Lecture :..... 14

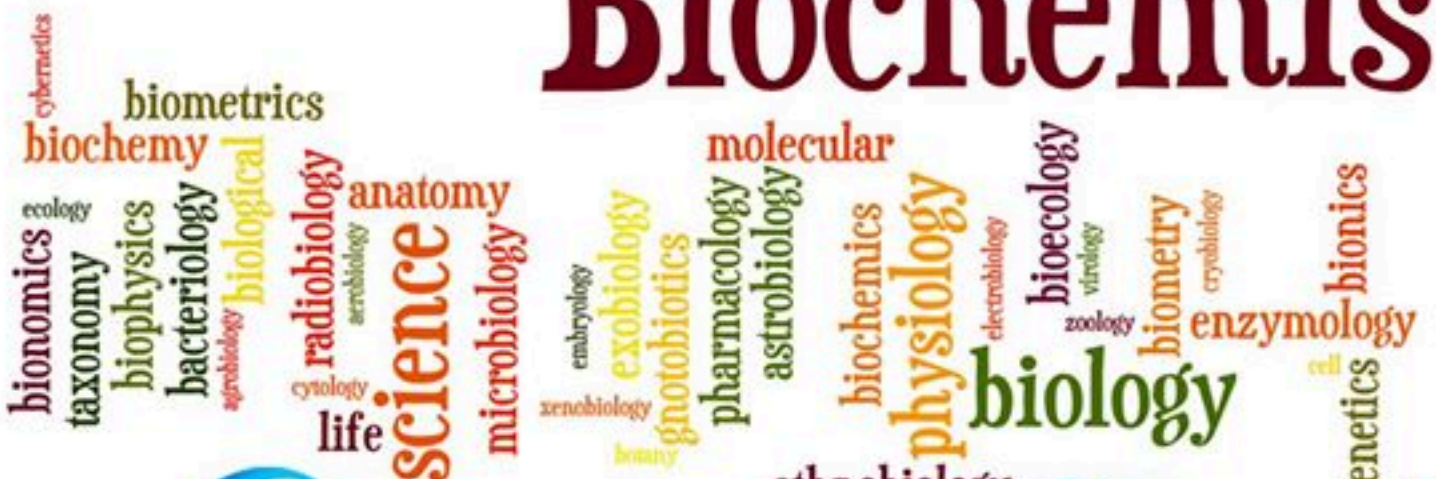
Dr. Name :..... Dr.Mamoun Ahram

Done By :..... Loay Zaghloul

☐ Slide ■ Sheet

Medical Committee
The University of Jordan

Biochemistry



Mousa Suboh

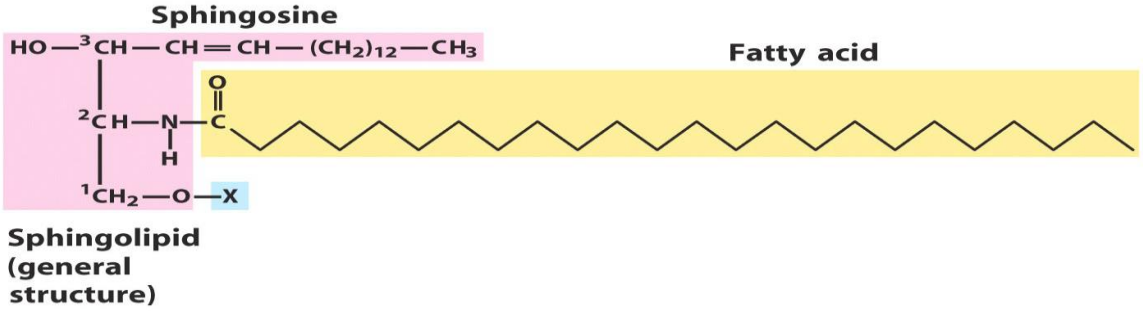
Sphingolipids

Are lipid molecules which have sphingosine backbone which has a distinct fatty acid chain connected to carbon number 2.

