomicron.
- ❖ Very low density lipoproteins (VLDL).
- ❖ Low density lipoproteins (LDL).
- ❖ High density lipoproteins (HDL).
- ❖ Free fatty acids – Albumin complex

Arrangement of lipoprotein on their Size and Density

Lipoprotein class	Size	Density
Chylomicrone	1000 to 10,000A	Less than 0.96
VLDL	300 to 700A	Upto 1.006
LDL	150 to 250A	Upto 1.063
HDL	75 to 100A	Above 1.063



Chylo-
microne

VLDL

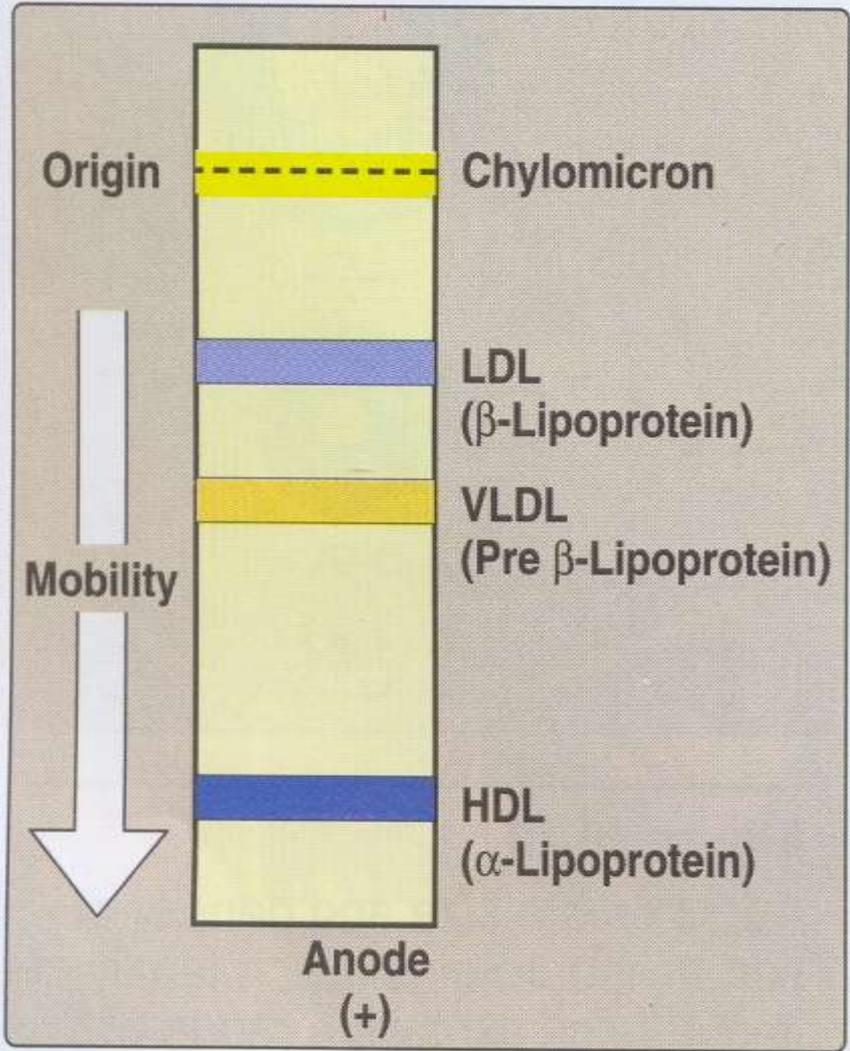
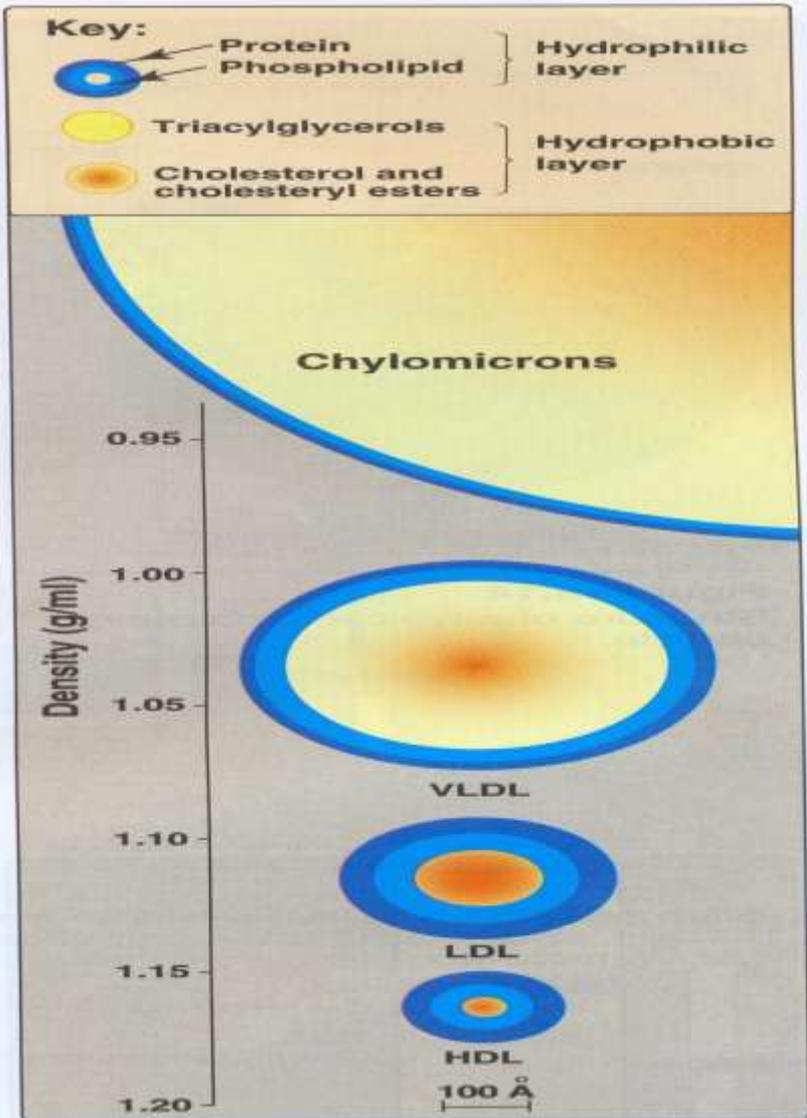
LDL

