Lipid Transport & Storage

Lipids are transported in the blood as lipoproteins.

Lipoproteins

Lipids must be transported between various tissues & organs for utilization & storage. Since lipids are insoluble in water, the problem of how to transport them in the aqueous blood media is solved by associating nonpolar lipids (triacylglycerol & cholesteryl esters) with amphipathic lipids (phospholipids & free cholesterol) & proteins to make water-soluble lipoproteins which transport lipids in the blood.

There are four major groups of lipoproteins in the blood which are:

(1) Chylomicron: derived from the intestine for the transport of triacylglycerol & other lipids absorbed from the intestine.

(2) Very low density lipoprotein (VLDL, or pre-β-lipoprotein): derived from the liver & to less extent from the intestine for the export of triacylglycerol.

(3) Low-density lipoprotein (LDL, or β-lipoprotein): represents the final stage in VLDL catabolism.

(4) High-density lipoprotein (HDL, or α-lipoprotein): derived from the liver & to less extent from the intestine. It involved in cholesterol transport & also in VLDL & chylomicron metabolism.

In addition there are two minor groups of lipoproteins in the blood that present in transient time, these are:

(1) Chylomicron remnant: derived from chylomicron catabolism.

(2) VLDL remnant (Intermediate-Density Lipoprotein [IDL]): derived through the way of VLDL catabolism into LDL.

The density of a lipoprotein decreases as the proportion of lipid to protein increases, these four major lipoproteins from the lowest density (highest diameter) to highest density (lowest diameter) are chylomicron, VLDL, LDL & HDL.

Triacylglycerol is the predominant lipid in chylomicron & VLDL, whereas cholesterol & phospholipid are the predominant lipids in LDL & HDL respectively.

Lipoproteins may be separated according to their electrophoretic properties into α-, β- & pre-β-lipoproteins.

Composition of the Lipoproteins in Plasma of Humans

				Composition			
Lipoprotein	**Source**	**Diameter (nm)**	**Density (g/mL)**	**Protein (%)**	**Lipid (%)**	**Main Lipid Components**	**Apolipoproteins**
Chylomicrons	Intestine	90–1000	< 0.95	1–2	98–99	Triacylglycerol	A-I, A-II, A-IV, B-48, C-I, C-II, C-III, E
Chylomicron remnants	Chylomicrons	45–150	< 1.006	6–8	92–94	Triacylglycerol, phospholipid cholesterol	B-48, E
VLDL	Liver (intestine)	30–90	0.95–1.006	7–10	90–93	Triacylglycerol	B-100, C-I, C-II, C-III, E
IDL	VLDL	25–35	1.006–1.019	11	89	Triacylglycerol, cholesterol	B-100, E
LDL	VLDL	20–25	1.019–1.063	21	79	Cholesterol	B-100
HDL	Liver, intes-tine,					Phospholipids, cholesterol	A-I, A-II, A-IV, C-I, C-II, C-III, E

Lipoprotein Structure

Lipoprotein consists of:

1)- Nonpolar lipid core consists mainly of triacylglycerol & cholesteryl ester.

2)- Single surface layer surround the nonpolar lipid core consist of amphipathic lipids mainly phospholipid & free cholesterol molecules which are oriented so that their polar groups face outward to the aqueous medium.

3)- Apolipoprotein (apoprotein) which is the protein moiety of a lipoprotein, some apolipoproteins are integral & cannot be removed, whereas others are free to transfer to other lipoproteins, these apolipoproteins are of many types in which one or more apolipoproteins are present in each lipoprotein.

The main types of apoproteins are:

i- Apo A: include Apo A-I, A-II & A-IV, represent the major apolipoproteins of HDL, also present in chylomicron.

ii- Apo B: include mainly:

a- Apo B-100: synthesized in the liver, it represents the major apolipoprotein of LDL, also found in VLDL.

b- Apo B-48: synthesized in the intestine, found in chylomicron.

Therefore, apo B is present in all lipoproteins except HDL.

iii- Apo C: include Apo C-I, C-II & C-III, they are freely transferable between several different lipoproteins.

iv- Apo E: found in all lipoproteins except LDL.

