1st Year MBBS

CVS Module
Lecture on Compound lipids
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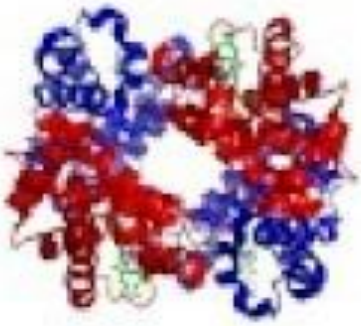
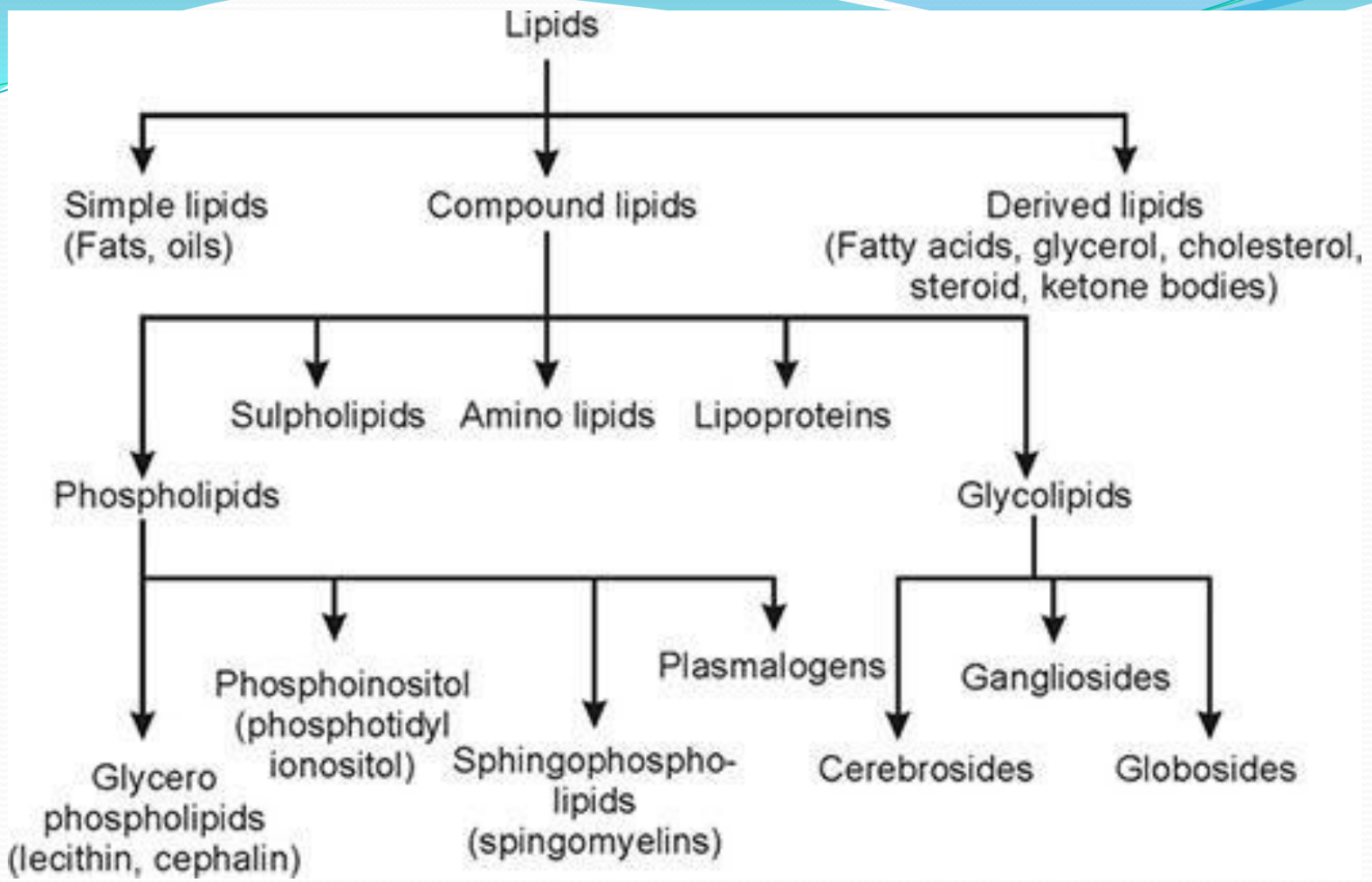
BioMolecules



COMPOUND LIPIDS


Lipids
Simple lipids
(Fats, oils)
Compound lipids
Derived lipids
(Fatty acids, glycerol, cholesterol,
steroid, ketone bodies)
Sulpholipids
Amino lipids
Lipoproteins
Phospholipids
Glycolipids
Plasmalogens
Phosphoinositol
(phosphotidyl
ionositol)
Gangliosides
Glycero
phospholipids
(lecithin, cephalin)
Sphingophospho-
lipids
(spingomyelins)
Cerebrosides
Globosides

II. Compound Lipids: These are Esters of fatty acids, containing

an alcohol

fatty acids

and some other group

- Phospholipids
- Glycolipids
- Sulpholipids
- Lipoproteins

COMPOUND LIPIDS

1) **PHOSPHOLIPIDS:**

Definition:

Phospholipids are compound lipids, in addition to fatty acids and glycerol/ or other alcohol,phospholipids also contain a phosphoric acid residue, nitrogen containing base and other substituents.

Classification:

Is based on the type of alcohol present in the phospholipids. They are classified mainly into following three groups:

A.GLYCEROPHOSPHATIDES

B.PHOSPHOINOSITIDES

C.PHOSPHOSPHINGOSIDES

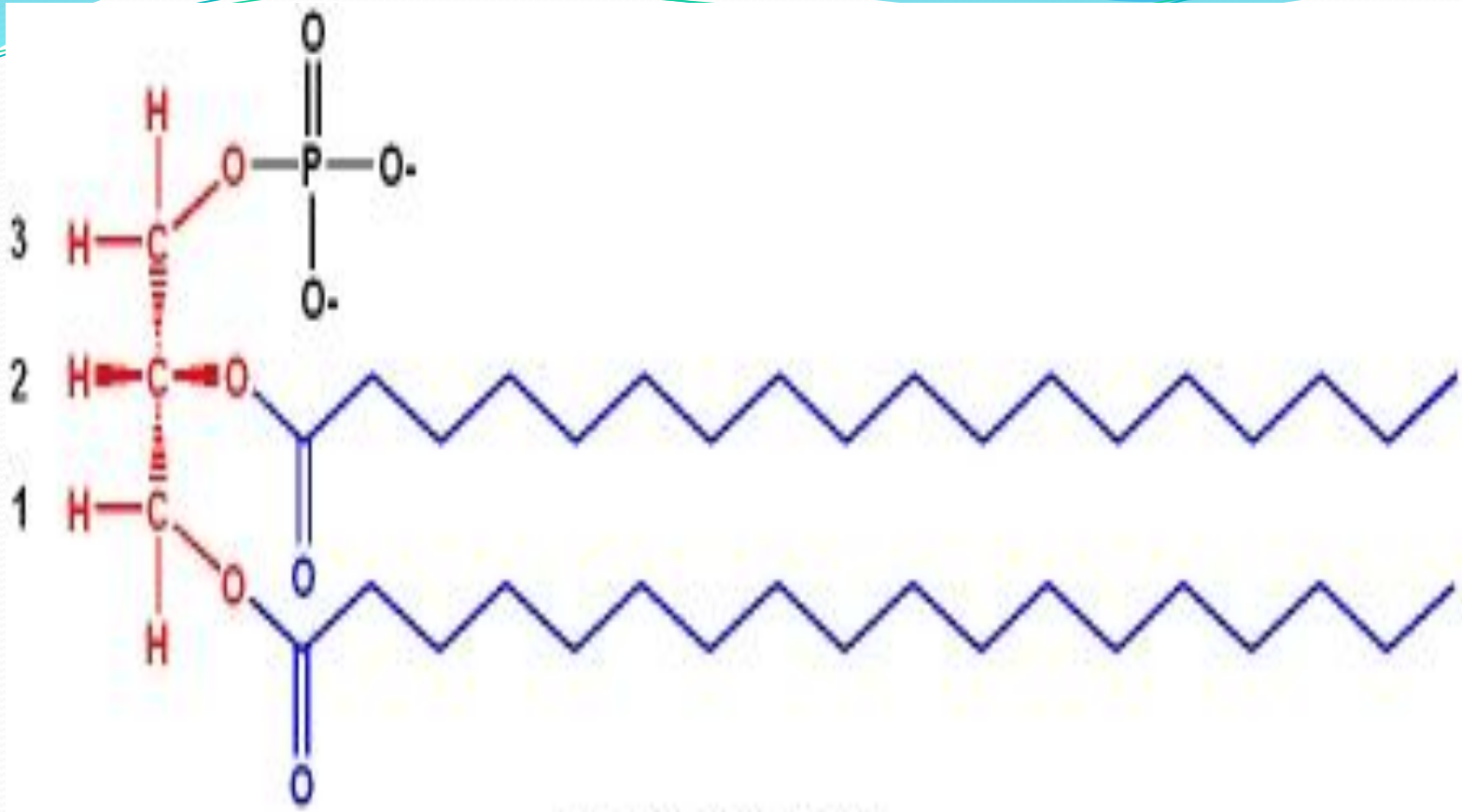
A: **Glycerophosphatides:**

In this glycerol is the alcohol group.