HDL

	TG	C & CE	PL	Apo protein
Chylo- microne	90 %	5 %	3 %	2 %
VLDL	60 %	20 %	15 %	5 %
LDL	08 %	50 %	22 %	20 %
HDL	05 %	25 %	30 %	40 %

Lipoprotein composition

Arrangement of lipoprotein based on DENSITY & ELECTROPHORETIC MOBILITY

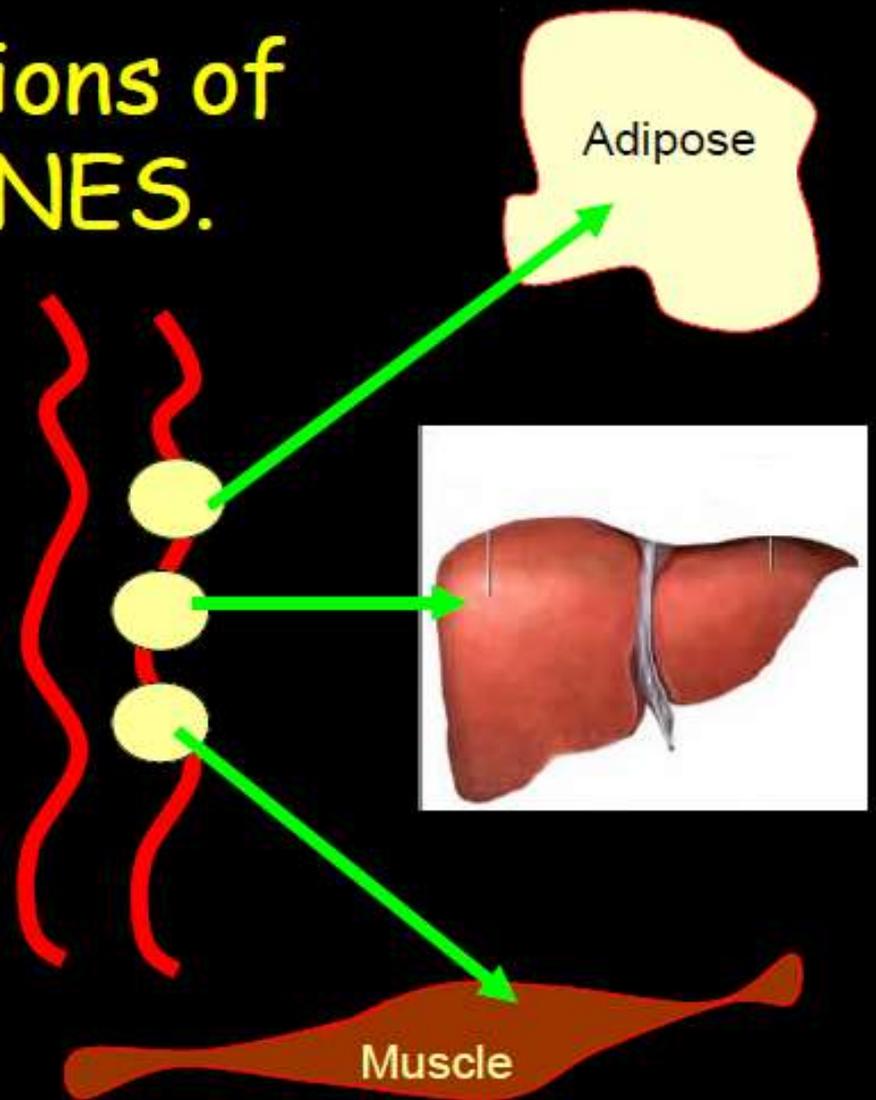


Functions of apolipoproteins?

- ❖ Provide recognition sites for cell surface receptors.
- ❖ Serves as coenzymes
- ❖ Some are required as a structural part and can not be replaced or removed.

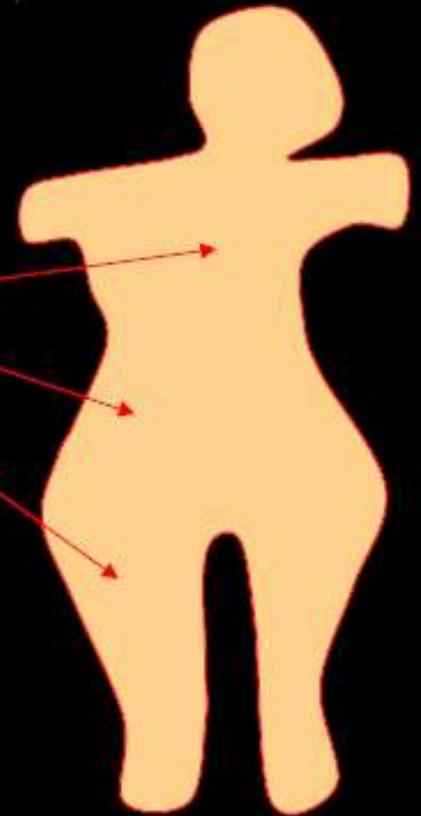
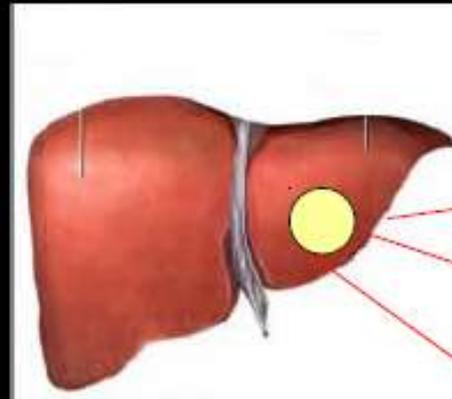
Write the functions of CHYLOMICRONES.

