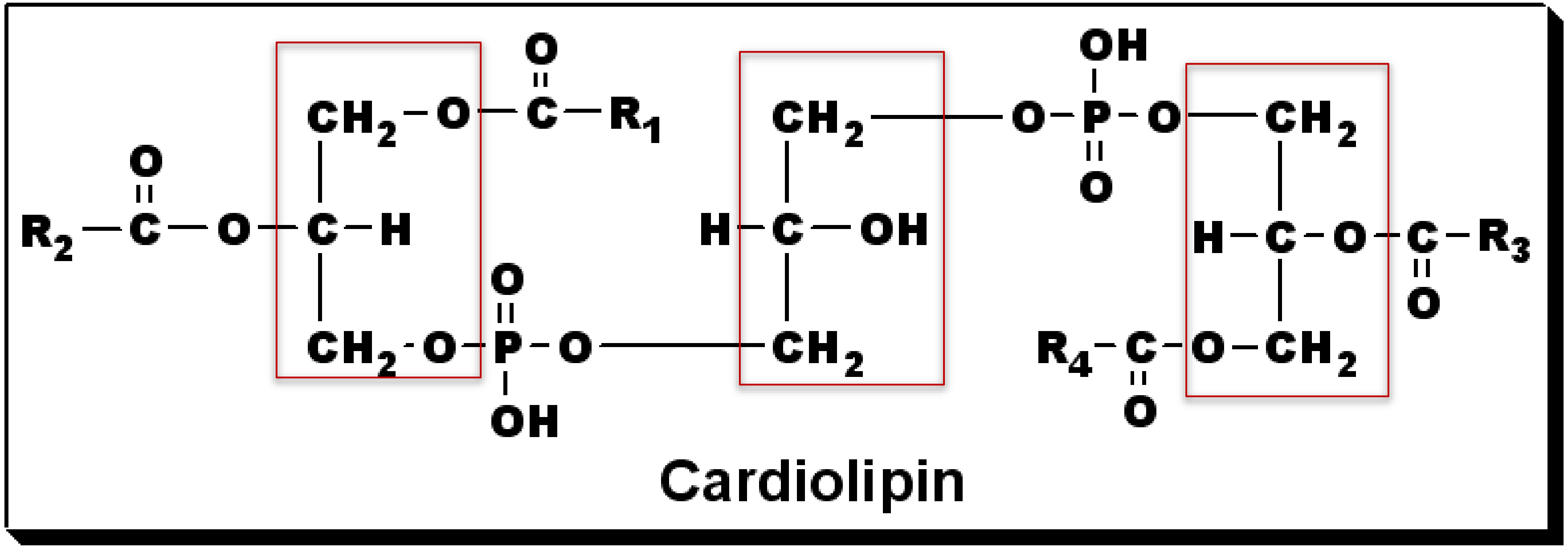
Glycerophospholipids - Cardiolipins

- Diphosphatidyl-glycerol
- Found in the inner membrane of mitochondria
- Initially isolated from heart muscle (cardio)
- Structure: 3 molecules of glycerol, 4 fatty acids & 2 phosphate groups

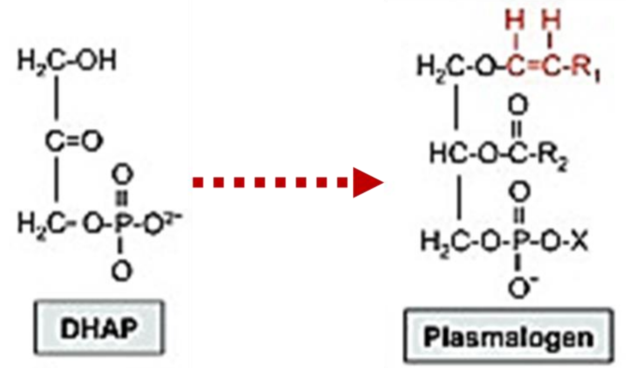


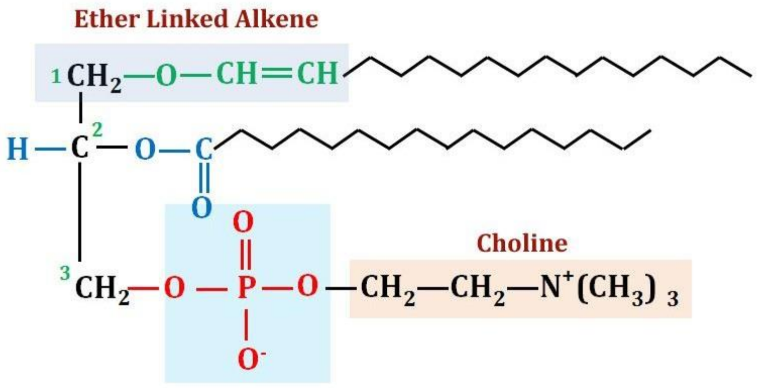
Further explanation regarding the previous slide:

This type is a large and complicated type of glycerophospholipids. § The Structure is → 3 molecules of glycerol ,4 fatty acids & 2 phosphate groups. § It seems like that you get two glycerophospholipids and join them together via a glycerol molecule . § The two terminal glycerol molecules form the backbone of the cardiolipins and the two phosphate groups from the both are attached with the first and third carbon of the third middle glycerol molecule.

Plasmalogens

- They are found in the cell membrane phospholipids fraction of brain & muscle, liver, and semen.
- They have a protective role against reactive oxygen species
- Structure:
  - Precursor: Dihydroxyacetone phosphate
  - Unsaturated fatty alcohol at C1 connected by ether bond
  - In mammals: at C3; phosphate + ethanolamine or choline
- Major classes of plasmalogens
  - Ethanolamine plasmalogen (myelin-nervous tissues)
  - Choline plasmalogen (cardiac tissue)
    - Platelet activating factor
  - Serine plasmalogens





Plasmalogen

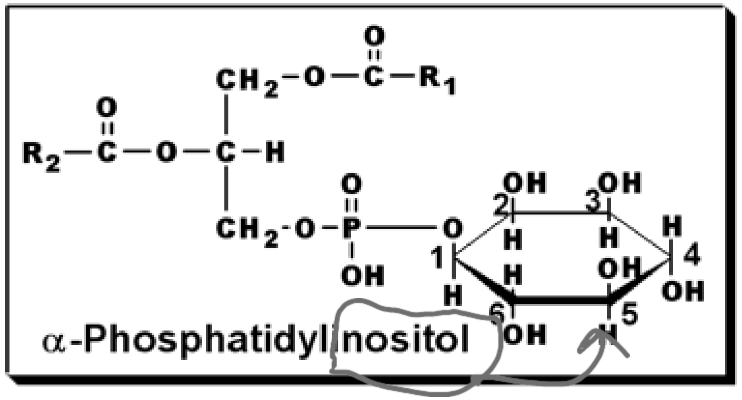
Further explanation regarding the previous slide:

•Look deeply to the structure in the photo, you have a glycerol molecule, at the first carbon we have a carbon chain, but it is not a fatty acid, we have a single oxygen with one double bond (it is a fatty alcohol connected by ether bond), while the second carbon chain has two oxygens, means that we have fatty acid (carboxylic group), and it is considered as ester bond. § On the third carbon we have a phosphate group connected to - for example- choline group and therefore we consider it as glycerophospholipid.

They have a protective role against reactive oxygen species (A highly active oxygen with an electron that reacts with the body's molecule and has harmful effects like cancers, we need to get rid of them).