Examples:

Phosphatidyl ethanolamine (cephalin), phsophatidyl choline (Lecithin), phospatidyl serine, plasmalogens, phosphatidic acid, cardiolipins and phosphatides.

Phosphatidic acid consists of a glycerol backbone, with, in general, a saturated fatty **acid** bonded to carbon-1,
an unsaturated fatty **acid** bonded to carbon-2,
and a phosphate group bonded to carbon-3.



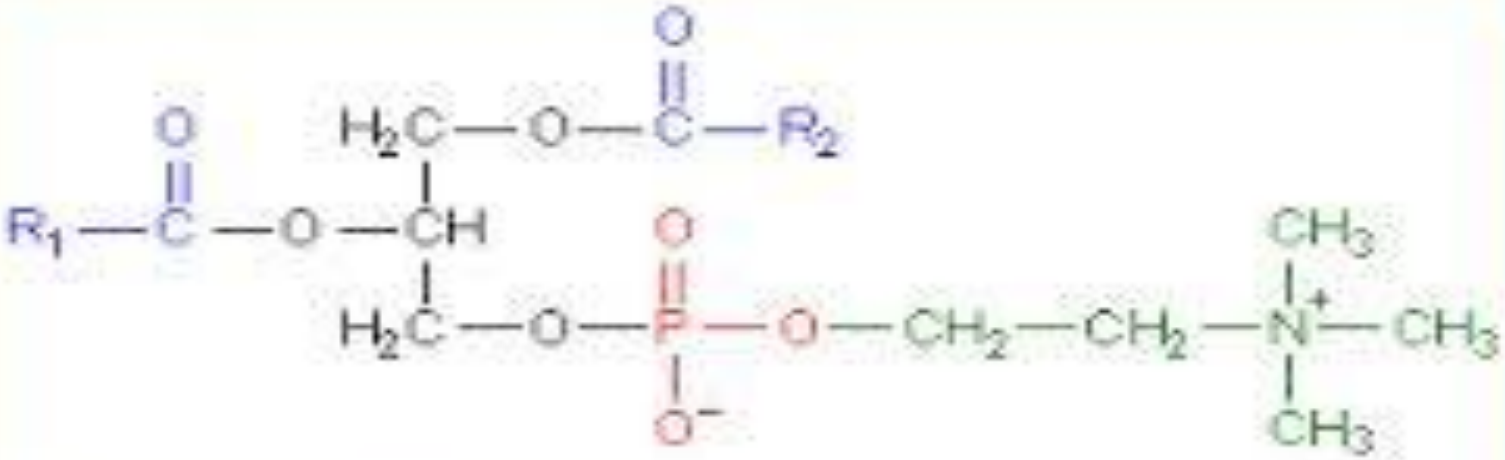
Phosphatidic Acid

PHOSPHATIDYL CHOLINE (LECITHIN)

- It is widely distributed in animals in liver, brain, nerve tissues, sperm and egg-yolk, having both metabolic and structural functions.

On hydrolysis, lecithin yields:

glycerol, fatty acids, phosphoric acid and nitrogenous base choline.

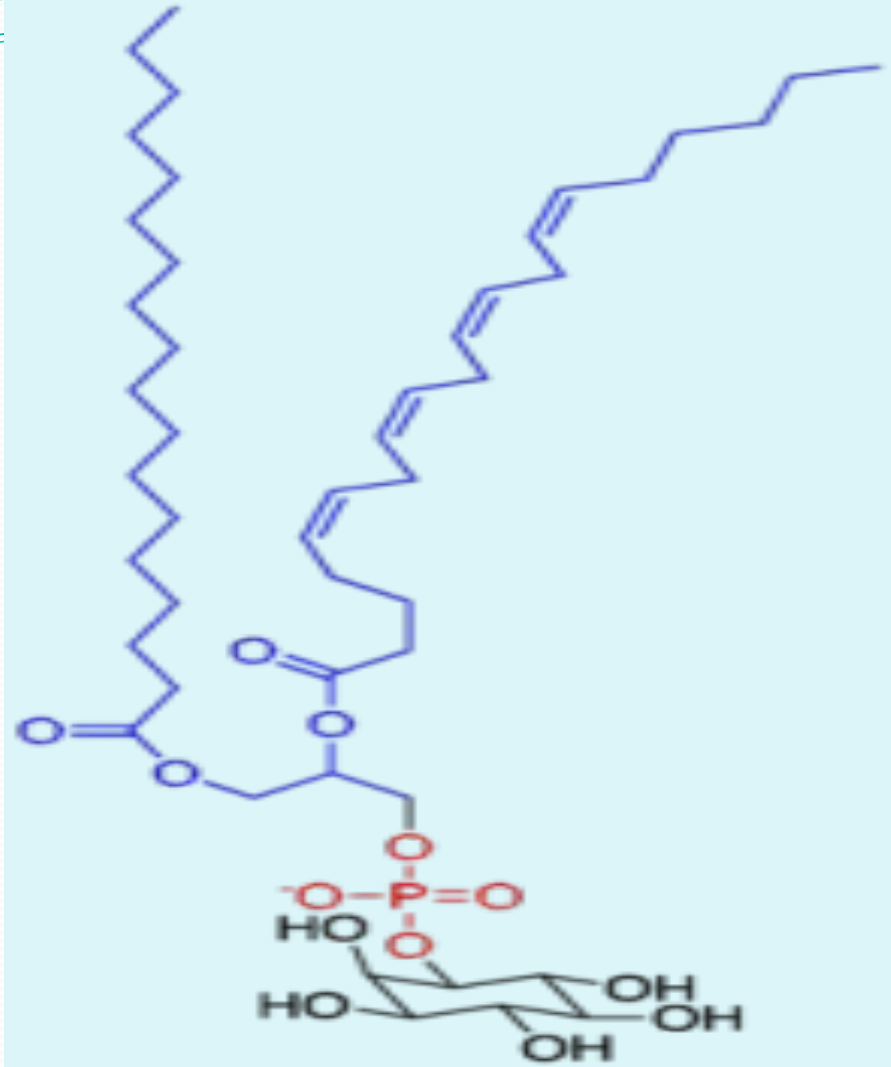


phosphatidylcholine

B: Phospho-inositides:

In this group, inositol is the alcohol,

e.g., phosphatidyl inositol (lipositol).


O
O
O
O
O
O
O
P
HO
HO
OH
OH
OH

C: **Phospho-sphingosides:**

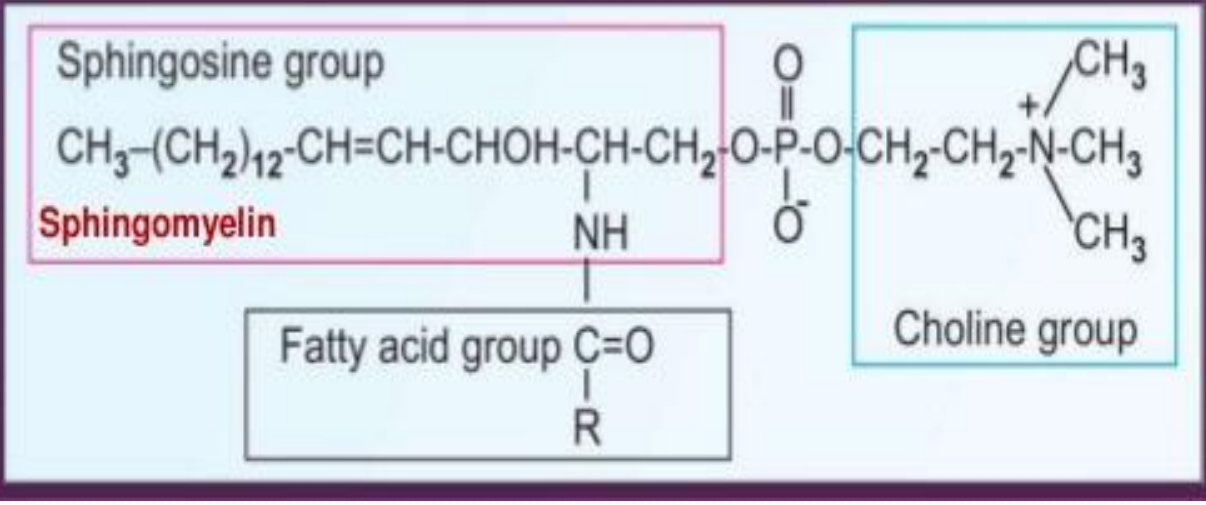
Alchohol present is sphingosine (also called as sphingol), an unsaturated amino alcohol,

e.g., sphingomyelin.

This does not contain a glycerol,instead it has an 18carbon unsaturated amino alcohol called SPHINGOSINE.its found in large amounts in brain and nervous tissues,and a very small amount in other tissues.