- Transport mainly Exogenous Triacylglycerol from intestine to Liver, adipose tissue and muscle.
- TAG either absorbed from food or Synthesized in enterocytes)



Write the functions of Very Low Density Lipoproteins (VLDL)

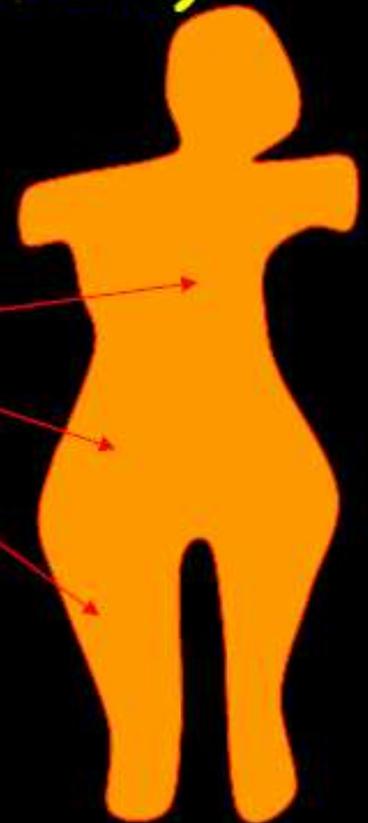
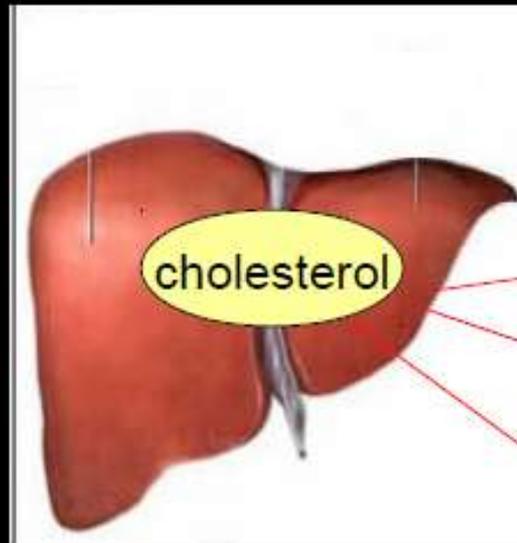
- Transports mainly endogenous Tri acyl glycerols from Liver to extra hepatic tissues



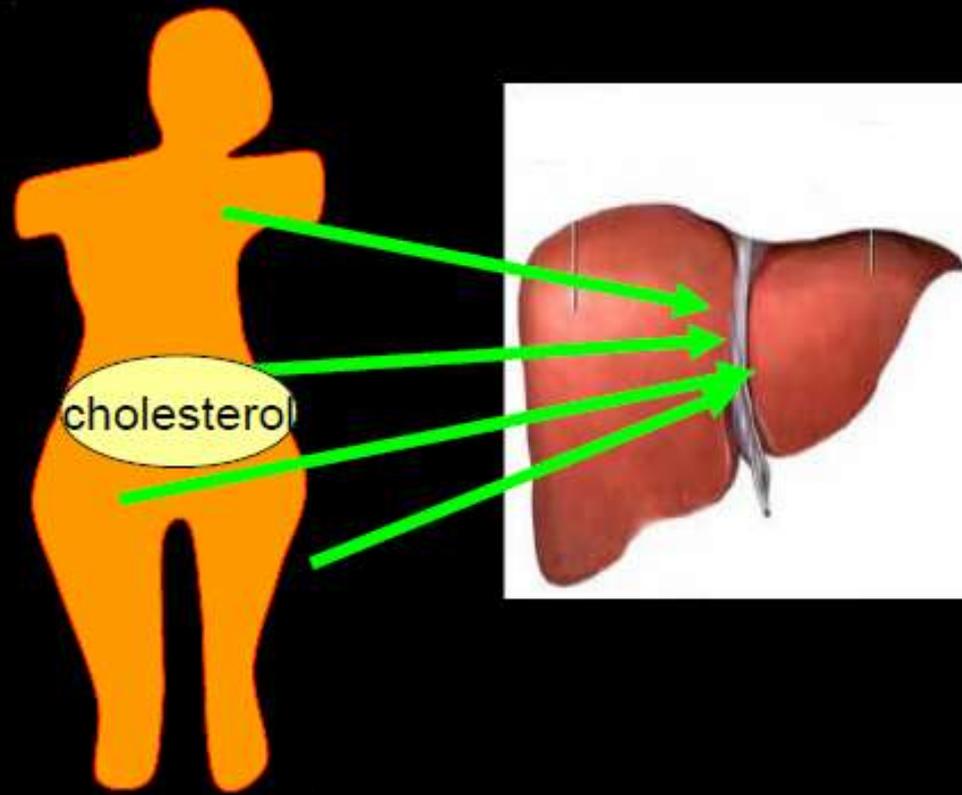
- Endogenous Tri acyl glycerols
Synthesized in hepatocytes

Write the functions of Low Density Lipoproteins (LDL)

- Transports mainly Cholesterol and cholesteryl esters from Liver to extra hepatic tissues