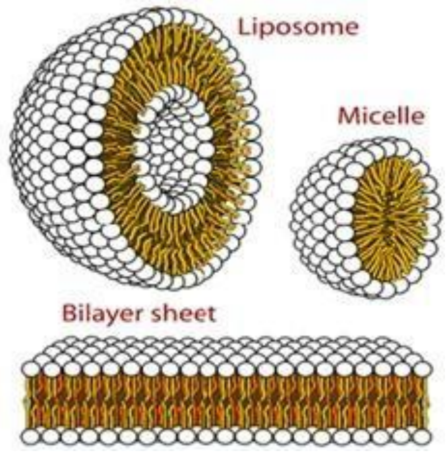
Glycerophospholipids - Inositides

- Phosphatidyl inositol
- Nitrogenous base: cyclic sugar alcohol (inositol)
- Structure: glycerol, saturated FA on carbon 1, unsaturated FA on carbon 2 usually arachidonic acid, ester groups, phosphoric acid, & inositol
- Source: Brain tissues



- Functions:
    - Major component of cell membrane
    - Second messenger during signal transduction
    - On hydrolysis by phospholipase C, phosphatidyl-inositol-4,5-diphosphate produces diacyl-glycerol (DAG) & inositol-triphosphate (IP3); which liberates calcium

The different structures of phospholipids



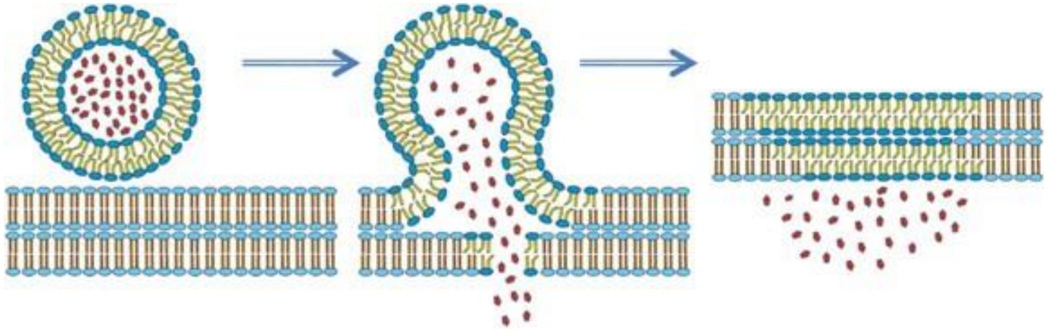
Amphipathic molecules are dynamic and they have different ways to move(1- lateral movement within the same leaflet , 2- rotation around itself, 3- flipflop (very rare because there are hydrophilic part will enter within hydrophobic region to be flopped so the energy requirement is too high)

How do these glycerol phospholipids (as a major components of the cell membranes) form the structure of the cell membrane?

As you all know in the membrane we have a bilayer of phospholipids and sphingolipids (keep in your mind that phospholipids are more abundant) because they have the hydrophobic tail region and the hydrophilic region (or the polar heads), they can't exist as one layer because the aqueous environment is surrounding them from all sides; from the inside (cytosolic side) and from the outside (ECM side); so they have to get these two layers in opposite direction so they would get the hydrophobic regions away from the aqueous environment, this way the cytosol can face the polar heads of the phospholipids and the ECM and interstitial fluid of the cell membrane will face the polar heads, so this structure cannot stay as a bilayer sheet because the ends from the sides will get exposed to the aqueous environment and this is unstable so they have to form a more stable structure which is a ball-like structure that's made of the bilayer the inside is hydrophilic and the outside is hydrophilic as well and this structure is called liposome and it is very similar to what happens in the cell membranes but different than micelles because the micelle is just made of one layer of amphipathic molecules with the core being hydrophobic and the exterior (outside) surface being polar.

Focus here that the micelle on the inside is hydrophobic, but the liposome on the inside is hydrophilic. Look at the picture and focus

Uses of liposomes: delivery

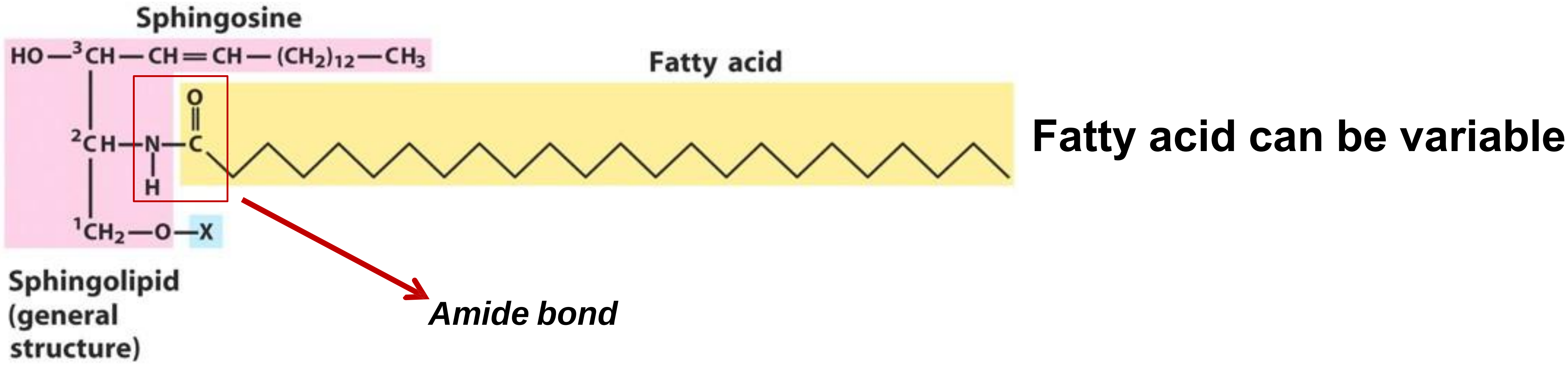


The importance of liposomes other than organizing cell membranes is that it can be used to deliver a drug. How does that work ?

So for example, you can load your drug inside a liposome and insert in between these phospholipids some protein types that specifically bind to a receptor or a molecule on your target cell which allows fusion of the liposomal bilayer leaflet (phospholipids that make the structure of liposome) and the cell membrane of the targeted cell (the cell you want to deliver the drug to) and then liposomes release the content inside it (drug) into the target cell.

Sphingolipids

- Sphingolipids are found in the plasma membranes(but less than phospholipid) of all eukaryotic cells and is highest in the cells of the central nervous system
- The core of sphingolipids is the long-chain amino alcohol, sphingosine



Further explanation regarding the previous slide:

•Glycerophospholipid consist from glycerol and f.A and phosphate and it is predominant lipids in plasma membrane.

Sphingolipid can be contribute in plasma membrane but less than phospholipid

Sphingosine is an 18 carbon molecule and on the first carbon there is an OH group which interacts with an X group to make different types of sphingolipids, the second carbon is connected to an amino group that interacts with the carboxyl group of a fatty acid making the second tail of the molecule (amide linkage), the rest of the molecule is a long hydrophobic chain that makes up the second tail of the sphingolipids.

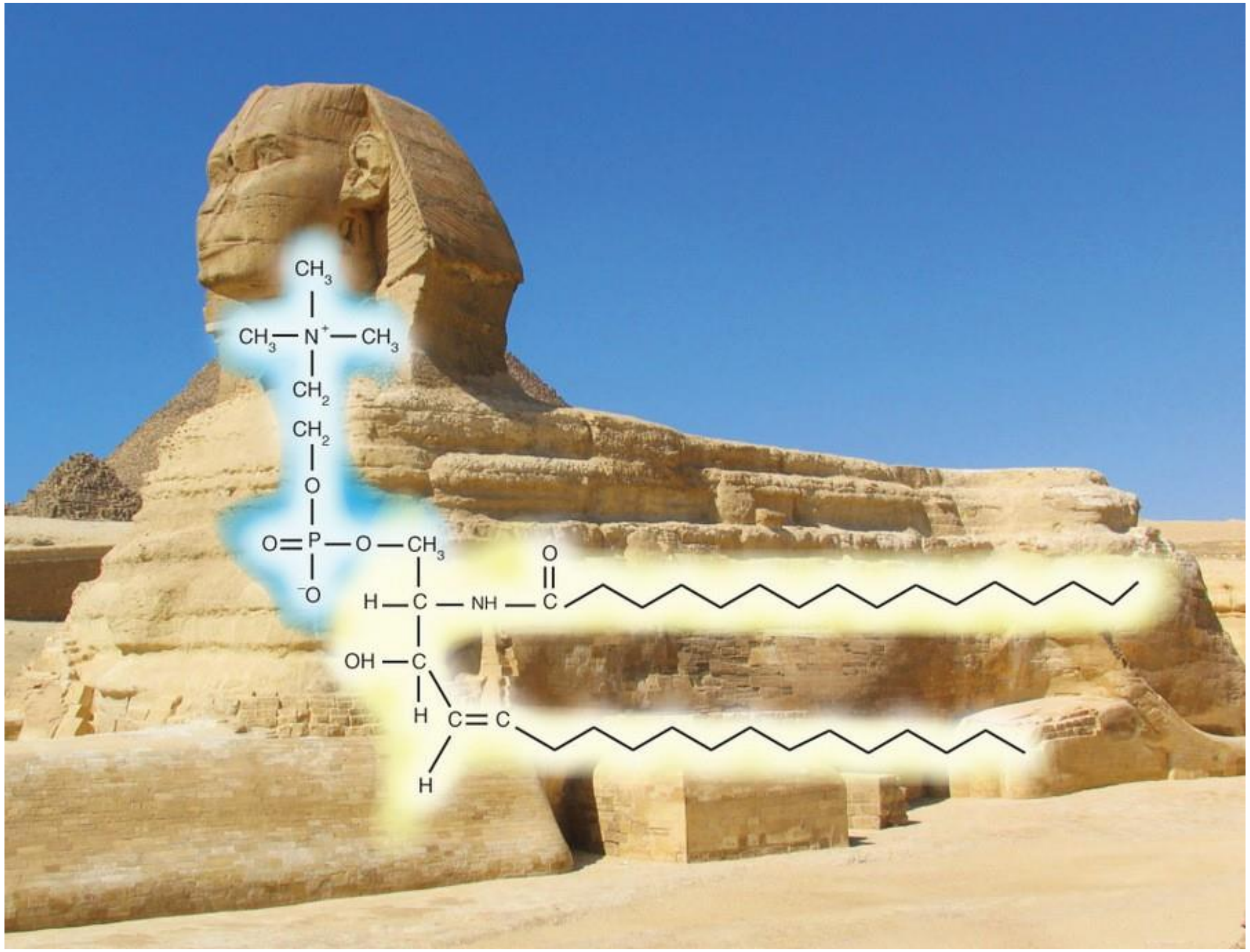
The presence of Nitrogen on carbon no.2 indicates that it is sphingosine

