



LIPOPROTEINS

Lecture-10

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- Lipids absorbed from the diet and synthesized by the liver and adipose tissue must be transported between various cells and organs for utilization and storage.

- Lipids are insoluble in water, the problem of transportation in the aqueous plasma is solved by associating nonpolar lipids (triacylglycerols and cholesteryl esters) with amphipathic lipids (phospholipids and cholesterol) and proteins to make water-miscible lipoproteins.

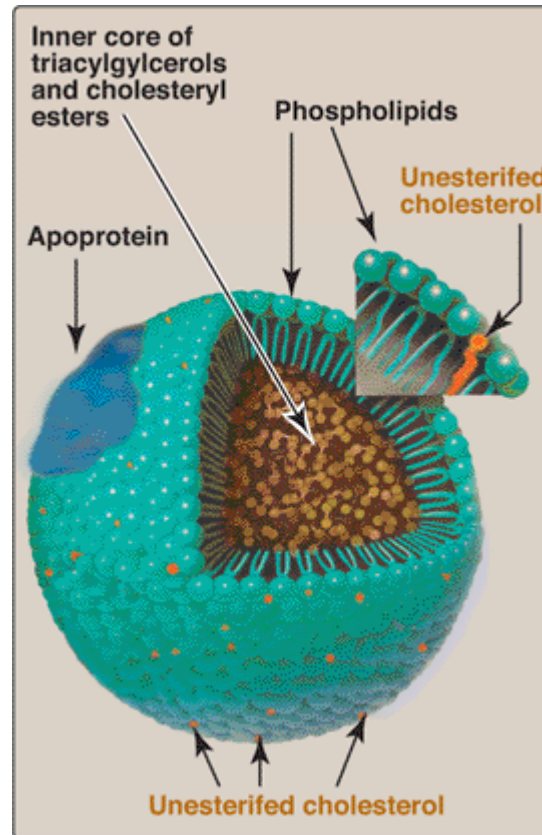
LIPOPROTEINS

- The plasma lipoproteins are spherical macromolecular complexes of lipids and specific proteins (apolipoproteins or apoproteins).
- The lipoprotein particles include chylomicrons, very-low-density lipoproteins (VLDL), low-density lipoproteins (LDL), and high-density lipoproteins (HDL).
- They differ in lipid and protein composition, size, density, and site of origin.
- Lipoproteins function both to keep their component lipids soluble as they transport them in the plasma and to provide an efficient mechanism for transporting their lipid contents to (and from) the tissues.

COMPOSITION OF PLASMA LIPOPROTEINS

- Lipoproteins are composed of a neutral lipid core (containing triacylglycerol, and cholesteryl esters) surrounded by a shell of amphipathic apolipoproteins, phospholipid, and nonesterified cholesterol.
- These amphipathic compounds are oriented so that their polar portions are exposed on the surface of the lipoprotein, thus making the particle soluble in aqueous solution.
- The triacylglycerol and cholesterol carried by the lipoproteins are obtained either from the diet (exogenous source) or from de novo synthesis (endogenous source).
- Lipoprotein particles constantly interchange lipids and apolipoproteins with each other; therefore, the actual apolipoprotein and lipid content of each class of particles can be somewhat variable.

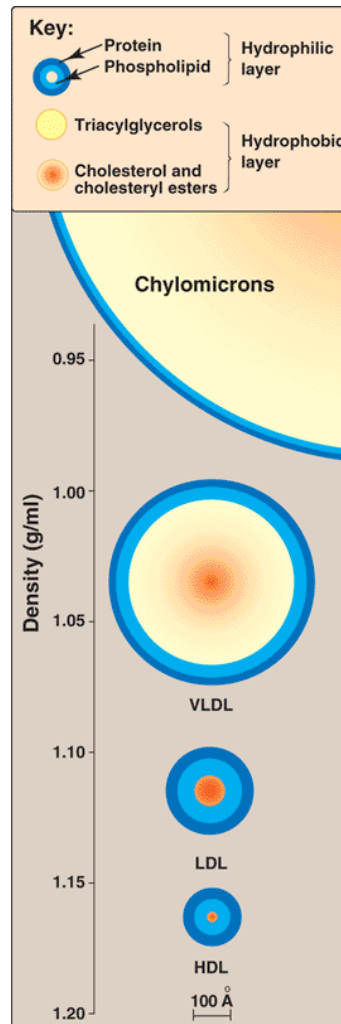
STRUCTURE OF A TYPICAL LIPOPROTEIN PARTICLE.