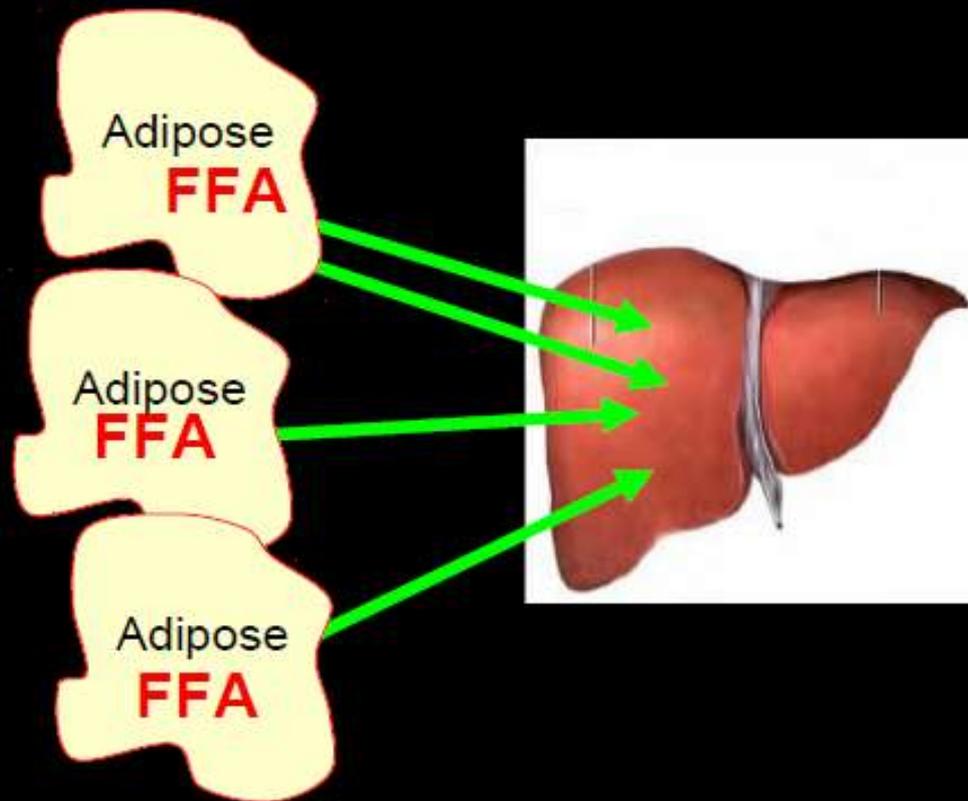


Write the functions of High Density Lipoproteins (HDL)



- Transports mainly Cholesterol and Cholesteryl esters from **extra hepatic tissues to Liver**
- Serves to hold apo-c & apo-e for use

Write the functions of Free fatty acid Albumin complex



- Transports mainly free fatty acids released from adipose tissue to Liver for oxidation

Enzymes in lipoprotein metabolism

- **Lecithin cholesterol acyl transferase (LCAT):**
 - Catalyses transfer of Sn2 FA of phospholipids to cholesterol.
 - Converts polar cholesterol to non polar cholesteryl esters
 - Shift of cholesterol from periphery to core
- **Lipoprotein lipase & Heparin sensitive lipase:**
 - Catalyses hydrolysis of chylomicron and VLDL
 - Located on capillary surface
 - Responsible for generating FA and glycerol in tissue

Enzymes in lipoprotein metabolism

□ **Hepatic lipase:**

- Catalyses hydrolysis of TAG and Phospholipids of HDL and IDL
- Located in sinusoids of liver
- Responsible for metabolic degradation of HDL and IDL

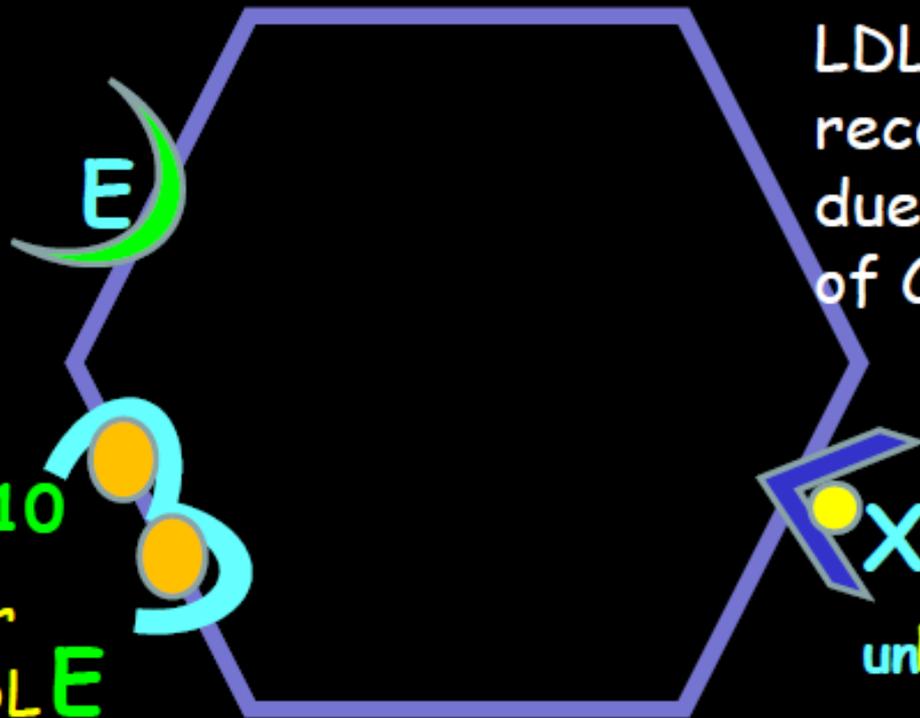
Enzymes in lipoprotein metabolism

□ Acid lipase & Intracellular lipase:

- Catalyses hydrolysis of TAG and cholesteryl esters in lysosomes
- Located in lysosome ,
- Optimum pH is acidic
- Responsible for degradation of lipoprotein taken up by receptor mediated endocytosis