Mysterious lipids

Sphynx → *sphingolipids*

Trivia

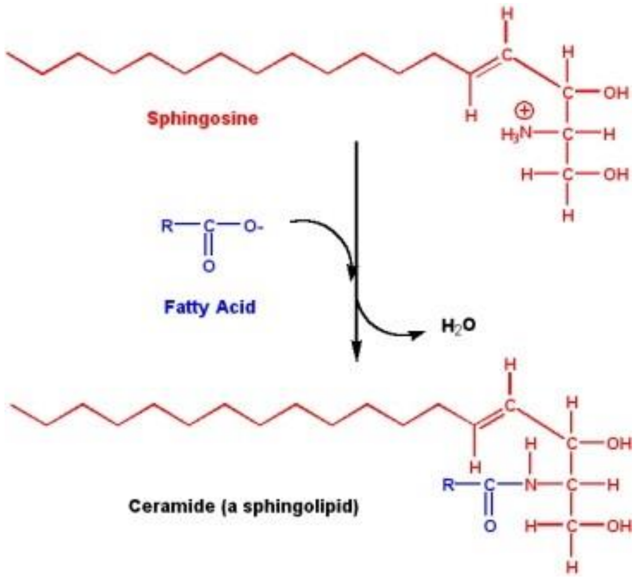
Named for the Sphinx of Thebes, who killed passersby that could not solve her riddles



Ceramide

The simplest sphingolipid

The father of sphingolipids is called ceramide whereas the father molecule of glycerol phospholipids is the phosphatidic acid with the simplest head group (hydrogen) attach ed to the phosphate group

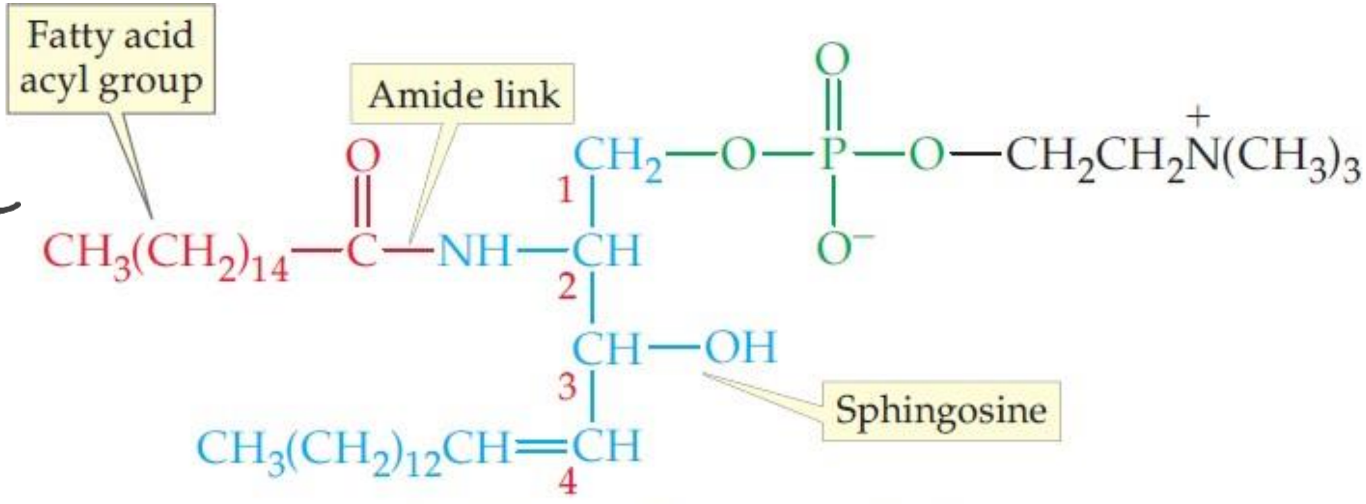


A molecule of sphingosine with one fatty acid to it and still we didn't attach anything to the head group, this is considered as a ceramide (it's a type of sphingolipids, it's the simplest sphingolipids

Types of sphingolipids

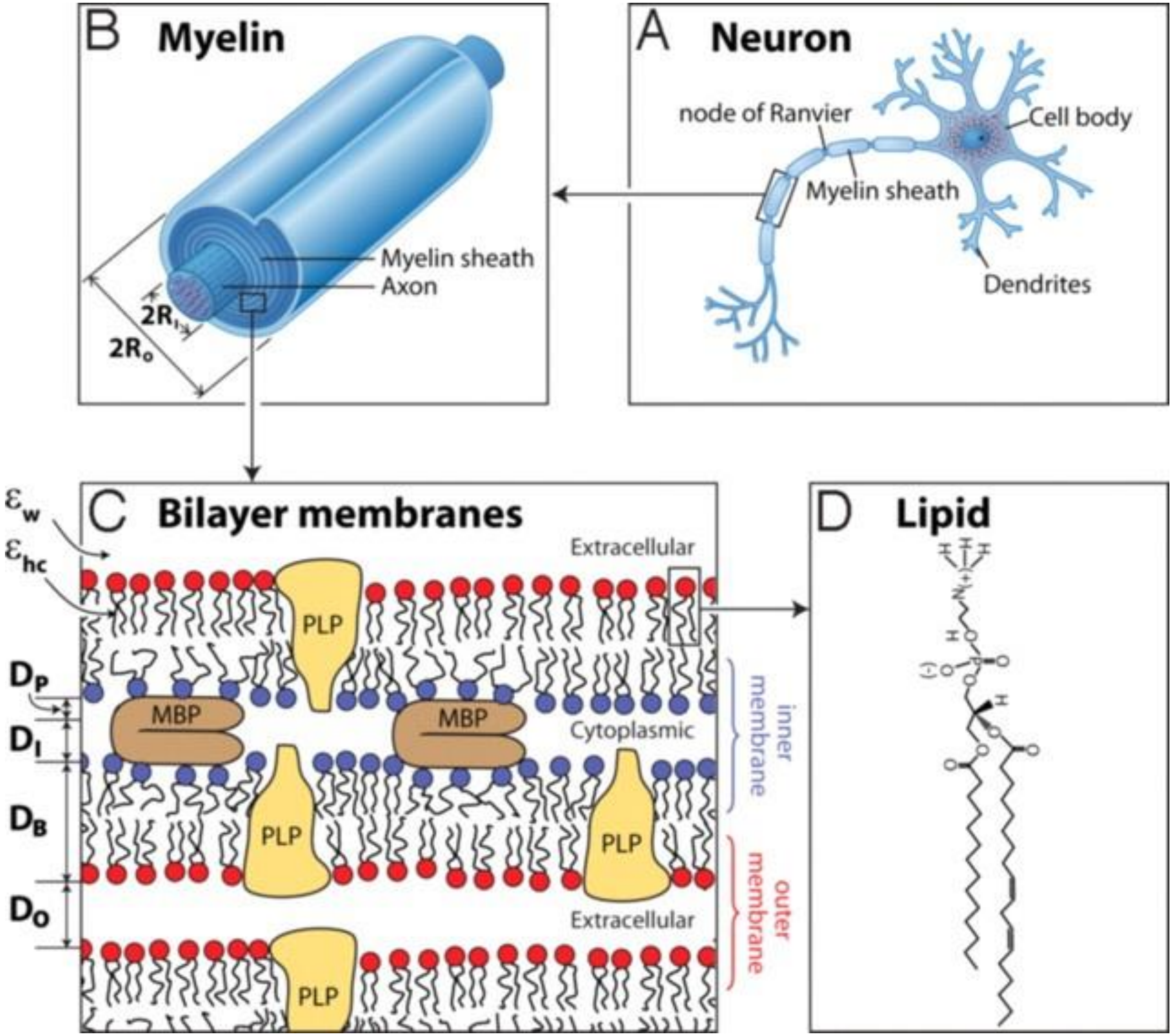
- The sphingolipids are divided into two subcategories:
  - Sphingomyelin (Consider as phospholipid)
    - It is a sphingolipid that is a major component of the coating around nerve fibers.
    - The group attached to C1 is a phosphocholine
  - Glycosphingolipid (or glycolipids)