SIZE AND DENSITY OF LIPOPROTEIN PARTICLES

- Chylomicrons are the lipoprotein particles lowest in density and largest in size, and contain the highest percentage of lipid and the lowest percentage of protein.
- VLDLs and LDLs are successively denser, having higher ratios of protein to lipid.
- HDL particles are the densest.
- Plasma lipoproteins can be separated on the basis of their electrophoretic mobility, or on the basis of their density by ultracentrifugation.

APPROXIMATE SIZE AND DENSITY OF SERUM LIPOPROTEINS



APOLIPOPROTEINS:

- The apolipoproteins associated with lipoprotein particles have a number of diverse functions, such as providing recognition sites for cell-surface receptors, and serving as activators or coenzymes for enzymes involved in lipoprotein metabolism.
- Some of the apolipoproteins are required as essential structural components of the particles and cannot be removed (in fact, the particles cannot be produced without them), whereas others are transferred freely between lipoproteins.
- Apolipoproteins are divided by structure and function into five major classes, A through E, with most classes having subclasses, for example, apolipoprotein (or apo) A-I and apo C-II.

CLASSIFICATION OF LIPOPROTEINS

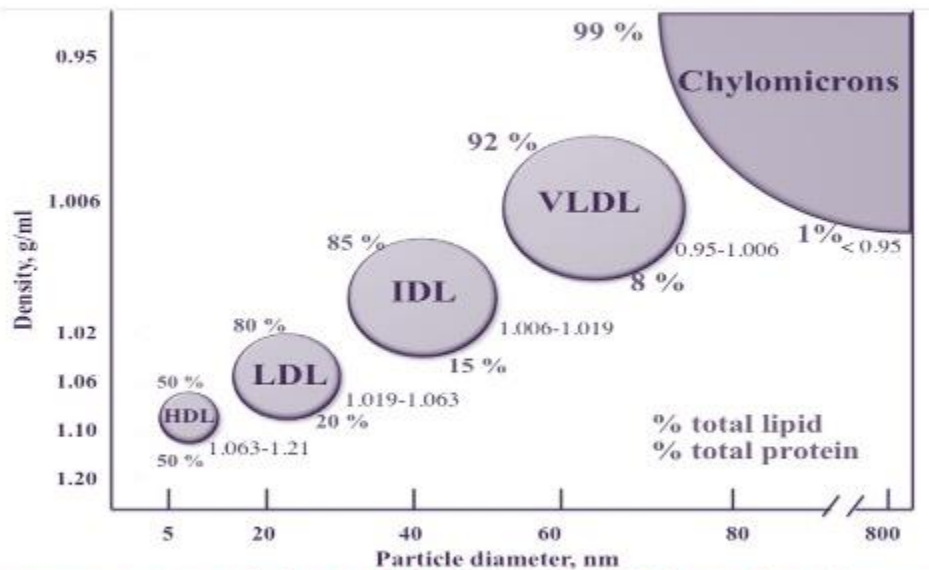
- Lipoproteins can be classified in three ways
- 1. Based on density- They are separated by Ultracentrifugation. Depending upon the floatation constant (Sf), five major groups of lipoproteins have been identified that are important physiologically and in clinical diagnosis.

- Chylomicrons, derived from intestinal absorption of triacylglycerol and other lipids; Density is generally less than 0.95 while the mean diameter lies between 100- 500 nm.

- (ii) Very low density lipoproteins (VLDL), derived from the liver for the export of triacylglycerol; density lies between 0.95-1.006 and the mean diameter lies between 30-80 nm.
- (iii) Intermediate density lipoproteins (IDL) are derived from the catabolism of VLDL, with a density ranging intermediate between Very low density and Low density lipoproteins i.e. ranging between 1.006- 1.019 and the mean diameter ranges between 25- 50nm.