Lipoprotein Receptors

Receptor for chylomicron remnants



Receptor for LDL does not recognize VLDL due to presence of C ii

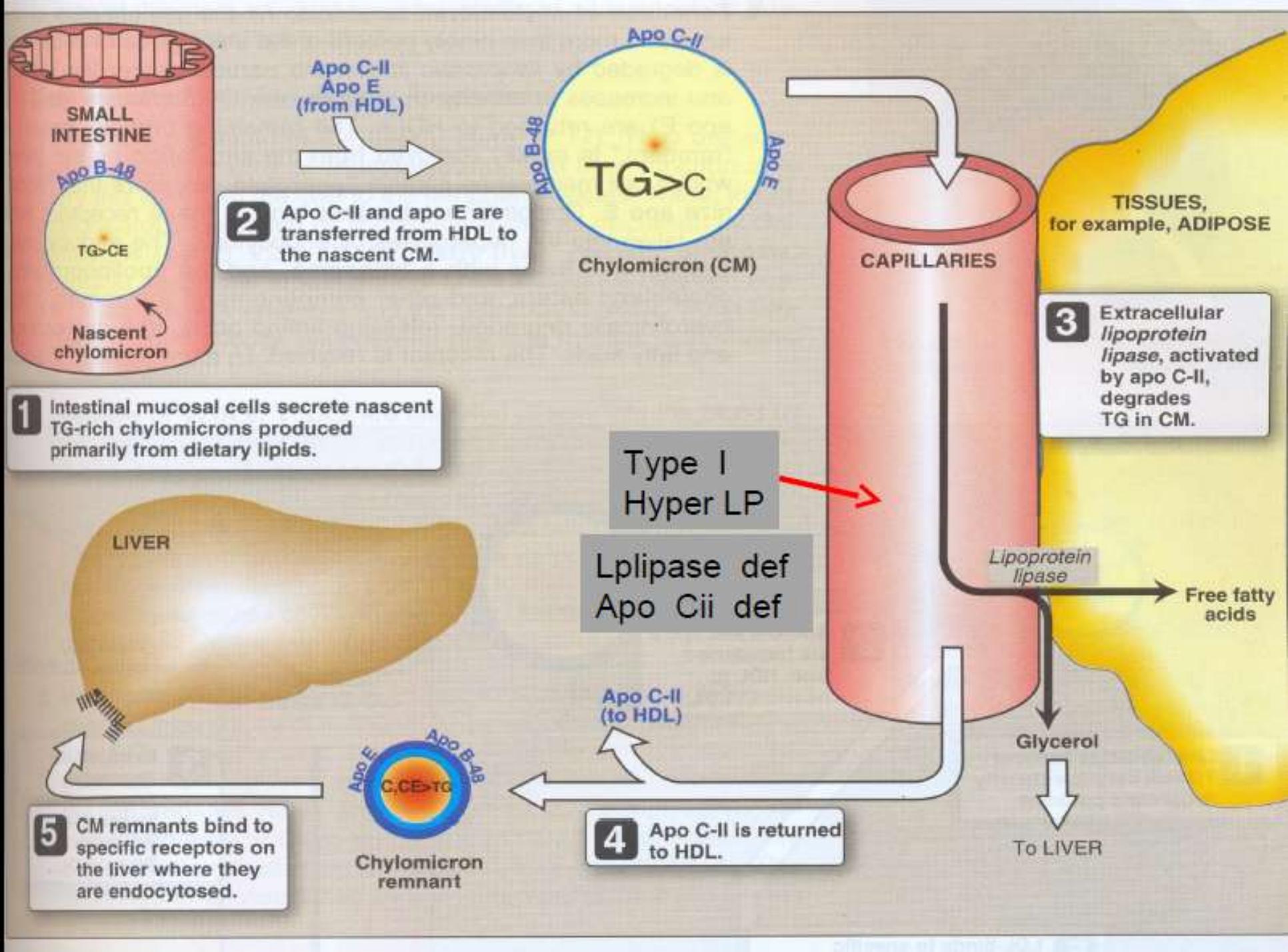
Receptor for LDL and IDL

unknown
Receptor for HDL

Apo C act as coenzyme for lipo protein lipase



***METABOLISM OF
CHYLOMICRONS***



1 Intestinal mucosal cells secrete nascent TG-rich chylomicrons produced primarily from dietary lipids.

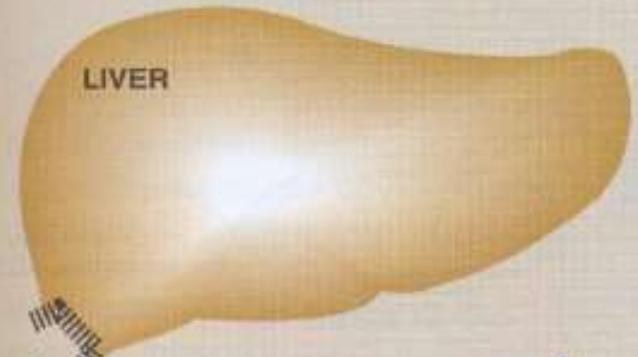
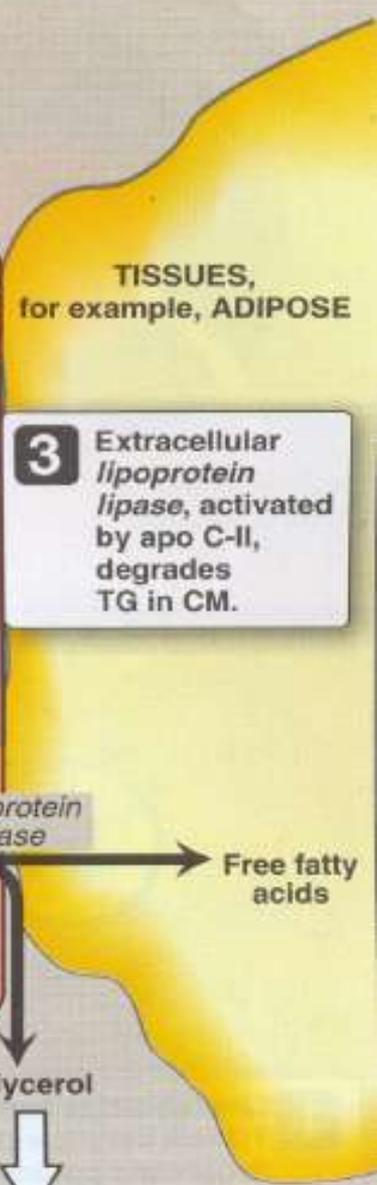
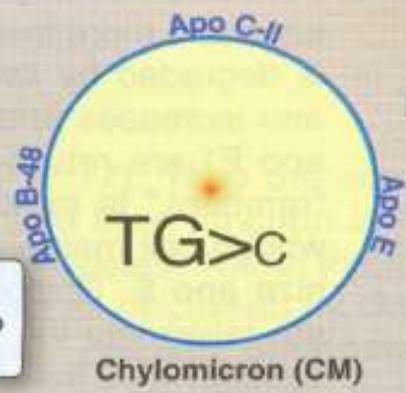
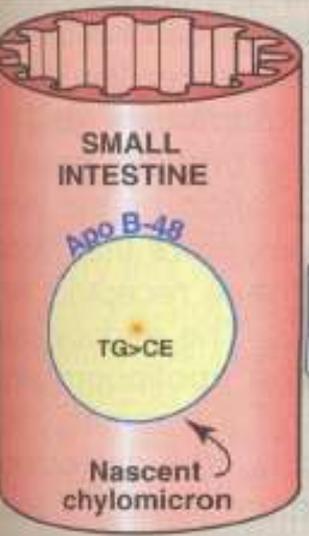
2 Apo C-II and apo E are transferred from HDL to the nascent CM.