Phosphosphingosides

- They contain **phosphoric acid** group.
- A common phosphosphingoside present abundantly in biomembranes, especially of the nervous system, is **sphingomyelin.** It contains choline.



On hydrolysis sphingomyelin yields

One molecule of fatty acid
Phosphoric acid
Nitrogenous base ------choline
sphingosine

OTHER PHOSPHOLIPIDS OF BIOLOGICAL IMPORTANCE

Phosphatidyl Serine:

A cephalin like phospholipid contains amino acid serine in place of ethanolamine found in brain and nervous tissues and small amount in other tissues. Also found in blood.

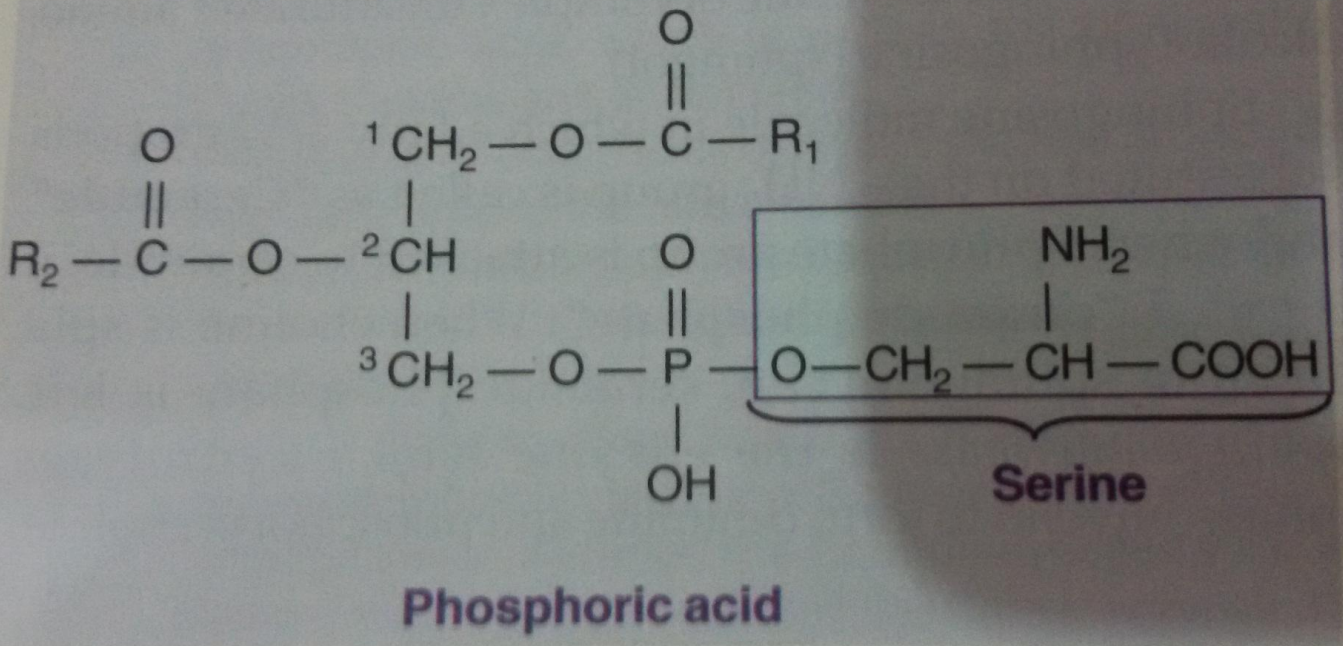


FIG. 4.14: PHOSPHATIDYL SERINE

- **Lysophosphatides:**

  These are phosphoglycerides containing only one acyl radical in α position, e.g., lysolecithin.

Plasmalogens:

- The plasmalogens make up an appreciable amount, about 10% of total phospholipids of brain and nervous tissue, muscle and mitochondria.

FIG. 4.14: PHOSPHATIDYL SERINE

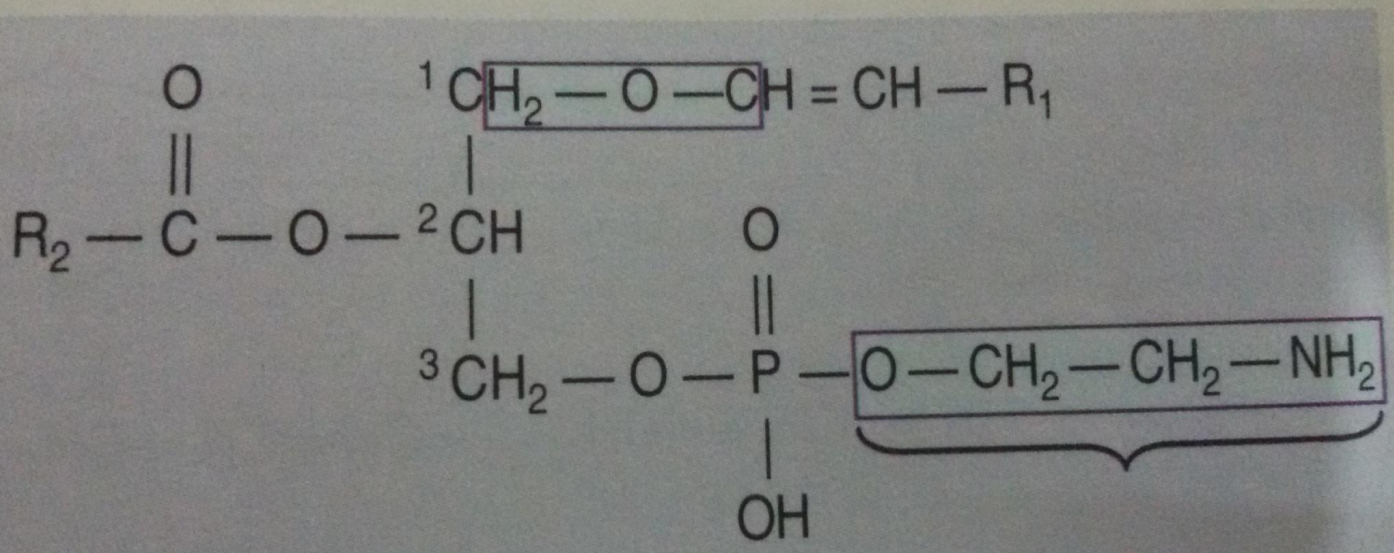


FIG. 4.15: PLASMALOGENS

- These compounds yield on hydrolysis:
- one molecule each of long chain aliphatic aldehyde,
- A fatty acid,
- glycerol ,
- PO_4 and
- A nitrogenous base which is usually ethanolamine, but may be sometimes choline.

FUNCTIONS OF PHOSPHOLIPIDS

Structural: Phospholipids participate in the lipoprotein complexes which are thought to constitute the matrix of cell walls and membranes, the myelin sheath, and of such structures as mitochondria and microsomes.

- Role in enzyme action:

  there are certain enzymes that need tightly bound phosphlipids for their actions e.g mitochondrial enzyme system involved in oxidative phosphorylation.

- Role in blood coagulation:

  phospholipids play an important role in blood coagulation process.

- Role in lipid absorption in intestine:

  during emulsification of lipid-water mixtures, lecithin lowers the surface tension of water which helps in emulsification process thus a pre-requisite in digestion and absorption of lipids from the GIT.

- Role in transport of lipids from intestine:

  exogenous TG is carried as lipoprotein complx,chylomicrons and PL play an active part in this process.

- Role in transport of lipids from liver:

  endogenous TG are carried from liver to various tissues as LP compx “Pre-β-LP (VLDL)”.PL is required for the formation of LP complx.

- Lipotropic action of lecithin:

  choline acting as lipotropic agents prevents formation of fatty liver,as lecithin can provide choline thus it acts as a lipotropic agent.

- Membrane phospholipids as source of arachadonic acid:

  PL of membrane are hydrolyzed by phospholipase A2 and provide the unsat.FA,which is utilized for synthesis of PG and leukotrienes.
- Insulation:PL of myelin sheaths provide the insulation around the nerve fibres.
- Cofactor:PL act as a cofactor for the activity of Lipo Protein lipase and Tri Glycerol lipase.

CLINICAL IMPORTANCE

1. Dipalmityl Lecithin(DPL): It acts as a surfactant and lowers the surface tension in lung alveoli. Surface activity is a phenomena by which the surface tension of the air alveolar lining interface is lowered with expiration due to presence of DPL. If DPL is absent the alveolar radius becomes smaller with expiration. The wall tension rises and the alveoli collapse. Absence of DPL in premature fetus produces collapse of lung alveoli which produces respiratory distress syndrome

2. Lecithine-Spingomyline ratio. L/S ratio in amniotic fluid has been used for the evaluation of fetal lung maturity

- If L/S ratio is >2 or > 5 indicates adequate fetal lung maturity and suggest that respiratory distress after delivery is not likely to develop
- Develivery of premature low weight fetus with L/S ratio 1 or <1 indicates that the infant will probably develop respiratory distress or hyaline membrane disease

3. Estimation of Lecithin

Estimation of Lecithin phosphorus in amniotic fluid is clinically more useful. Its value of 0.100mg/100dl indicates adequate fetal lung maturity.