The main functions of apolipoproteins are:

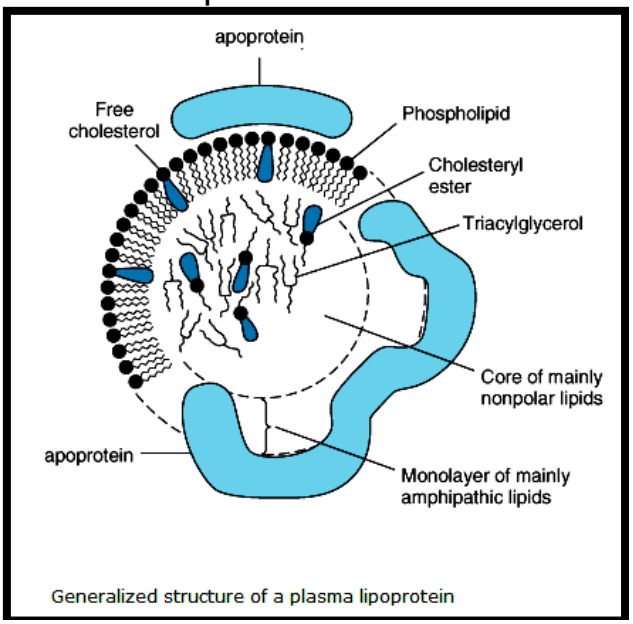
(I) Form important part of lipoprotein structure.

(2) Activate or inhibit enzymes:

A- Enzyme activators: as apo C-II for the activation of lipoprotein lipase, apo A-I for the activation of lecithin:cholesterol acyltransferase (LCAT).

B- Enzyme inhibitors: as apo A-II & apo C-III for the inhibition of lipoprotein lipase.

(3) Act as ligands for interaction with lipoprotein receptors in tissues, eg, apo B-100 & apo E for the LDL receptor, apo E for the LDL-receptor-related protein (LRP) & apo A-I for the HDL receptor.



Generalized structure of a plasma lipoprotein

Triacylglycerol Transport

Triacylglycerol is transported from the intestine mainly by chylomicron & from the liver by VLDL. Chylomicron is found in chyle so that it formed only by the lymphatic system draining the intestine & is responsible for the transport of triacylglycerol & other dietary lipids into the blood circulation, small quantities of VLDL are also found in chyle; however, most VLDL in the blood are of hepatic origin which transport triacylglycerol from the liver to the extrahepatic tissues.

Formation of Chylomicron & VLDL

There are similarities in the mechanisms of formation of chylomicron by intestinal cells & VLDL by hepatic parenchymal cells. Newly secreted or "nascent" chylomicron & VLDL contain only a small amount of apo C & apo E, & the full complement is acquired from HDL in the blood circulation, also chylomicron & VLDL contain apo B (apo B-48 in chylomicron & apo B-100 in VLDL), in addition to that chylomicron contains apo A.

Catabolism of Chylomicron & VLDL

Chylomicron & VLDL are rapidly catabolized through the following steps.

(Step 1): Triacylglycerol of chylomicron & VLDL are hydrolyzed into glycerol & fatty acids by **lipoprotein lipase** enzyme that located on the walls of blood capillaries of the muscle & adipose tissues, some of the released fatty acids return to the circulation attached to albumin as FFA, but the bulk is transported into the tissue mainly by muscle cells as energy source (undergoes oxidation) or by adipose cells as energy stores (forms triacylglycerol). Both phospholipids & apo C-II are required as activators for lipoprotein lipase activity, while apo A-II & apo C-III act as inhibitors. Insulin enhances lipoprotein lipase in adipocytes, therefore, this enzyme is also called **insulin sensitive lipase** enzyme.

(Step 2): Reaction with lipoprotein lipase results in the loss of 70–90% of the triacylglycerol content of chylomicron & VLDL in addition to the transfer of apo C of chylomicron & VLDL & apo A of chylomicron to HDL but not apo B & E, these changes result in the formation of chylomicron remnant(contains apo B-48 & E) & VLDL remnants (IDL)(contains apo B-100 & E) respectively, both these two remnants are relatively enriched in cholesterol & cholesteryl esters because of the loss of most its contents of triacylglycerol by lipoprotein lipase.