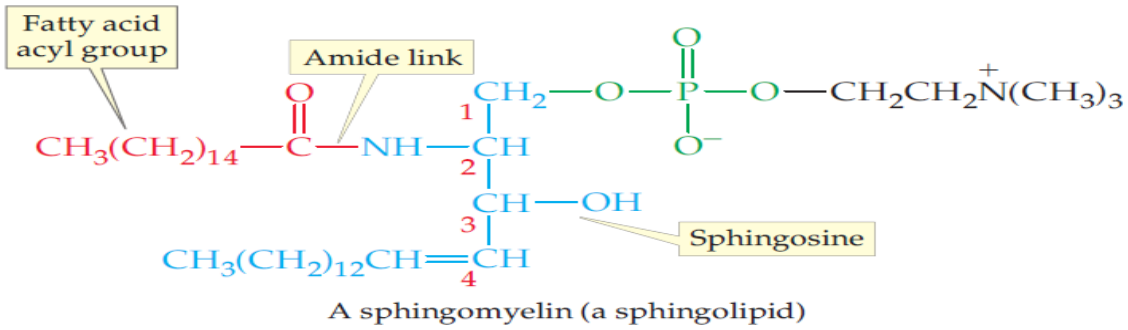
There are 2 types of sphingolipids:

1-phospholipids: phosphate group at carbon number one

2-glycolipids: sugar molecule at carbon one



The main type of sphingophospholipids is sphingomyolen, which has the same structure of a sphingolipid + a phosphate group to carbon #1 + **a choline group to carbon #1**



A sphingomyelin (a sphingolipid)

Depending on the type of sugar attached to carbon #1 we can classify glycolipids to 3 types:

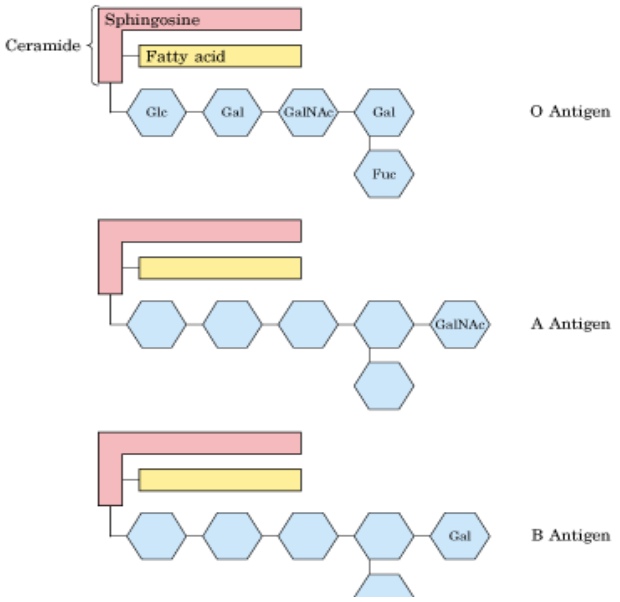
1-Cerebrosides: one monosaccharide attached to the molecule
A-Glucocerebrosides: glucose.
B-Galactocerebrosides: galactose modified addition of sulfate group known as sulfatide and it's mainly found in brain tissue in the central nervous tissue.

2-Gangliosides: 2 or more sugars attached to carbon number one, and at least one of them must be sialic acid .
Side note: they are found in intestinal cells targeted by cholera toxin in the human intestines, and this is the cause of toxicity and fatality of cholera toxin because it induces uncontrolled diarrhea which causes dehydration which leads to death.

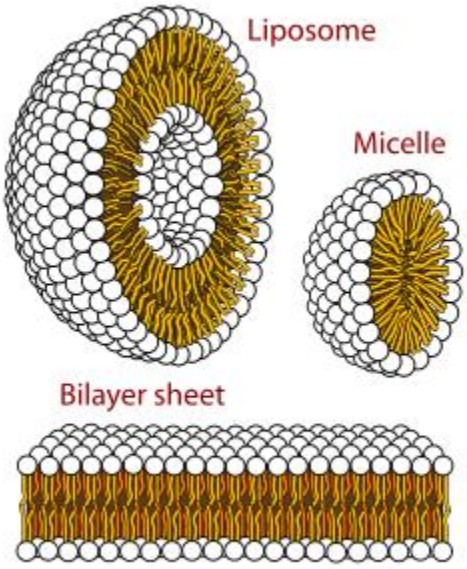
3-Globosides: 2 or more sugars.(not very common)

From the names we can notice that these names' suffixes cerebro and ganglio are found abundantly in the nervous system/tissue/cells, they are important for cell recognition and cell-cell interaction

Red blood cells and different antigens in blood types are found because of the presence of an extra sugar which is galactose and acetylgalactosamine and these sugars are mainly attached to sphingolipids in red blood cells.