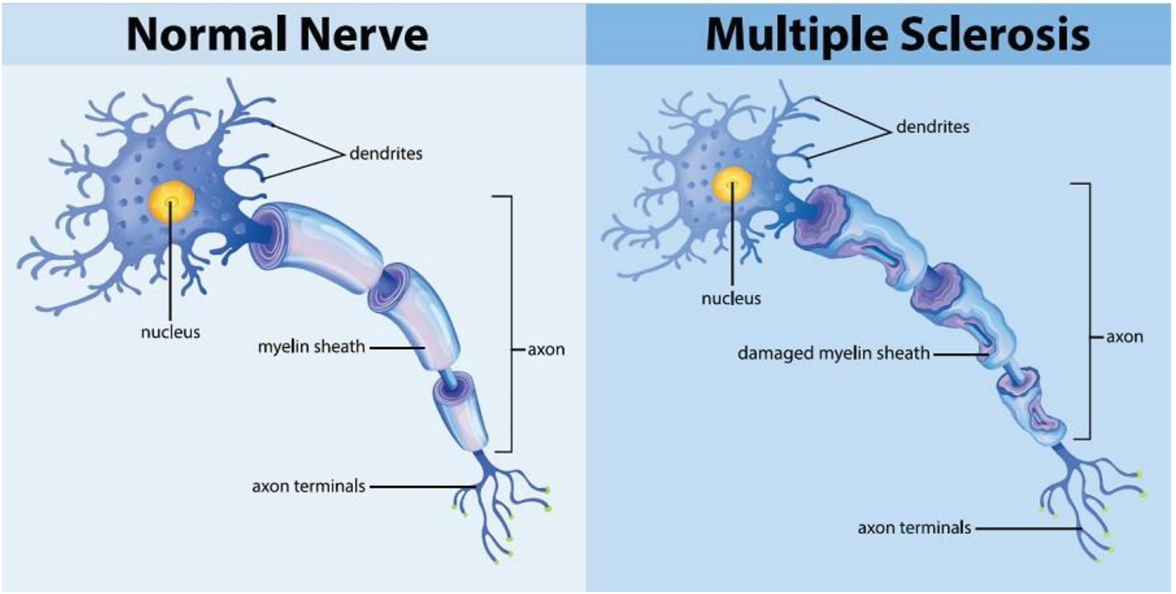
The first carbon is attached to phosphate and choline.
The second carbon which has the amino group is connected to the fatty acid.



A sphingomyelin (a sphingolipid)

Zooming into the myelin





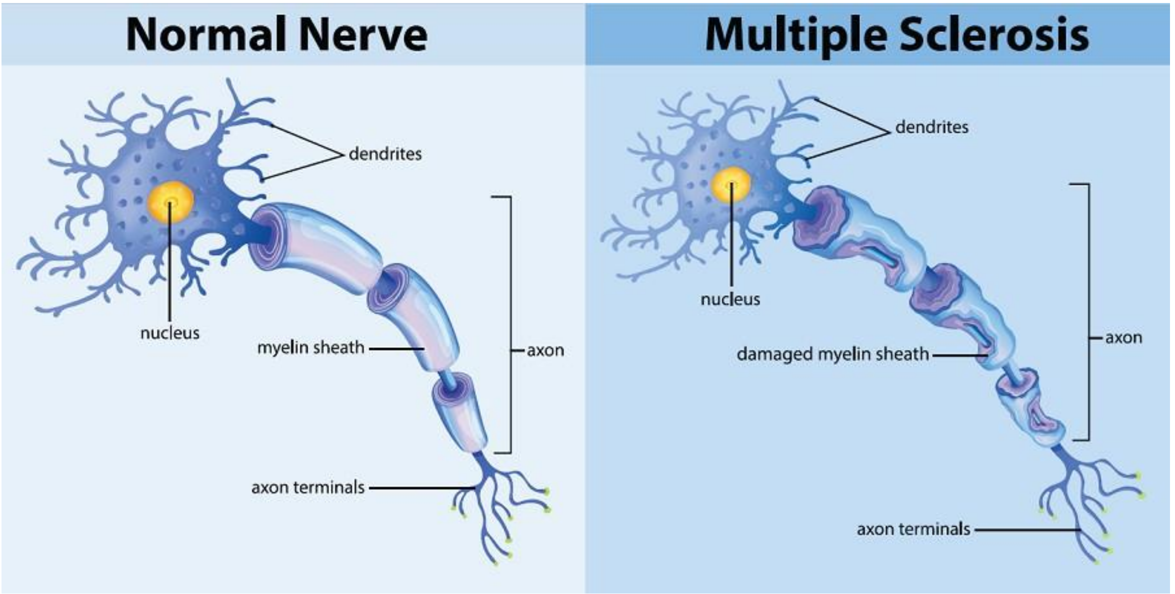
- Sphingomyelin is very abundant in myelin sheath and myelin sheath is a layer that is mostly made of sphingomyelin together with proteins and other molecules but the major component of it is Sphingomyelin and this type of molecules covers the axons of neurons (along which an action potential is transferred until it reaches the axon terminals and then it'll be transferred to other neurons through the synapses to result in a certain response).
- So this sphingomyelin as a lipid molecule is going to be an electrical insulator so it doesn't transmit electricity.

So what is the importance of this?

The myelin sheath is not continuous; it has some interruptions along it, and these interruptions where we don't have myelin sheath are called
(Nodes of Ranvier)

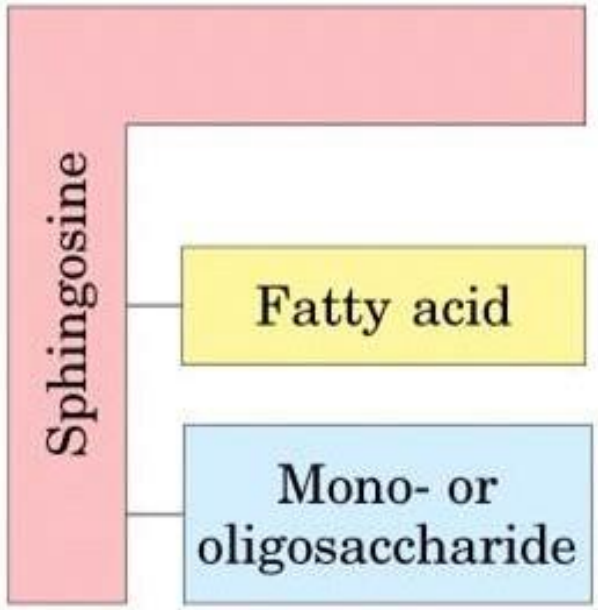
What is the importance of nodes of Ranvier?
Since the major component of the myelin sheath is a lipid molecule which is an insulator (doesn't transmit electricity), and the action potential transmission is actually a transmission of electricity because there is a movement of electrons (a movement of charged ions along the membrane to result in the action potential transfer along it), so this action potential is unable to be transmitted along the myelin sheath but it can jump between nodes of Ranvier (because these are connecting regions, they don't have this insulator material of myelin), so the action potential can jump from one node of Ranvier to another, so this way the action potential would move faster because it doesn't have to go along all the distance ; just from

•-An application on this is multiple sclerosis disease (التصلب اللويحي)and in this disease there is a problem in the sphingomyelin structure, so there would be a distortion in the myelin sheath and the transmission of action potential would be delayed and there are different types of neurons that can be affected and this results in different collection of signs and symptoms in the patients. -This disease usually affects young females and the reason behind it is unknown, the treatment for it is not yet known, there are some treatments that make patients' life better, but it is not a final treatment (not a treatment of the cause). - The family history plays a role in having this disease. - the cause of the disease is having a problem with the structure of the sphingomyelin in the myelin sheath of neurons of these patients. - If the affected neuron is related to vision, there would be an effect on the vision and if there is an effect on the balance there would be a problem in balance. -At different times along the life of these people, they would have different attacks with different signs and symptoms depending on the affected neurons and their function that would be compromised due to this problem.