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

4 Apo C-II is returned to HDL.

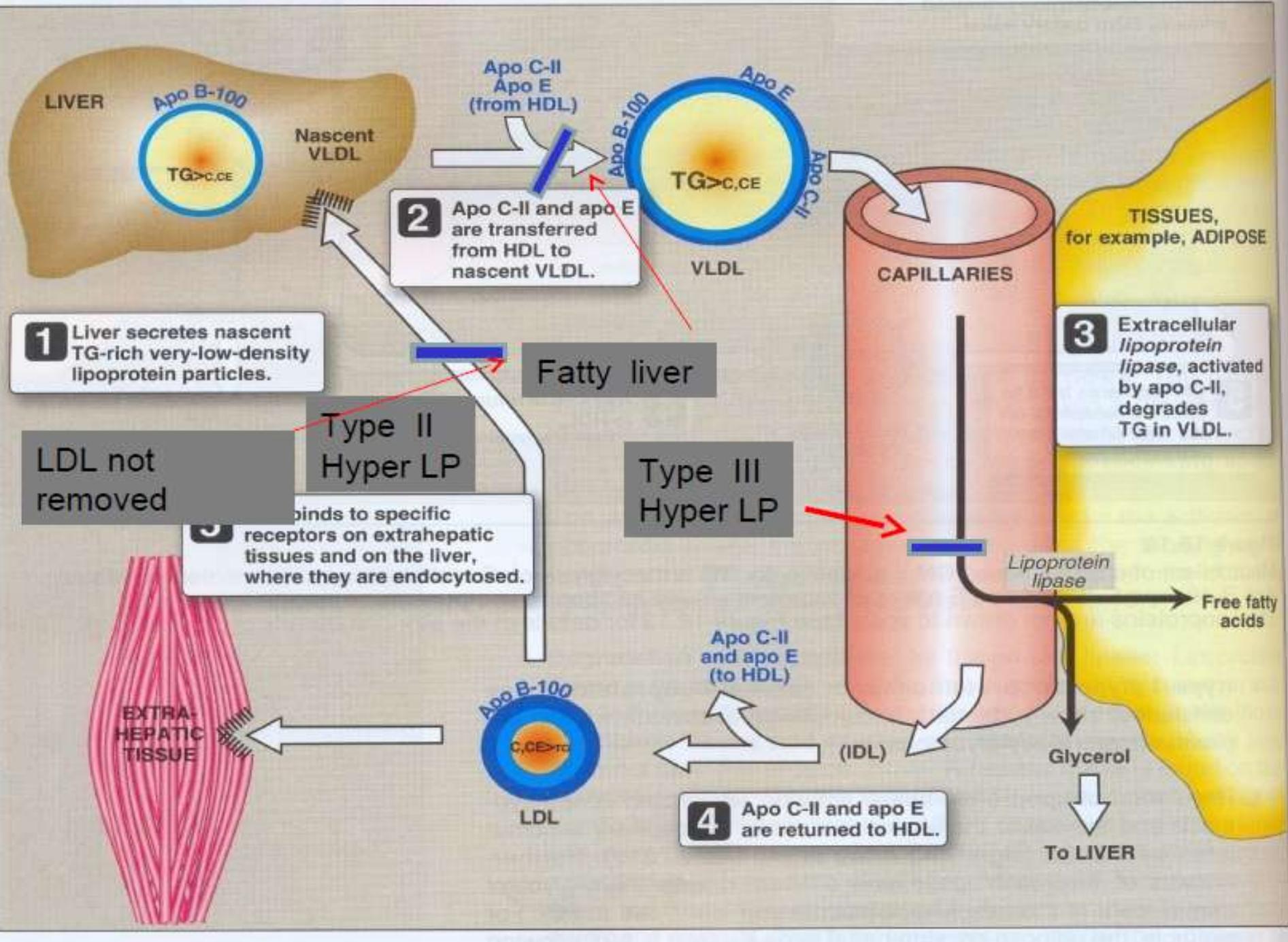
5 CM remnants bind to specific receptors on the liver where they are endocytosed.