- (iv) Low-density lipoproteins (LDL), representing a final stage in the catabolism of VLDL; density lies between 1.019-1.063 and mean diameter lies between 18-28 nm
- (v) High-density lipoproteins (HDL), involved in cholesterol transport and also in VLDL and chylomicron metabolism. Density ranges between 1.063-1.121 and the mean diameter varies between 5-15 nm.

Classification of Lipoproteins



Lipoproteins with high lipid content will have low density, larger size and so float on centrifugation. Those with high protein content sediment easily, have compact size and have a high density.

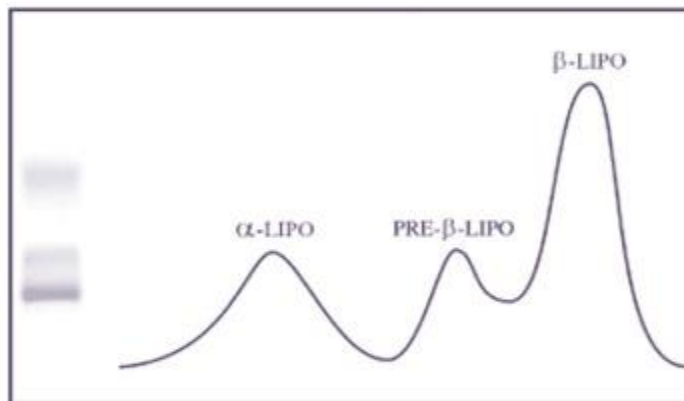
CLASSIFICATION OF LIPOPROTEINS

2-Based on electrophoretic mobilities Lipoproteins may be separated according to their electrophoretic properties into - α , pre β , β , and broad beta lipoproteins.

- The mobility of a lipoprotein is mainly dependent upon protein content.
- Those with higher protein content will move faster towards the anode and those with minimum protein content will have minimum mobility.

Classification of Lipoproteins

LIPOPROTEINS INTERPRETATION



Normal values range

Fraction	% Lipoproteine tot.
α -Lipo	20-48
Pre- β -Lipo	12-30
β -Lipo	45-70
Chilomicroni	0

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

- HDL are α , VLDL pre- β , LDL- β , and IDL are broad beta lipoproteins.
- Free fatty acid and albumin complex although not a lipoprotein is an important lipid fraction in serum and is the fastest moving fraction.
- Chylomicrons remain at the origin since they have more lipid content.
- VLDLs with less protein content than LDL move faster than LDL, this is due to nature of apoprotein present

CLASSIFICATION OF LIPOPROTEINS

3-Based on nature of Apo- protein content □ One or more apolipoproteins (proteins or polypeptides) are present in each lipoprotein.


- The major apolipoproteins of HDL (α -lipoprotein) are designated A.
- The main apolipoprotein of LDL (β -lipoprotein) is apolipoprotein B (B-100), which is found also in VLDL.
- Chylomicrons contain a truncated form of apo B (B-48) that is synthesized in the intestine, while B-100 is synthesized in the liver.
- Apo E is found in VLDL, HDL, Chylomicrons, and chylomicron remnants.

CLINICAL SIGNIFICANCE OF LIPOPROTEIN METABOLISM

- Fatty Liver is an abnormal accumulation of certain fats (triglycerides) inside liver cells.
- Hepatic triacylglycerol synthesis provides the immediate stimulus for the formation and secretion of VLDL.
- Impaired VLDL formation or secretion leads to nonmobilization of lipid components from the liver, results in fatty liver.

PRIMARY DISORDERS OF PLASMA LIPOPROTEINS

- Inherited defects in lipoprotein metabolism lead to the primary condition of either hypo- or hyperlipoproteinemia .
- In addition, diseases such as diabetes mellitus, hypothyroidism, nephrotic syndrome, and atherosclerosis are associated with secondary abnormal lipoprotein patterns that are very similar to one or another of the primary inherited conditions.

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The End