Glycolipids

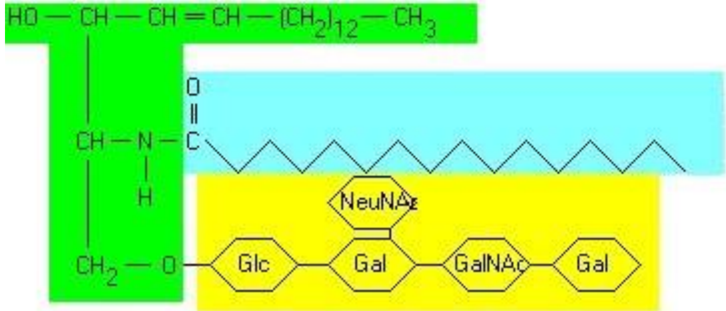
- Sphingolipids can also contain carbohydrates attached at C-1 and these are known as glycolipids
- Glycolipids are present on cell membranes and act as cell surface receptors that can function in cell recognition (e.g., pathogens) and chemical messengers
- There are three types of glycolipids
  - Cerebrosides (Contain a monosaccharide)
  - Globosides (Contain two or three sugars)
  - Gangliosides (contain three or more sugar)



Glycolipids

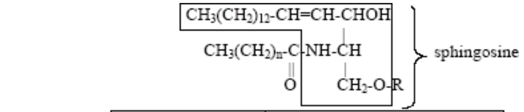
- Cerebrosides: the simplest glycolipids, contain a single hexose (galactose or glucose).
- Globosides and gangliosides are more complex glycolipids.
- Both contain glucose, galactose, and N-acetylgalactosamine, but gangliosides must also contain sialic acid.

Galactocerebroside Glucocerrebroside

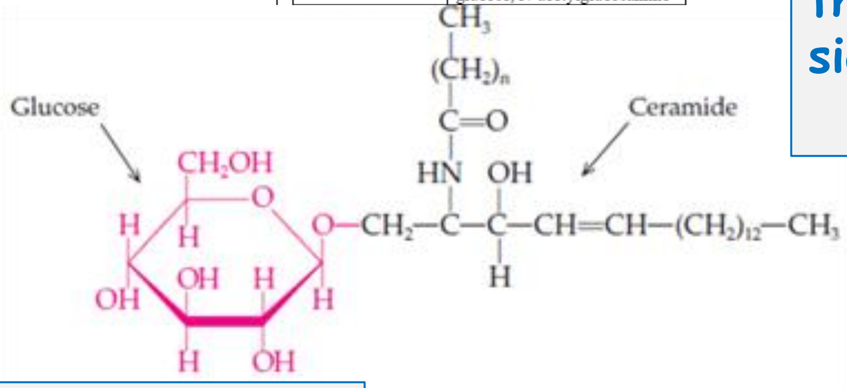


Gangliosides are bound by cholera toxin in the human intestine facilitating its endocytosis into the cells.

Cholera causes severe diarrhea , so sphingolipids are considered as a target for toxins



Sphingolipid type	R group
Ceramide	H
Sphingomyelin	phosphocholine
Cerebroside	monosaccharide (galactose or glucose)
Globoside	two or more sugars (galactose, glucose, N-acetylglucosamine

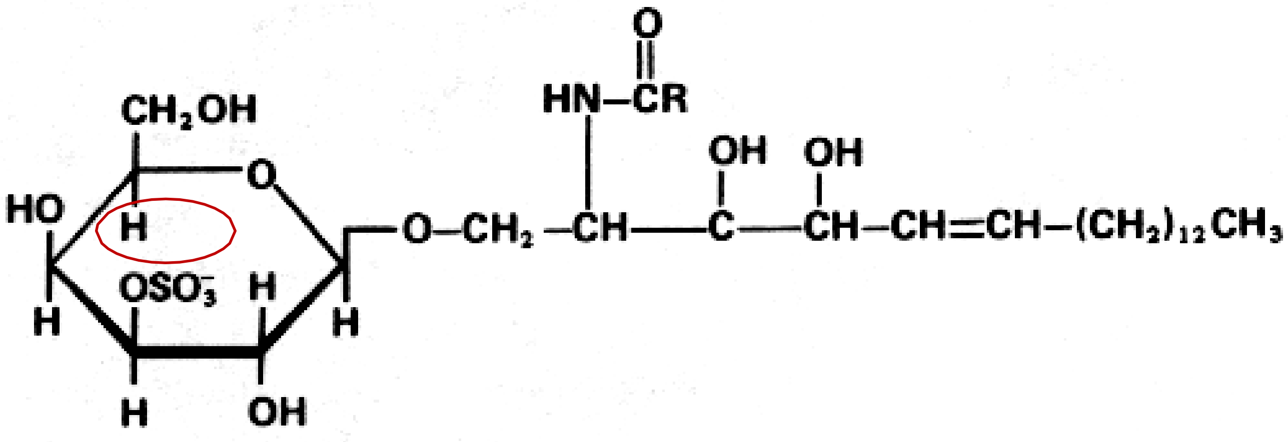


Glucocerebroside

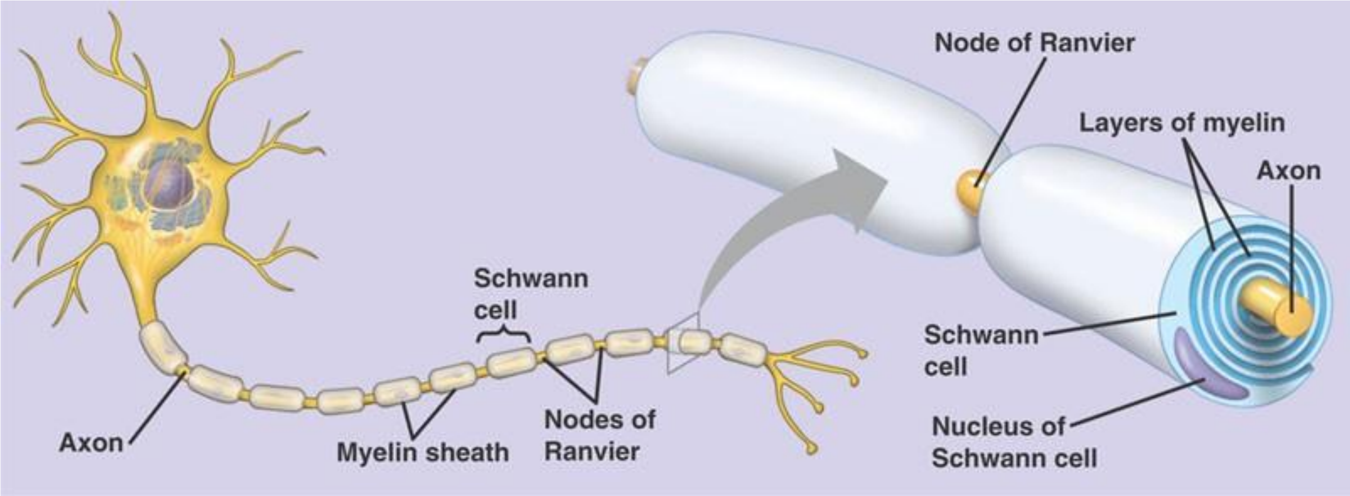
- Globoside :- contains more than one sugar molecules
- Ganglioside :- it contains more than one sugar molecules and sialic acid

Sulfatides

- Synthesized from galactocerebroside
- Abundant in brain myelin **(Myelin sheath)**