2 *GLYCOLIPIDS*

Lipids containing carbohydrate mostly are called glycolipids. They contain a special alcohol called sphingosine or sphingol *in addition to fatty acids* but does **not contain** phosphoric acid or glycerol. *These are of* ***two types:***

- Cerebrosides
- Gangliosides

Cerebrosides (Glycosphingosides)

Cerebrosides occur in large amounts in the white matter of brain and in the myelin sheaths of nerve. They are not found in embryonic brain but develops as medullation progresses. In smaller amounts they appear to be very widely distributed in animal tissues

. In medullated nerves the concentration of cerebrosides are much higher than in non-medullated nerve fibres.

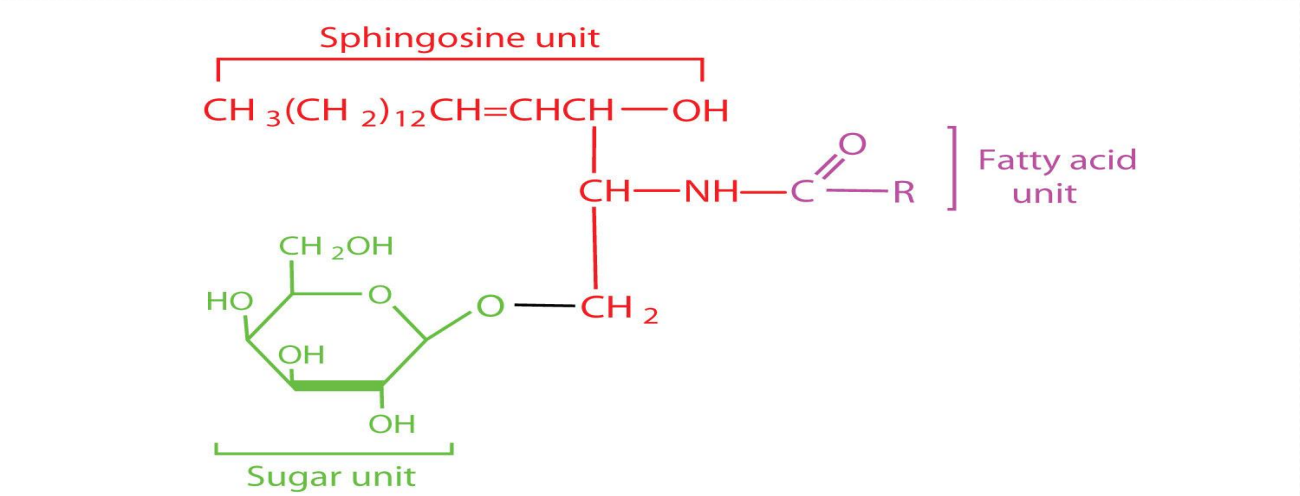
Structure: A cerebroside is considered to be built on the following:

FA of high molecular weight

Sphingosine

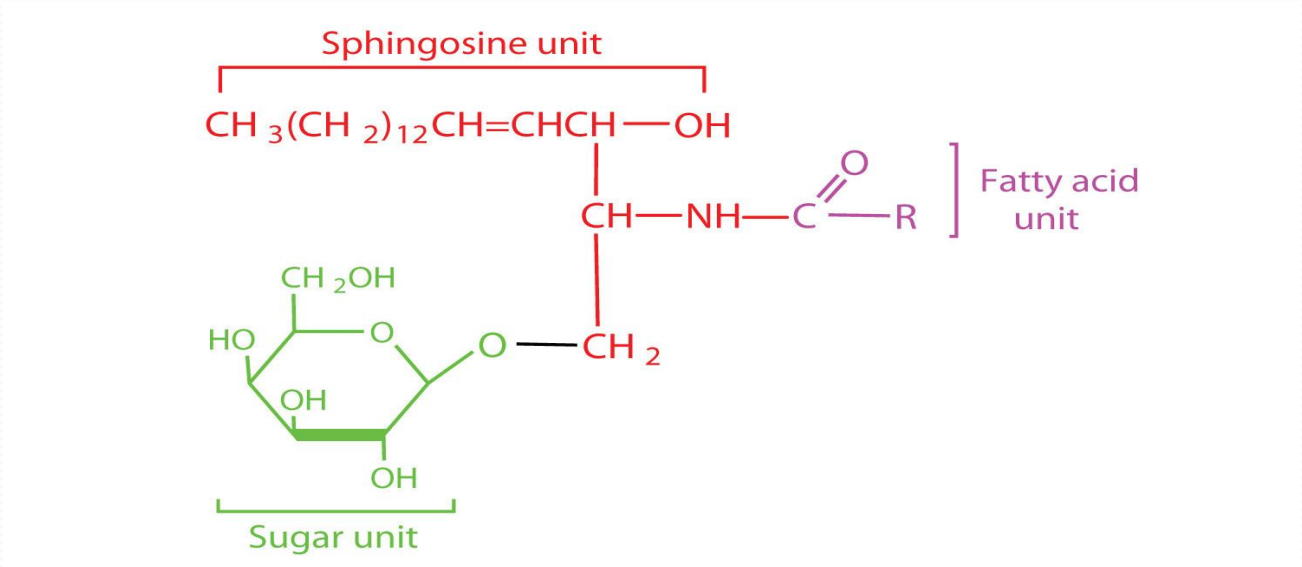
usually galactose but sometimes may be glucose.

There is no glycerol, no phosphoric acid and no nitrogenous base.



Thus, a cerebroside, on hydrolysis, yields:

- **a sugar, usually galactose, but sometimes glucose**
- **a high molecular weight fatty acid and alcohol, sphingosine or dihydrosphingosine.**



Clinical aspect

Gaucher's disease: it is an inherited disorder of cerebrosides metabolism(lipidosis)

Both adults and infants are affected.

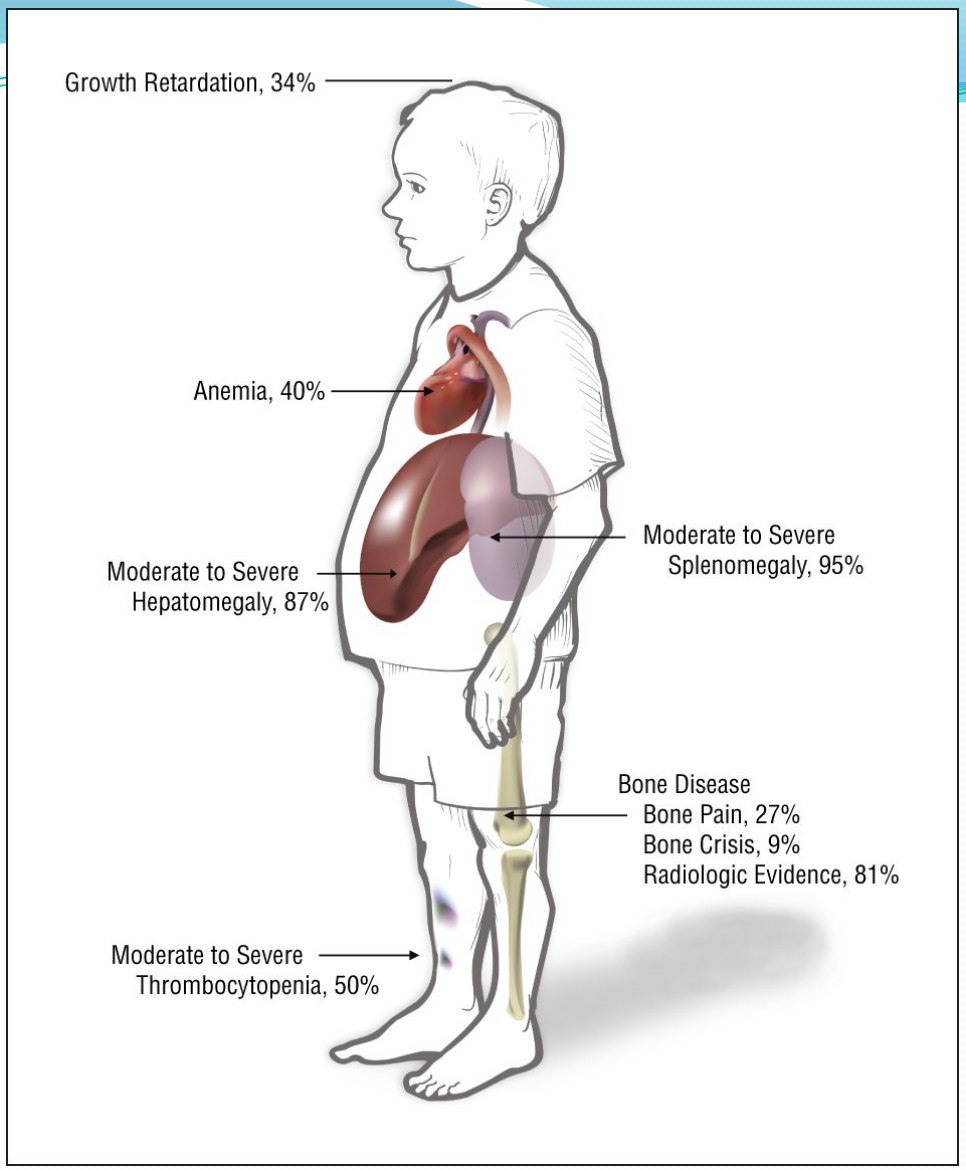
In infancy and childhood: there's acute onset with a rapid course and death in several years.