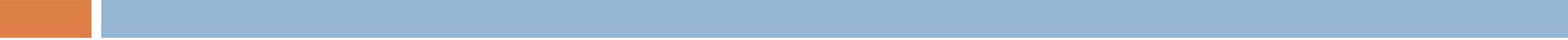
Type I Hyper LP
Lplipase def
Apo Cii def



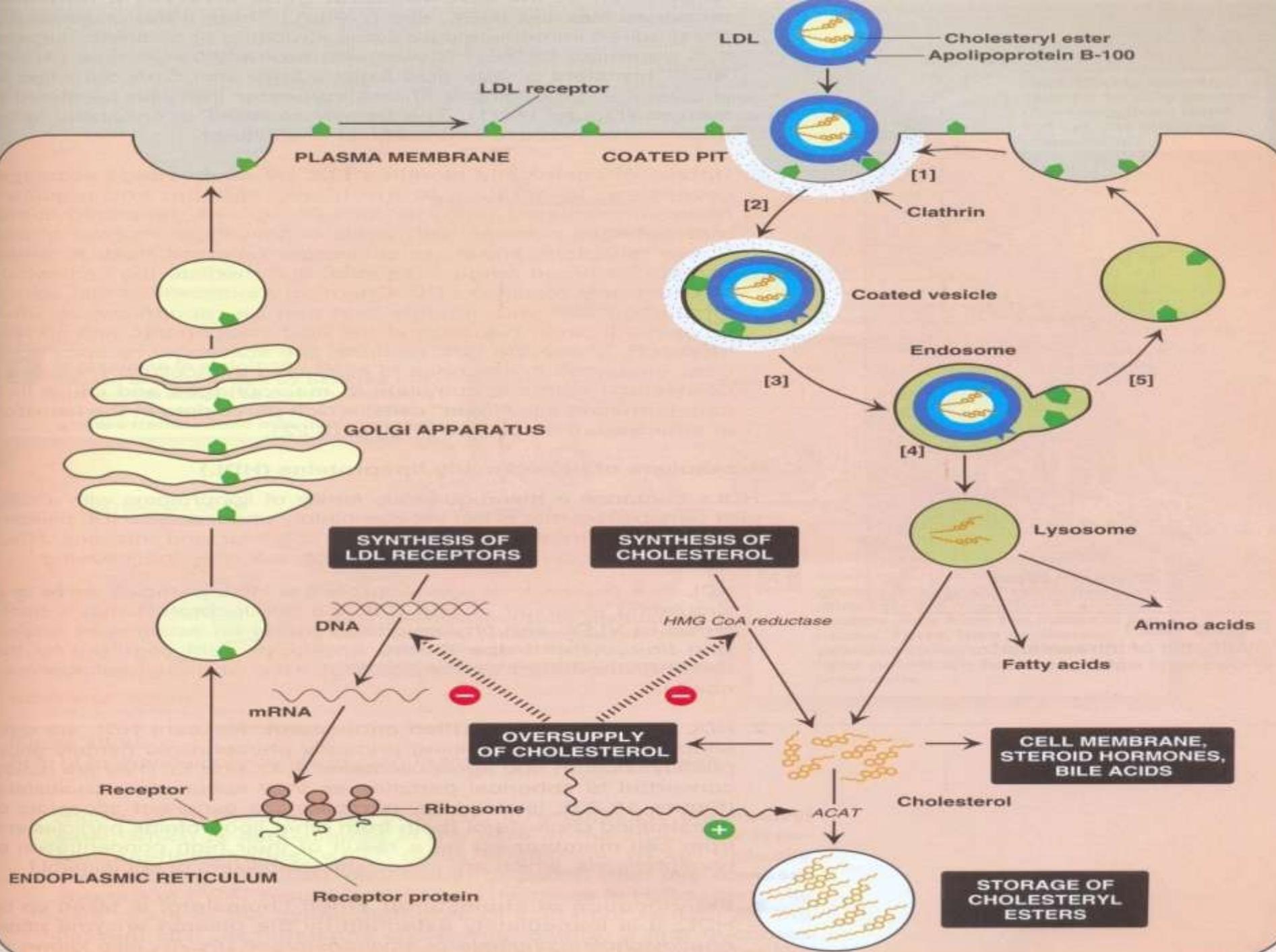


METABOLISM OF VLDL AND LDL



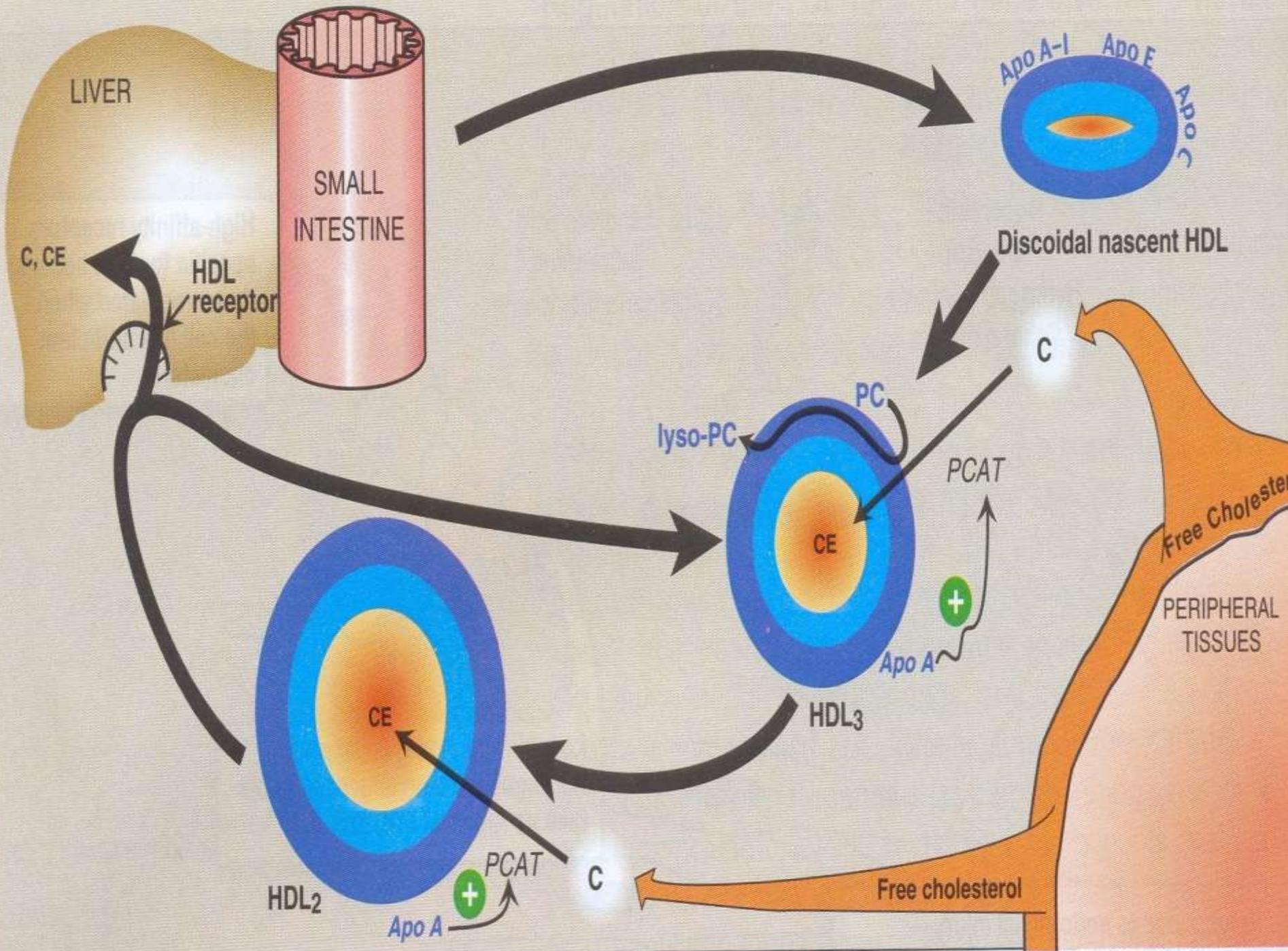


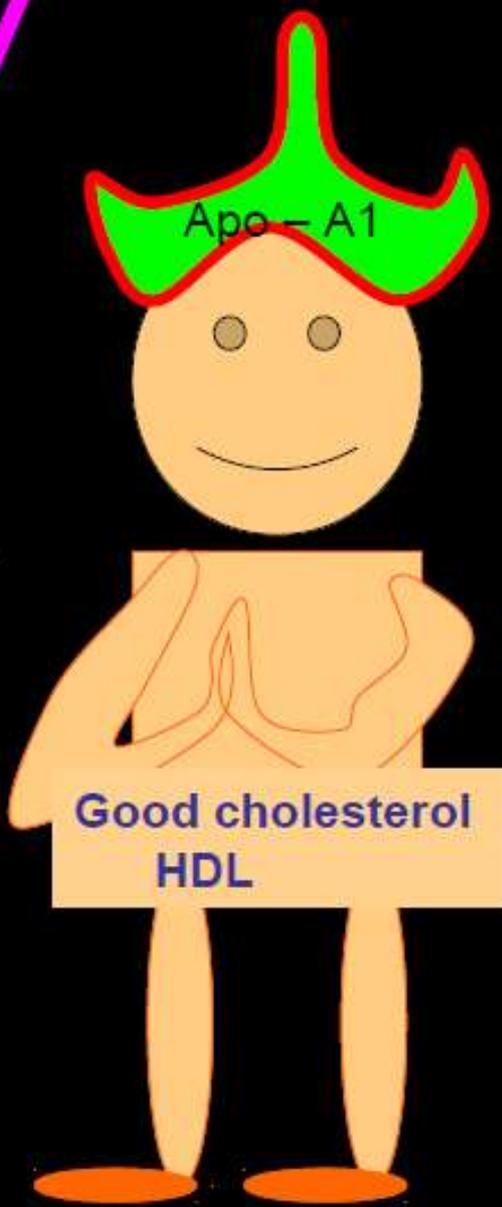
CELLULAR UPTAKE AND DEGRADATION OF LDL





METABOLISM OF HDL





Lipoproteins and Disease

- Hyperlipoproteinemias and hypolipoproteinemias are due to malfunctions in the synthesis and catabolism of lipoproteins.

HYPERLIPOPROTEINEMIA

TYPE -- I

- Deficiency of enzyme lipoprotein lipase
- VLDL and Chylomicrons are not utilized
- High TAG level in the blood

□ **HYPERLIPOPROTEINEMIA TYPE -- II**

- Lack of removal of LDL from the blood
- Not recognising Apo B100 in LDL receptor
- High Cholesterol level in the blood
- High risk of CHD and

□ **HYPERLIPOPROTEINEMIA TYPE – III**

- Deficiency of enzyme mobilizing
- VLDL and LDL from circulation
- Apo E deficient, impairs uptake
- IDL level increase in the blood

□ **HYPERLIPOPROTEINEMIA TYPE -- IV**

- Due to imbalance between
- synthesis and clearance of VLDL in circulation

HYPERLIPOPROTEINEMIA TYPE – V

Lipoprotein lipase deficient or utilization of VLDL and Chylomicrons

HYPO LIPOPROTEINEMIA & A BETA LIPOPROTEINEMIA

- Serum LDL and VLDL level decreased due to absence of Apo B
- Lack of formation of Chylomicron after high fatty meal
- Result malabsorption, steatorrhea and cholesterol deposition under skin as

HYPO LIPOPROTEINEMIA –II

- Deficiency of HDL due to absence of Apo A1
- Result cholesterol ester deposition in skin , cornea and blood vessels.
- Increased risk of premature CHD

Diseases associated with lipoprotein metabolism

Diseases	Genetic defects	Risk
LPL defect	Reduced level of LPL	Pancreatitis
Apo C-11 defect	Inability to synthesize Apo C-11	Pancreatitis
A beta lipoproteinemia	Inability to synthesize Apo B	Neurological defect
An alpha lipoproteinemia	Inability to synthesize Apo A	Cholesteryl esters storage in abnormal sites