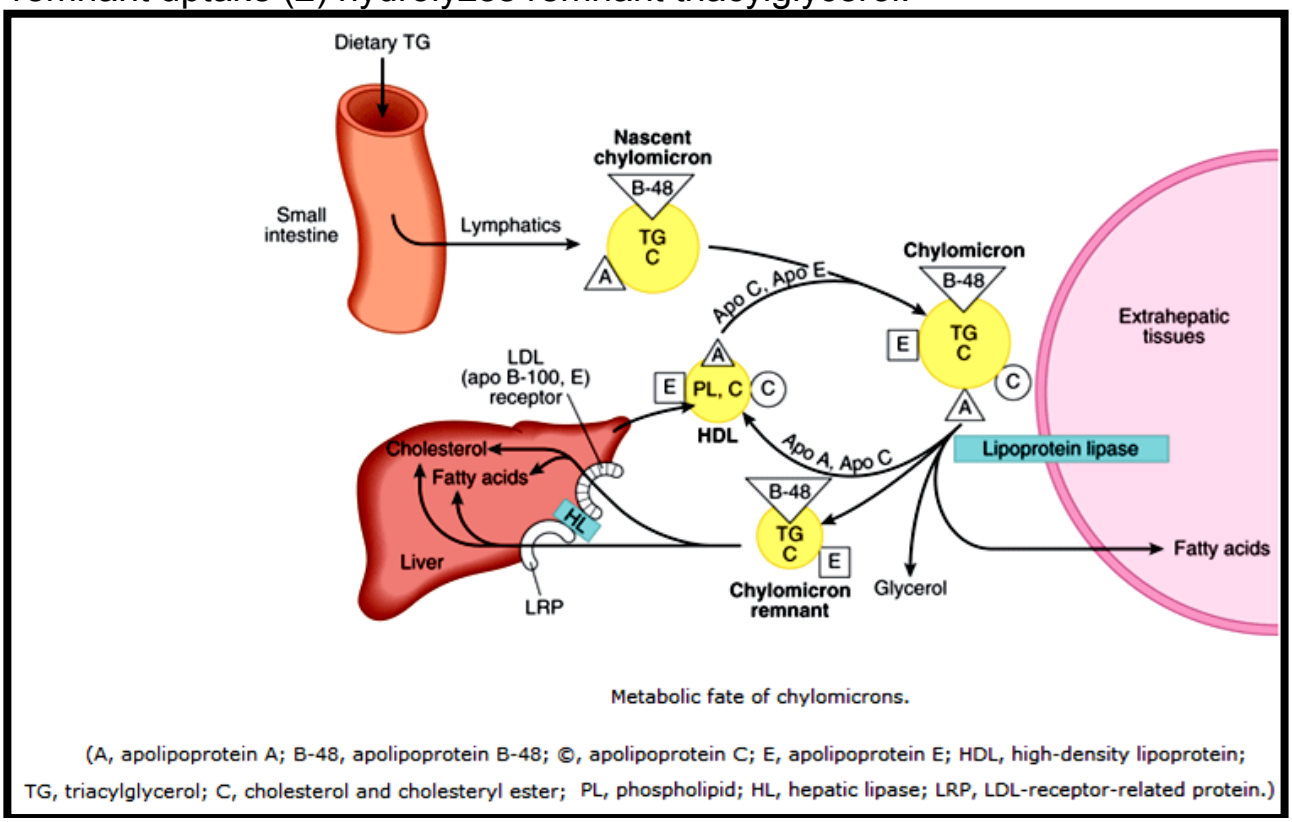
(Step 3): The liver is responsible for the uptake of chylomicron remnant & IDL by receptors-mediated endocytosis as follow:

A- Chylomicron remnants are taken up by the liver via two receptors, the LDL receptor (sensitive to apo B-100, E) & LRP (sensitive to apo E).

B- IDL may be taken up by the liver directly via the LDL receptor (sensitive to apo B-100, E) or it may loss its apo E & its content of triacylglycerol to be converted into LDL (contains only apo B-100) which is taken up directly via the LDL receptor (sensitive to apo B-100, E). In humans, a relatively large proportion of IDL forms LDL. Approximately 70% of LDL receptors are present