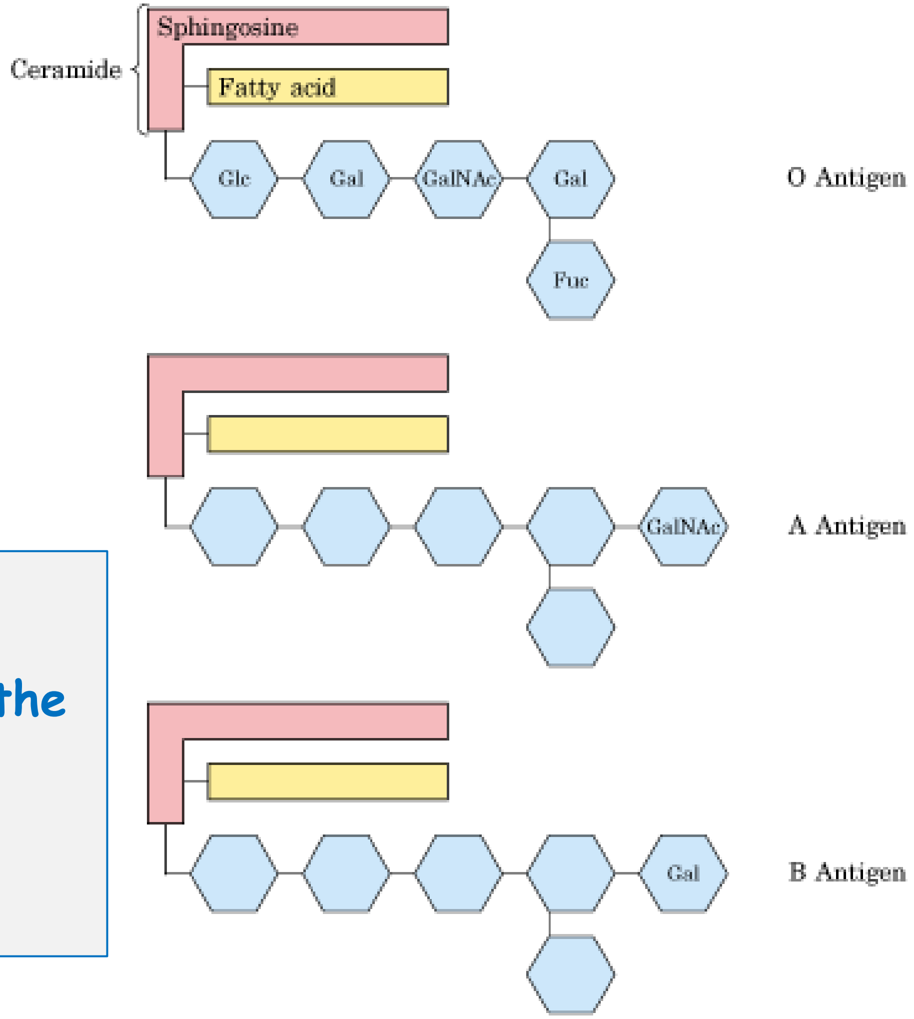
Galactose



- A type of sphingolipids
-it's a glycolipid that contains a sulfate group in the sugar that attached to the sphingosine backbone (modified sugar)

Sphingolipids and blood groups

- Sphingolipids serve in intercellular communication and as the antigenic determinants of the ABO blood groups.
- Some are used as receptors by viruses and bacterial toxins.

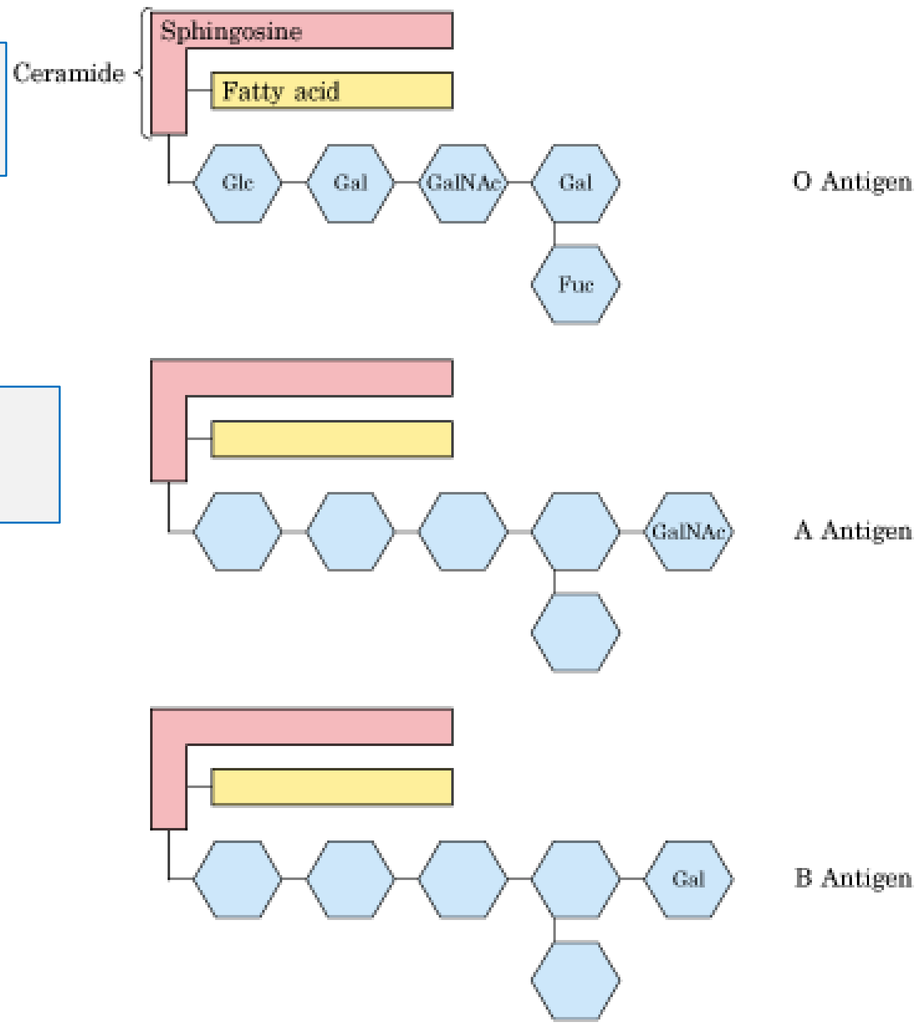


the blood type is defined by The sugar molecule in the sphingolipids of the plasma membrane of the RBC
(and also it can be defined by the sugar molecules of the glycolipids and glycoproteins)

Type O doesn't attach either N-acetylgalactosamine or galactose

Type A is attached to N-acetylgalactosamine in the end of the oligosaccharide

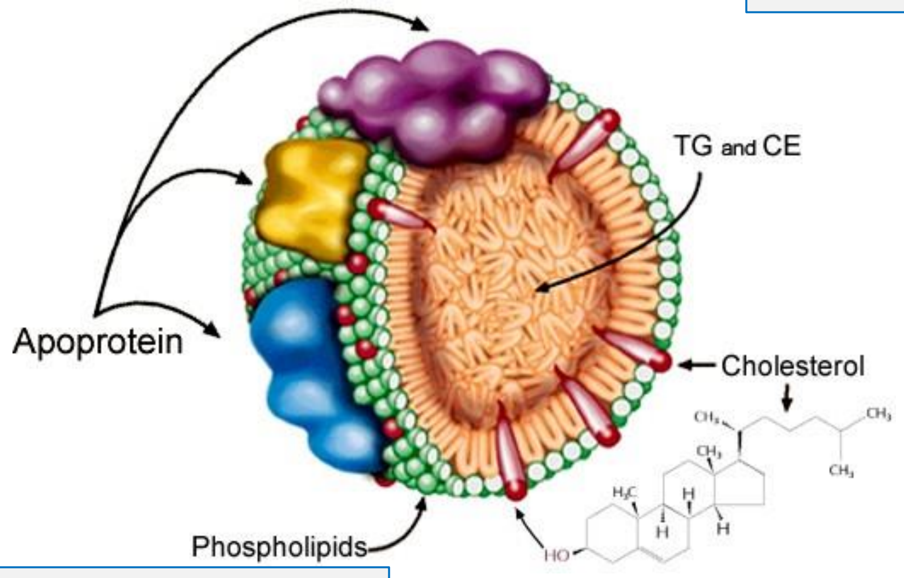
Type B is attached to galactose in the end of the oligosaccharide