Infant will : loose wt

fail to grow

progressive mental retardation

spasticity later flaccidity


Growth Retardation, 34%
Anemia, 40%
Moderate to Severe
Hepatomegaly, 87%
Moderate to Severe
Splenomegaly, 95%
Bone Disease
Bone Pain, 27%
Bone Crisis, 9%
Radiologic Evidence, 81%
Moderate to Severe
Thrombocytopenia, 50%

2. In adult:

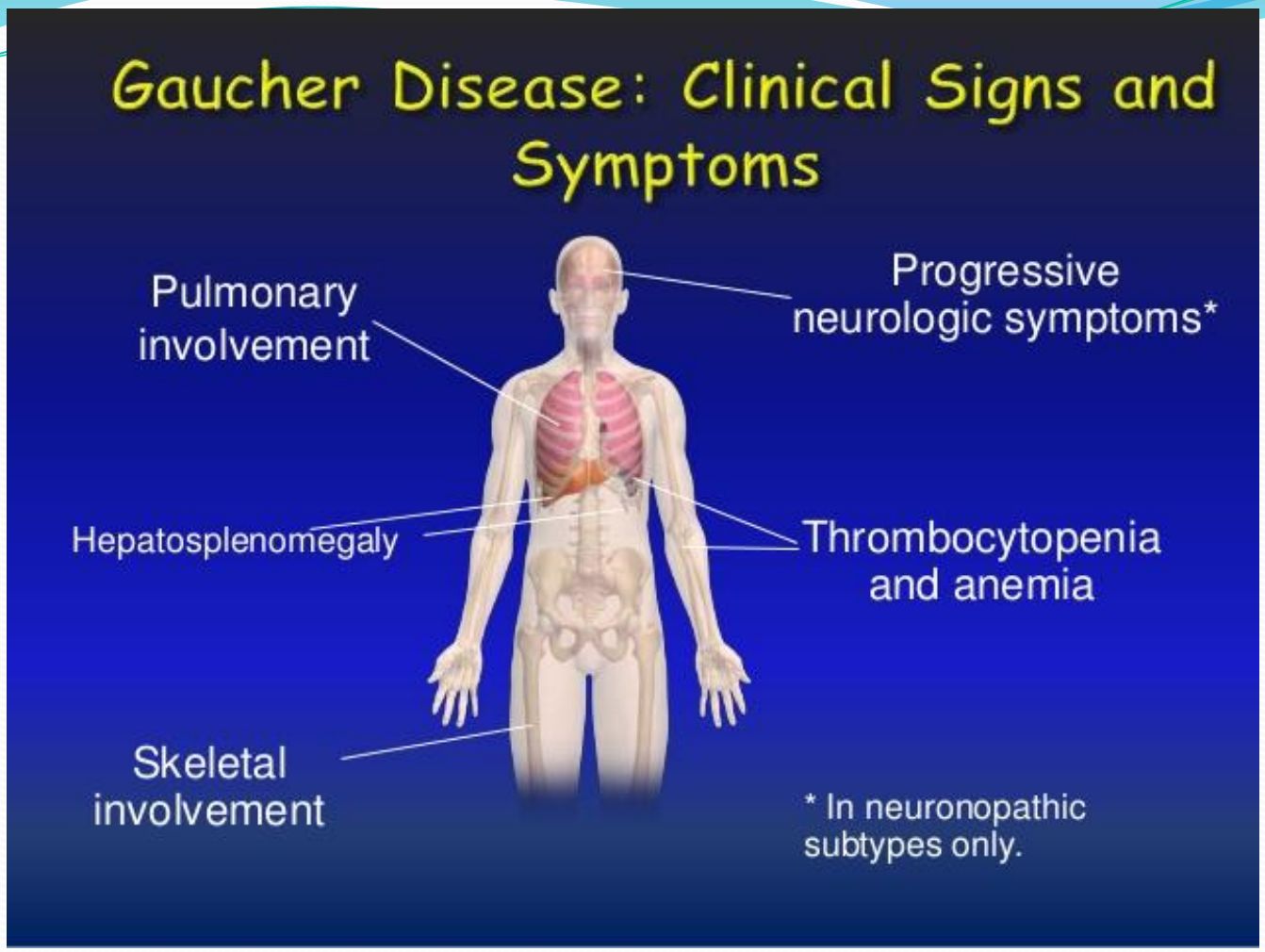
- there's progressive enlargement of spleen,may reach upto umblicus or below.
- Characteristic bone pain,due to replacement of marrow cells by histiocytes that are loaded with lipids,which will lead to:

progressive aneamia

leucopenia

thrombocytopenia

tendency to bleeding and secondary infections


Gaucher Disease: Clinical Signs and Symptoms
Pulmonary involvement
Progressive neurologic symptoms*
Hepatosplenomegaly
Thrombocytopenia and anemia
Skeletal involvement
* In neuronopathic subtypes only.

GANGLIOSIDES

The highest concentrations are found in gray matter of brain.

BIOMEDICAL IMPORTANCE

The gangliosides are mainly components of membranes,therefore,they can serve as specific membrance binding sites (receptor sites) for circulating hormones and thereby influence various biochemical processes in the cell.

CLINICAL ASPECT

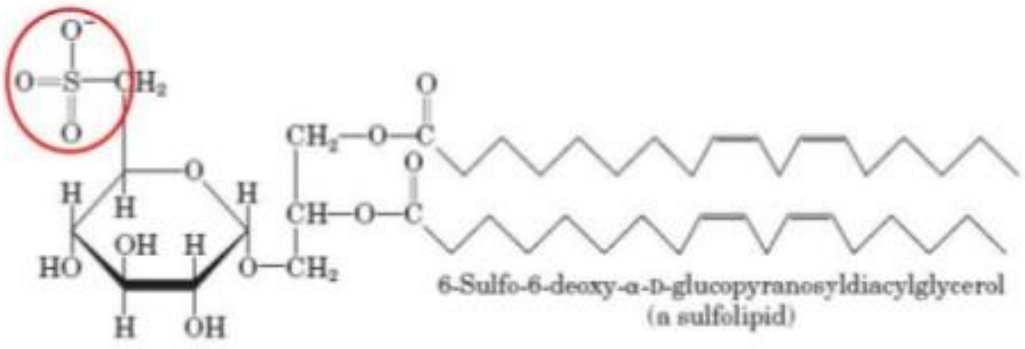
- **Tay-Sachs Disease (GM2 Gangliosidosis):**
- Accumulation of gangliosides in brain and nervous tissues takes place.
- It is a rare inherited disorder,in infants there's progressive development of idiocy and blindness soon after birth.
- .

There maybe seizures and association of macrocephaly.
Prognosis is bad and death usually follows

3 SULPHOLIPIDS

- They are sulphate esters of glycolipids.Lipids material containing sulphur are present in various tissues,found in kidney,liver,brain and certain tumors.it is abundant in white matter of brain.

Sulfolipids

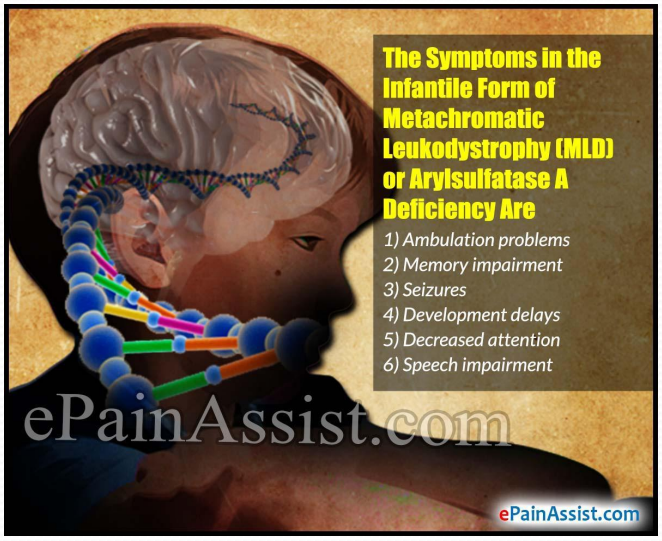


Sulfolipids have a sulfonated glucose residue joined to a diacylglycerol in glycosidic linkage. They also exist predominantly in chloroplast

CLINICAL ASPECT

- Metachromatic leukodystrophy:MLD it is an inherited disorder,in which sulphatide gets accumulated in various tissues.
- It is of 2 types:

1. Late infantile type:manifests usually before 3yrs. There is :



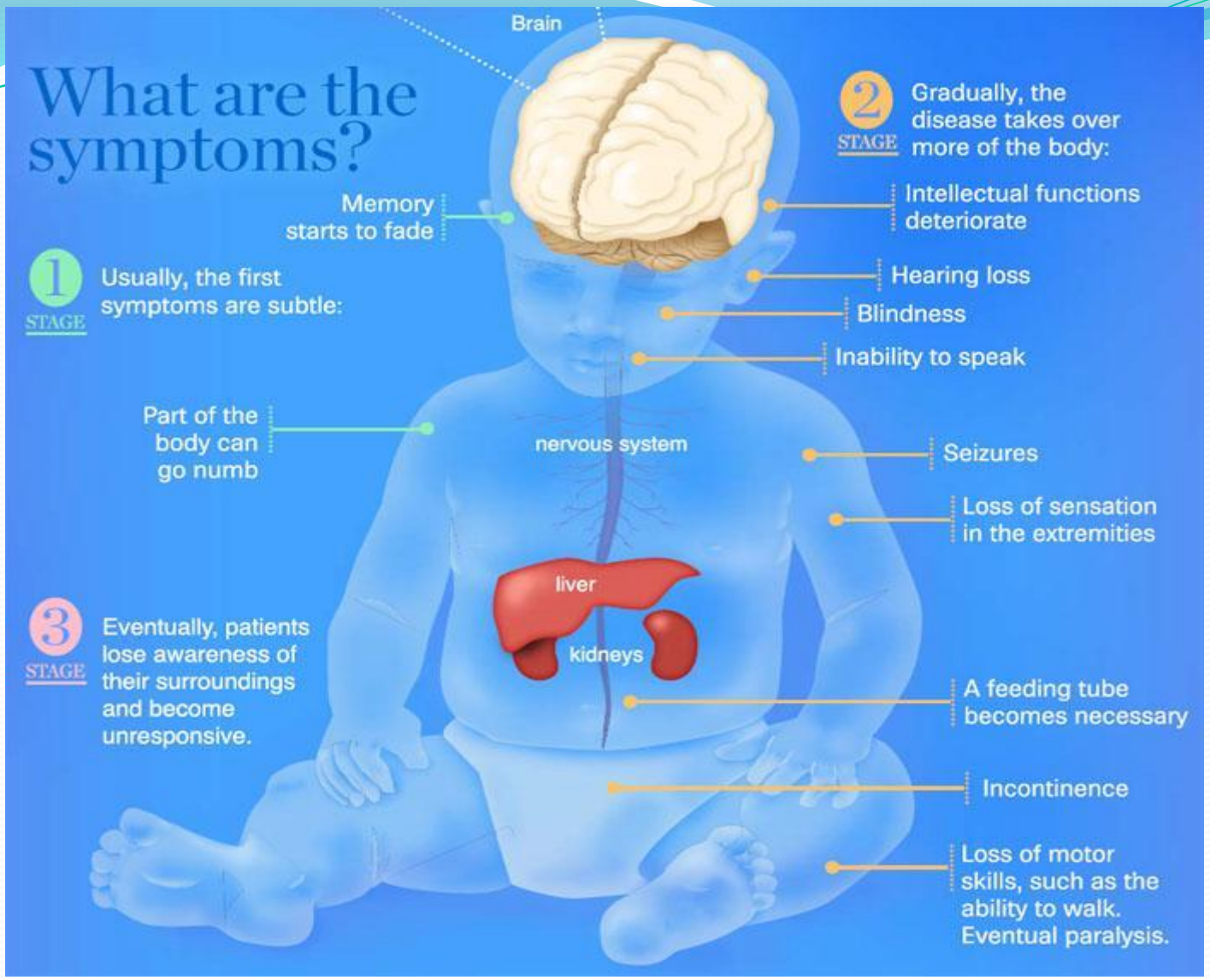
weakness

ataxia

hypotonus & paralysis

difficulty in speech

optic atrophy


What are the symptoms?
Brain
1 STAGE
Usually, the first symptoms are subtle:
Memory starts to fade
Part of the body can go numb
2 STAGE
Gradually, the disease takes over more of the body:
Intellectual functions deteriorate
Hearing loss
Blindness
Inability to speak
nervous system
Seizures
Loss of sensation in the extremities
liver
kidneys
3 STAGE
Eventually, patients lose awareness of their surroundings and become unresponsive.
A feeding tube becomes necessary
Incontinence
Loss of motor skills, such as the ability to walk. Eventual paralysis.

2 Adult type:initially there are psychiatric manifestations and later there is progressive dementia.

LIPOPROTEINS

THEIR CHEMISTRY AND ASSOCIATED DISEASES

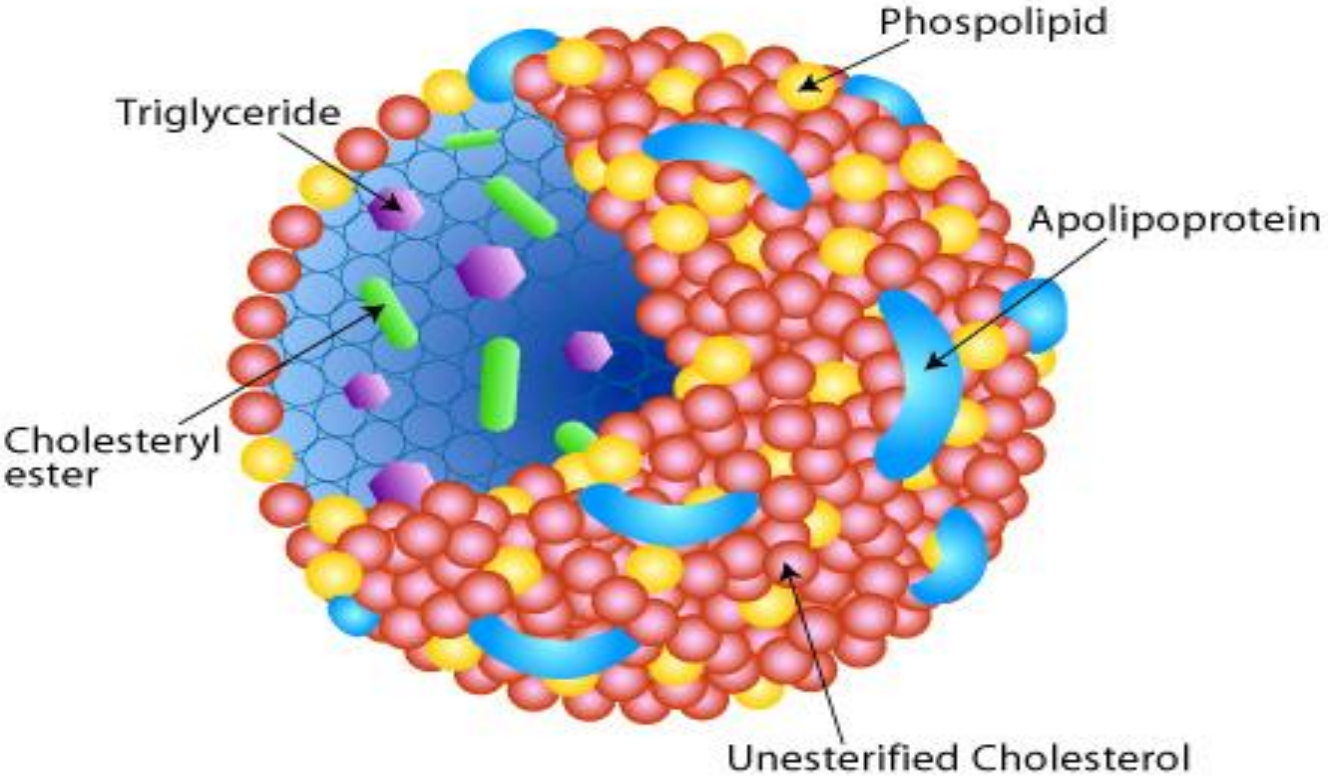
Lipoproteins- Introduction

- 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.