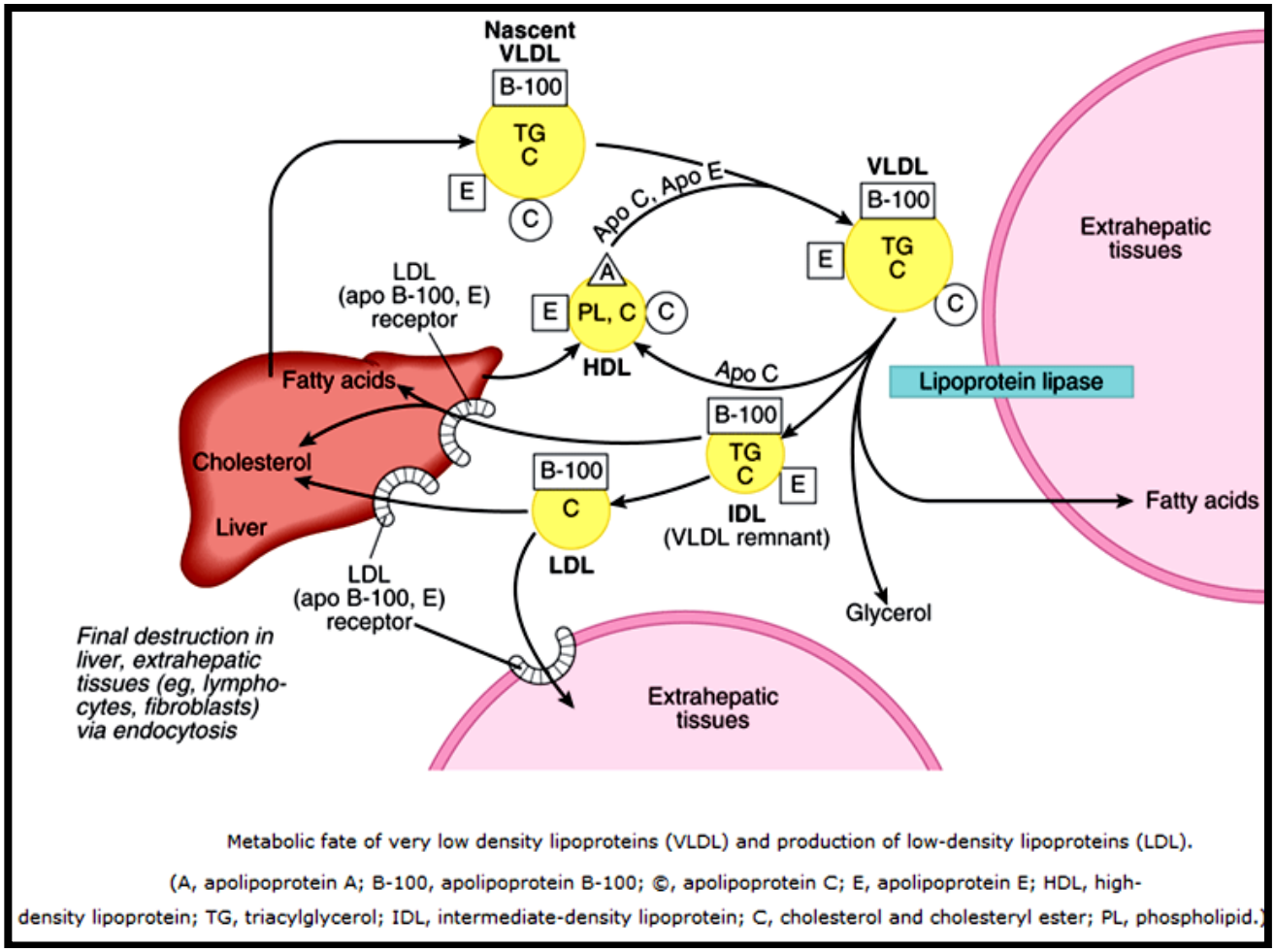
in the liver & 30% in the extrahepatic tissues. When these receptors are saturated, the excess LDL is taken up by macrophages present in blood vessels initiating atherosclerosis. Therefore, a positive correlation was exists between the incidence of atherosclerosis & the plasma concentration of LDL.

In this process, the **hepatic lipase** enzyme has a dual role: (1) facilitate remnant uptake (2) hydrolyzes remnant triacylglycerol.



Metabolic fate of chylomicrons.

(A, apolipoprotein A; B-48, apolipoprotein B-48; ©, apolipoprotein C; E, apolipoprotein E; HDL, high-density lipoprotein; TG, triacylglycerol; C, cholesterol and cholesteryl ester; PL, phospholipid; HL, hepatic lipase; LRP, LDL-receptor-related protein.)



Metabolic fate of very low density lipoproteins (VLDL) and production of low-density lipoproteins (LDL).

(A, apolipoprotein A; B-100, apolipoprotein B-100; ©, apolipoprotein C; E, apolipoprotein E; HDL, high-density lipoprotein; TG, triacylglycerol; IDL, intermediate-density lipoprotein; C, cholesterol and cholesteryl ester; PL, phospholipid.)