Lipoproteins

Lipoproteins are particles made of protein and lipids
-they look like Micelle

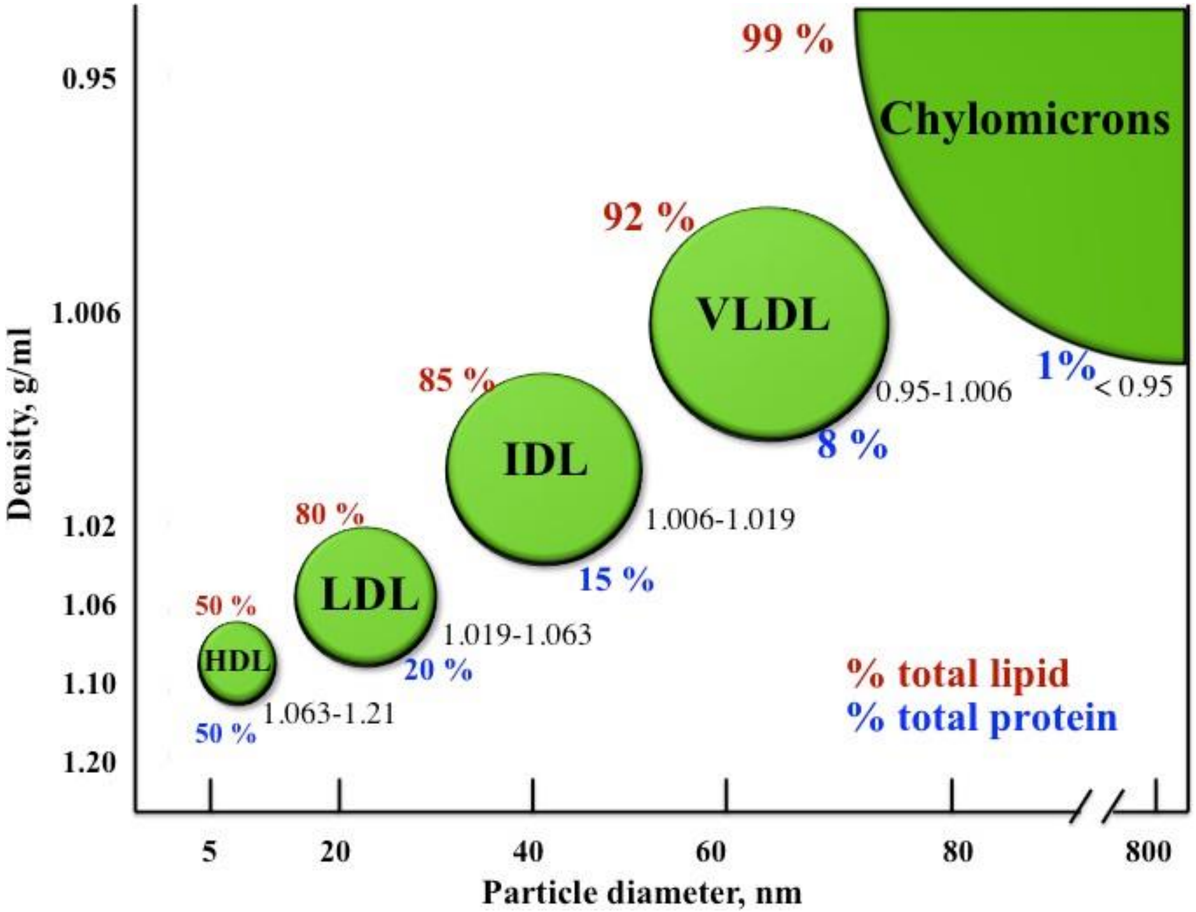
They diver in size , density , content
And function



(Specifically the triacylglycerols)

As lipid content increases, the density decreases

Function: transport of different types of lipids (cholesterol, cholesterol esters, phospholipids & triacylglycerols) in blood plasma.



There are five main types of lipoproteins And each one is responsible of transporting lipids from one place to another.

1 / Chylomicrons :-
Are responsible of transporting dietary lipids from intestines to the liver

2/ Very low-density lipoprotein (VLDL) :-
It Transports lipids from the liver to the blood (Then VLDL is converted to IDL which is converted to LDL)

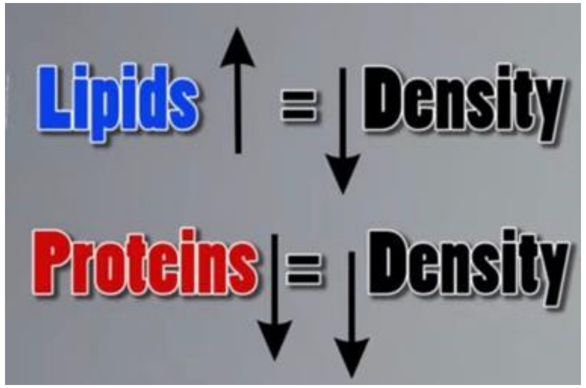
3/ IDL
It's just a transitional one

4/ low-density lipoproteins (LDL):-
Caries cholesterol from the liver to other tissues

5/ High-density lipoprotein (HDL):-
Returns access cholesterol from peripheral tissues to the liver

---

1/ dietary lipids is absorbed by the intestine and carried via chylomicrons , chylomicrons 'll transport the triacylglycerols to the tissues , while the remaining cholesterol from the dietary lipids will be taken up by the liver (s we can say that chylomicrons gives the tissues triacylglycerols while it delivers the cholesterol to the liver)
(للتوضيح أكثر الدكتور قال انه chylomicron رح ياخذ الدهون الممتصة
ويطلع على الأنسجة مليان triacylglycerols لما يعطيهم
ما بتبقى الا الكولسترول وبيعطيه للكبد)



As The liver is a central organ for fatty acid synthesis and considered as a storage of cholesterol ,so your liver makes cholesterol and sends it to other parts of your body where you need it .

2/ then VLDL carries the lipids from the liver and travels in the blood stream to other organs and tissues, so these tissues will extract triglycerides from VLDL

During this extraction , VlDL is converted to IDL which will converted to LDL (during this transition the triacylglycerols are removed and what we have remaining in the lipoprotein (LDL)is cholesterol)

(يتم امتصاص [illegible] triacylglycerols from
the VLDL [illegible] لى
IDL لى ثم LDL

ليستلور [illegible]

3/ LDL will deliver cholesterol to the peripheral tissues peripheral tissues

•-the LDL is sometimes called bad cholesterol because:-

•1/ It carries cholesterol from the liver to the peripheral tissues

•2/ LDL accumulation in blood vessels induces atherosclerosis and heart attack

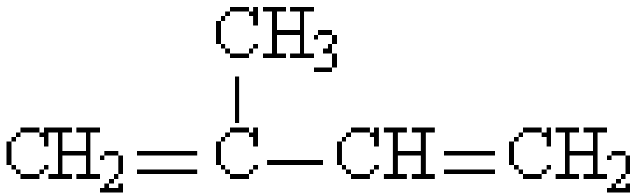
- HDL is known as the good cholesterol ,because:-

It carries the access cholesterol from the peripheral tissues to the liver (liver will get rid of it)

Steroids

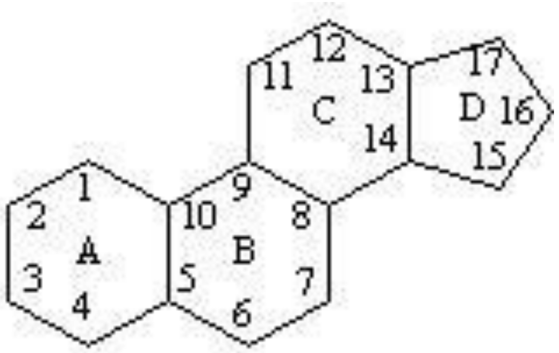
cholesterol is amphipathic. It has a polar head that contains a hydroxyl group, whereas the rest of the molecule is hydrophobic, consisting of the fused ring structure and a hydrocarbon tail

The precursor



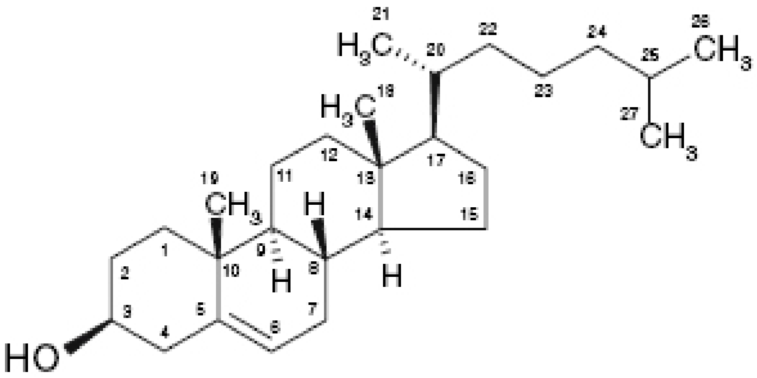
Isoprene

The nucleus



Steroid nucleus

The most common steroid



- Steroids are derived from cholesterol
- Isoprenyl is the precursor of cholesterol