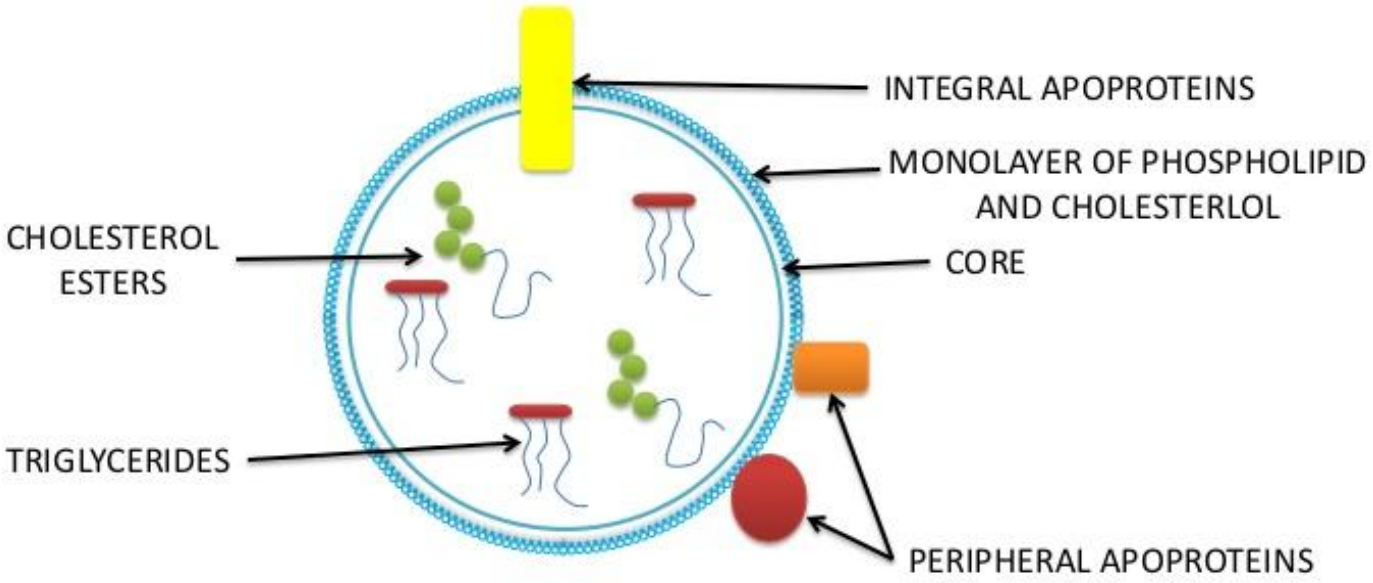
General Structure of Lipo proteins

- Lipoproteins consist of a nonpolar core and a single surface layer of amphipathic lipids
- The **nonpolar lipid core** consists of mainly **triacylglycerol** and **cholesteryl ester** and is surrounded by a **single surface layer** of **amphipathic phospholipid** and **cholesterol** molecules
- These are oriented so that their polar groups face outward to the aqueous medium.
- The protein moiety of a lipoprotein is known as an **apolipoprotein** or **apoprotein.**

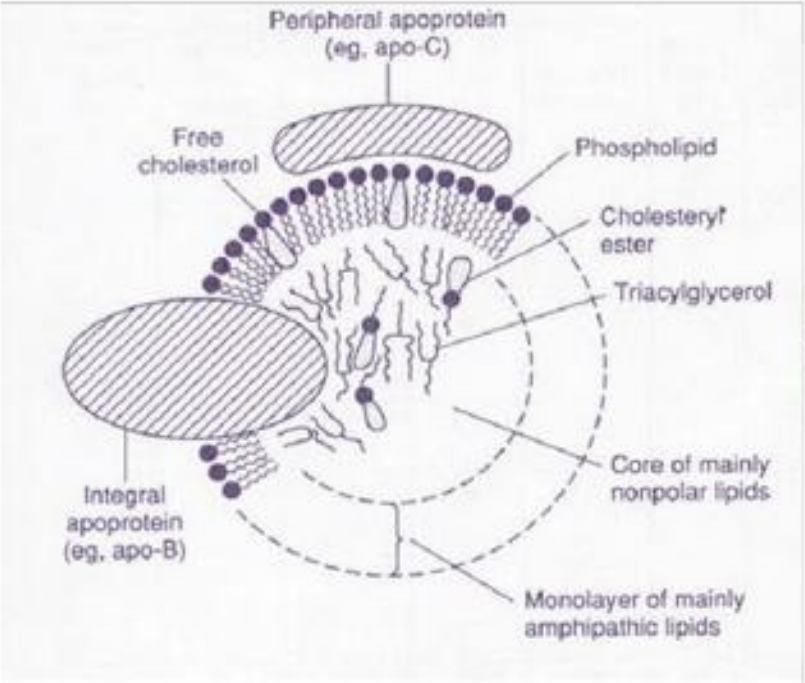
Lipoprotein Structure

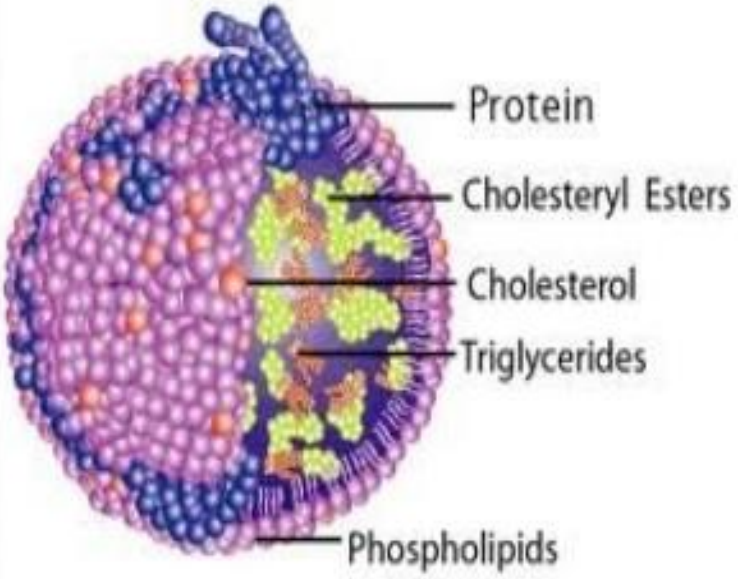


Structure of lipoprotein



General Structure of Lipo proteins



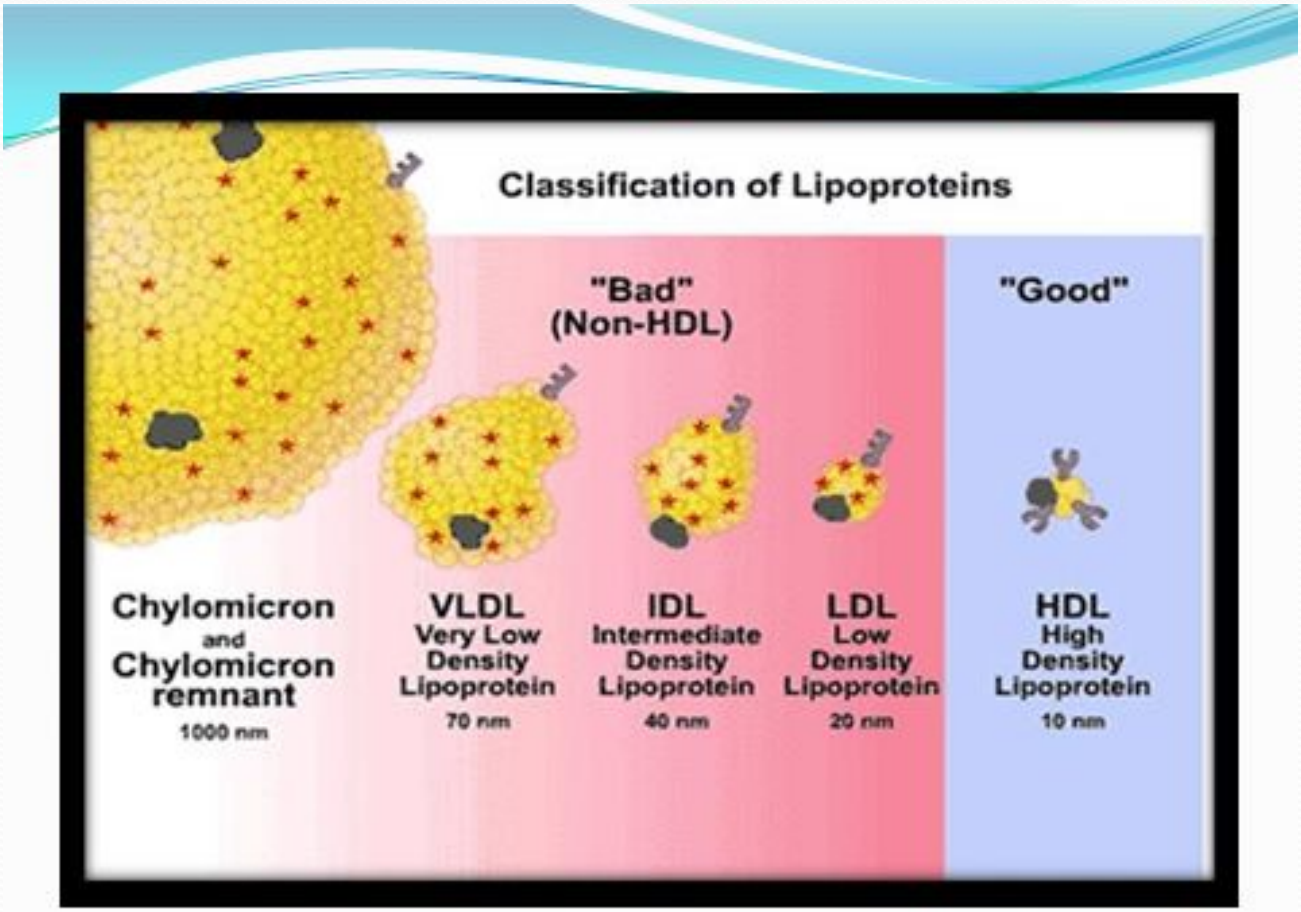


Some apolipoproteins are integral and cannot be removed, whereas others can be freely transferred to other lipoproteins.

CLASSIFICATION

- Three major classifications of Lipoproteins that are based depending on
- Density
- Electrophoretic mobility
- Nature of Apo-protein content

1. Based on Density :



Chylomicrons

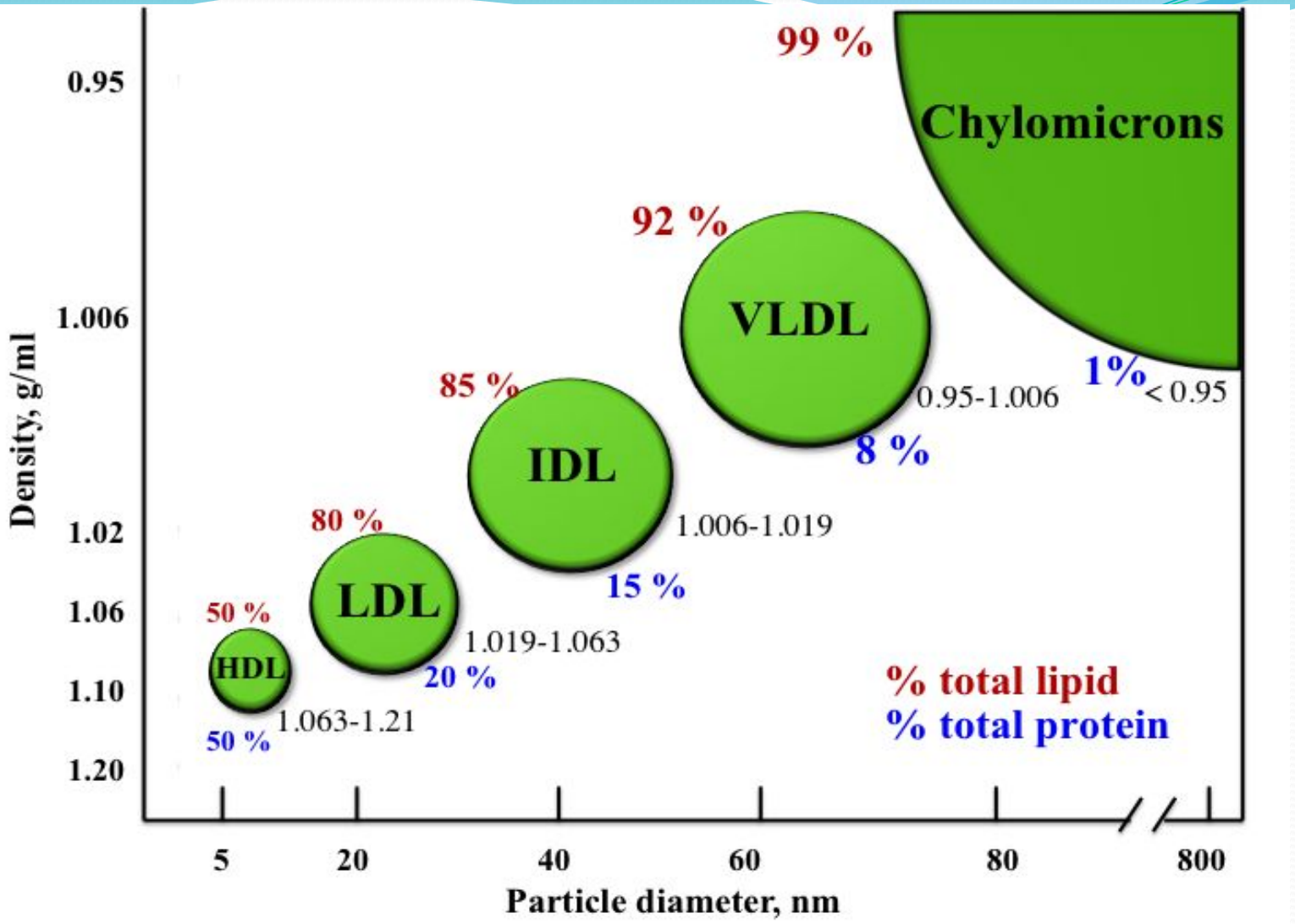
- Derived from intestinal absorption of triacyl gycerol and other lipids

- Very Low Density Lipoproteins (VLDL) :
- Derived from the liver for transport of triacylglycerol.

- Intermediate Density Lipoproteins (IDL) :
- These are derived from catabolism of VLDL.Their density range between VLDL and LDL

- Low Density Lipoproteins (LDL) :
- These represent the final stage of catabolism of VLDL.

- High Density Lipoproteins (HDL):
- Involved in transport of cholesterol and also metabolism of chylomicrons & VLDL .


99 %
Chylomicrons
92 %
VLDL
0.95-1.006
8 %
1%
< 0.95
85 %
IDL
1.006-1.019
15 %
80 %
LDL
1.019-1.063
20 %
50 %
HDL
1.063-1.21
50 %
% total lipid
% total protein
Density, g/ml
0.95
1.006
1.02
1.06
1.10
1.20
5
20
40
60
80
800
Particle diameter, nm

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

2) Based on electrophoretic mobilities (contd.)

- 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.
- Chylomicons 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, Chylomicons, and chylomicron remnants.

Functions of Apo proteins

(1) They can form part of the structure of the lipoprotein, e.g. apo B, structural component of VLDL and Chylomicons

(2) They are enzyme cofactors, e.g. C-II for lipoprotein lipase, A-I for lecithin: cholesterol acyl transferase (LCAT), or enzyme inhibitors, eg, apo A-II and apo C-III for lipoprotein lipase, apo C-I for cholesteryl ester transfer protein

(3) They act as ligands for interaction with lipoprotein receptors in tissues, e.g. apo B-100 and apo E for the LDL receptor, apo A-I for the HDL receptor.

Lipoproteins

Lipoprotein	Apoproteins	Function
Chylomicron	apoB-48, apoC, apoE	Transport TGs form intestine to liver/ other tissues
VLDL	apoB-100, apoC, apoE	Transport TGs from liver to adipose/ muscles.
IDL	apoB-48, apoC, apoE	Intermediary between VLDL and LDL
LDL	apoB-48	Transport cholesterol to peripheral tissues.
HDL	apoA, apoC, apoE, apoD	•Absorb cholesterol form peripheral tissues and transport it to liver •Reservoir for exchange of lipoproteins in VLDL and Chylomicron metabolism

Nomenclature of lipoproteins

	Diameter nm	Protein %	Triglycerides %	Cholesterol esters %
Chylomicron	75-1200	1	88	3
VLDL	30-80	10	56	15
IDL	25-30	10	29	34
LDL	18-25	~20	13	48
HDL	5-12	~50	13	30

Albumin Fatty acid complex

Primary Disorders of Plasma Lipoproteins (Dyslipoproteinemias)

- 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.
- All of the primary conditions are due to a defect at a stage in lipoprotein formation, transport, or degradation.

Primary Disorders of Plasma Lipoproteins (Dyslipoproteinemias)

Name	Defect	Characteristics
Hypolipoproteinemias		
Abetalipoproteinemia	No chylomicrons, VLDL, or LDL are formed because of defect in the loading of apo B with lipid.	Rare; blood acylglycerols low; intestine and liver accumulate acylglycerols. Intestinal malabsorption.
Familial alpha-lipoprotein deficiency Tangier disease Fish-eye disease Apo-A-I deficiencies	All have low or near absence of HDL.	Hypertriacylglycerolemia due to absence of apo C-II, Low LDL levels. Atherosclerosis in the elderly.

Primary Disorders of Plasma Lipoproteins (Dyslipoproteinemias)

Name	Defect	Characteristics
Hyperlipoproteinemia		
Familial lipoprotein lipase deficiency (type I)	Hypertriacylglycerolemia due to deficiency of LPL, abnormal LPL, or apo C-II deficiency causing inactive LPL.	Slow clearance of chylomicrons and VLDL. Low levels of LDL and HDL. No increased risk of coronary disease.
Familial hypercholesterolemia (type II a)	Defective LDL receptors or mutation in ligand region of apo B-100.	Elevated LDL levels and hypercholesterolemia, resulting in atherosclerosis and coronary disease.

Primary Disorders of Plasma Lipoproteins (Dyslipoproteinemias)- contd.

Name	Defect	Characteristics
Familial type III hyperlipoproteinemia (broad beta disease, remnant removal disease, familial dysbetalipoproteinemia)	Deficiency in remnant clearance by the liver is due to abnormality in apo E.	Increase in chylomicron and VLDL remnants , Causes hypercholesterolemia, xanthomas, and atherosclerosis.
Familial Hypertriacylglycerolemia (type IV)	Overproduction of VLDL often associated with glucose intolerance and hyperinsulinemia.	High cholesterol, VLDL, Subnormal LDL and HDL. Associated with Alcoholism, diabetes mellitus and obesity.
Hepatic lipase deficiency	Deficiency of the enzyme leads to accumulation of large triacylglycerol-rich HDL and VLDL remnants	Patients have xanthomas and coronary heart disease.


thank
you