-cholesterol is a 27 carbon compound

-cholesterol is composed of :-

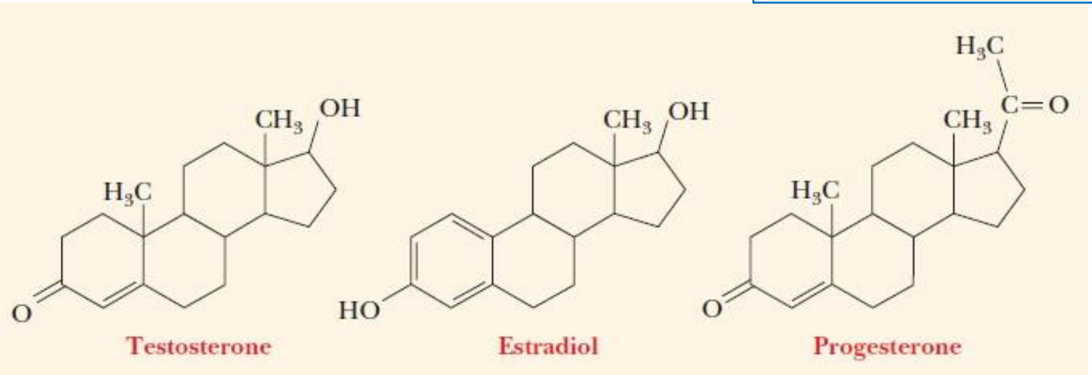
1a core of four rings structure called the steroid nucleus ,each ring is labeled A,B,C or D.(17 C)

2hydrophobic chain which's attached to carbon number 17 (10 carbon)

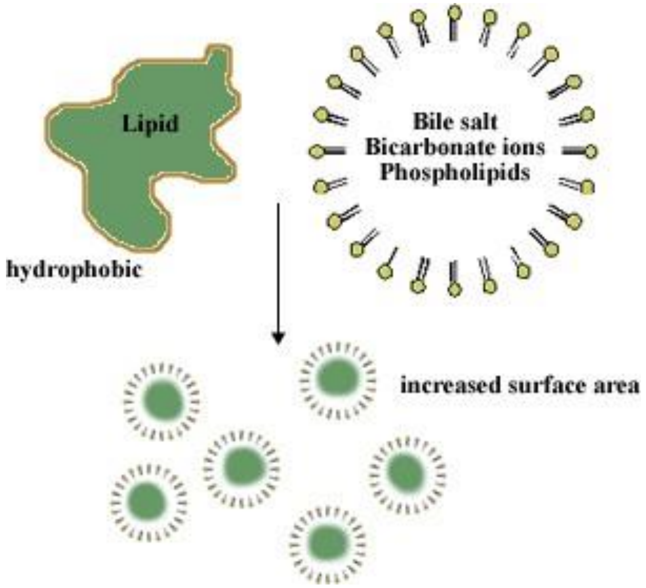
Products of cholesterol

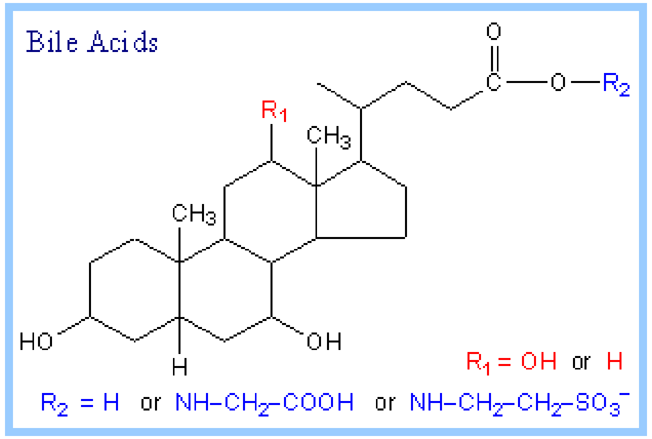
- Hormones
  - Sex hormones (androgens,. estrogens, progestins)
- Vitamin D
- Bile acids (intestinal absorption of fat)

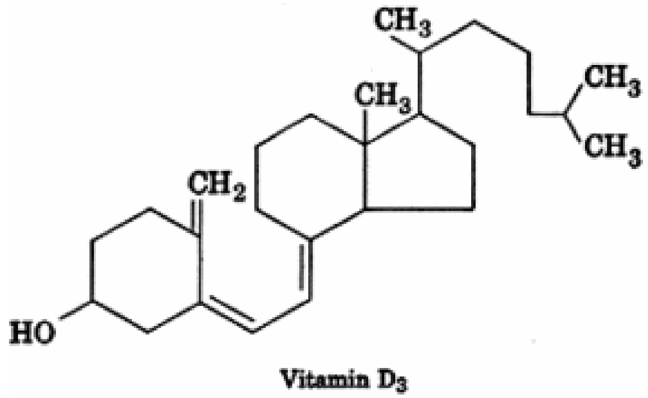
Note :-
Bile acid :-
اقر لمقرار



Also, cortisol is synthesized from cholesterol





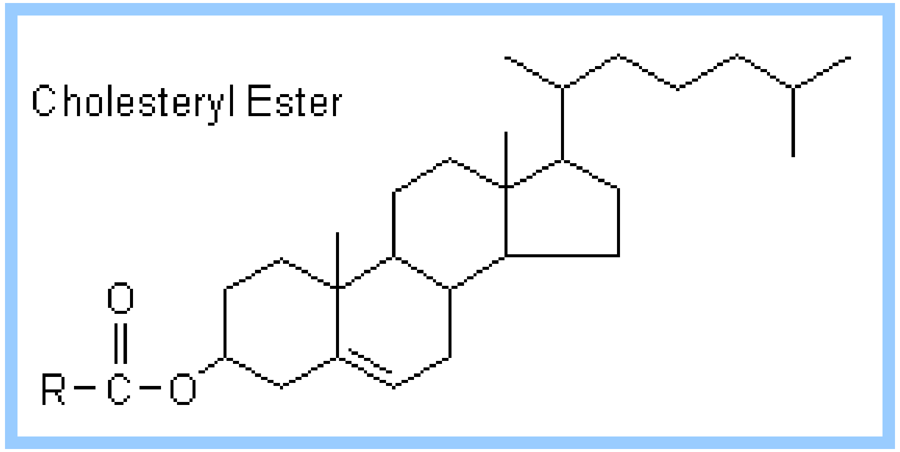


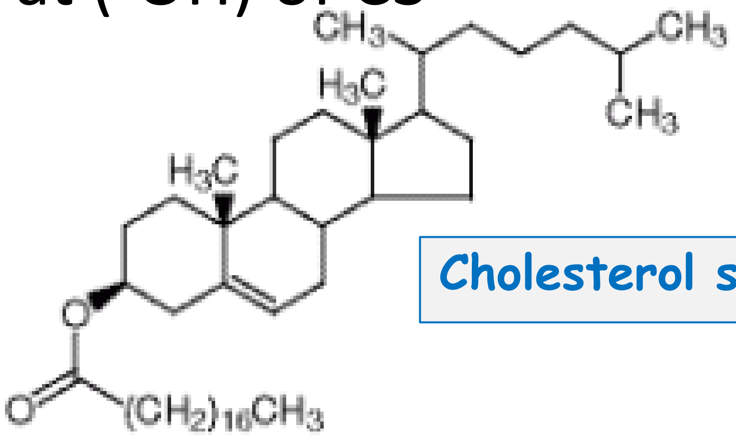
-we can derive different molecules from the cholesterol

The bile present in the gallbladder is derived from cholesterol
It is important to emulsification (to dissolve ,breaking big lipid molecules into small particles) to facilitate lipid absorbtion because it is presented as a big , hydrophobic molecules inside intestine

Cholesterol esters

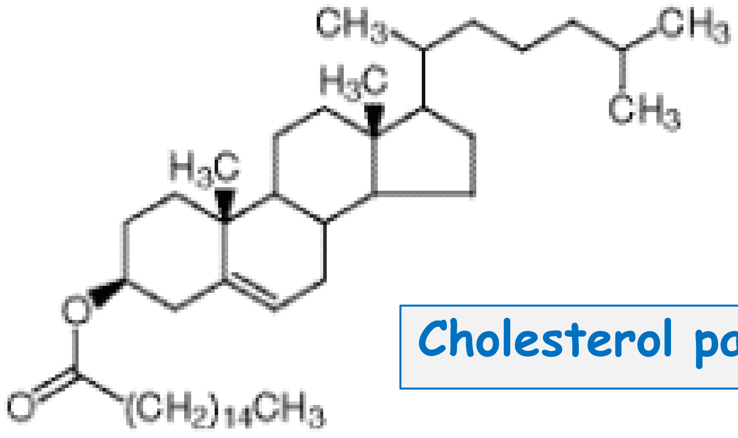
- A cholesterol with a fatty acid attached at (-OH) of C3





Cholesterol setearate

Name the molecules?



Cholesterol palmitate

Atherosclerosis

Extra note – the doctor didn't mention it

Arteriosclerosis is a type of vascular disease where the blood vessels carrying oxygen away from the heart (arteries) become damaged from factors such as high cholesterol, high blood pressure, diabetes and certain genetic influences.