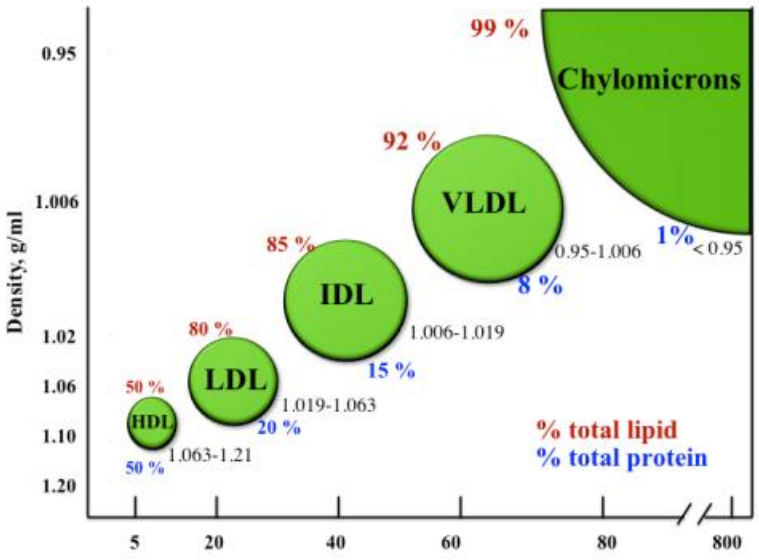


Lipoproteins



Are proteins that look like micelles (which look like balls with phospholipid heads to the outside and extending to the inside you have a fatty acid chain) now in addition to the phospholipid part we have proteins and that's why they are known as lipoproteins and they are holoproteins because they have a protein part and a non-protein part attached together, the main function of lipoprotein is <u>to transport lipids in our blood</u>, because lipids are hydrophobic and our blood is a hydrophilic environment, so there must be a way to transport lipids in the blood, and the only way to transport lipids in the blood is to package them inside lipoproteins so inside the lipoproteins you will have the different type of lipids mainly triglyceride and cholesterol and these type of proteins travel in blood between different type of tissues.

there are 4 principle lipoproteins:
1- chylomicrons.
2-VLDL (very-low-density lipoproteins).
3-LDL (low-density lipoproteins).
4-HDL (high-density lipoproteins)
They differ in size and density .



Looking at the previous

picture,we conclude that:
In size we can see that chylomicrons are the largest, followed by VLDL then LDL and the smallest is HDL.
in terms of density as lipid content increases density decreases, the Y-axis in the photo is reversed it goes from highest in the bottom to lowest, chylomicrons has the least density because they carry more lipids than the other ones, HDL from the name have the highest density because they carry the least lipids.

Function:

Note: " After you read the paragraph below,please refer to slide #60 to understand it more,don't look at the slide first it's a bit complicated"

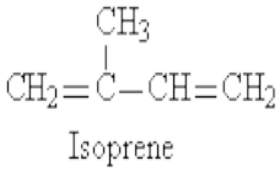
When you eat fat-rich meal, fats must be absorbed to the intestines. Because they are hydrophobic they tend to cluster together in hydrophilic environment, for them to be absorbed bile acids are needed, we will talk later about the bile acid, once they are absorbed they are packaged inside chylomicrons. Those chylomicrons carry triglycerides mainly and some cholesterol to the liver. Then after the liver is done doing whatever it does with them, the liver then packages lipids triglyceride and cholesterol inside VLDL, they come out of liver, travel in blood, as they travel in blood there are lipases (enzymes) which keep on removing triglycerides from the VLDL, as more triglycerides are removed from the VLDL, then they do not contain as much triglycerides so it has more cholesterol than triglycerides and VLDL are converted to LDL, so the function of LDL is to transport cholesterol to peripheral tissues, and that's why it's known as **bad cholesterol** ☹, peripheral tissue has excess cholesterol, they don't need it, they package cholesterol inside HDL and it carries cholesterol to the liver for elimination / excretion and that's why HDL is known **as good cholesterol** ☺, DO NOT MEMORIZE THE NUMBERS IN THE PHOTO. Just be able to compare relative data (densities and sizes) between the 4 groups.

In brief; chylomicrons carry more triglycerides than cholesterol and they transport dietary triglycerides, VLDL carry liver triglycerides and they carry more triglycerides, LDL carry more cholesterol because triglycerides are removed by lipases to peripheral tissue and finally HDL carry more cholesterol than triglycerides and they carry excess cholesterol from peripheral tissue to the liver to be eliminated (cholesterol scavengers).

Steroids

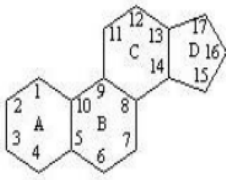
Are the type of lipids that have this particular structure to the right, they have 4 rings, 17 carbons.

The precursor

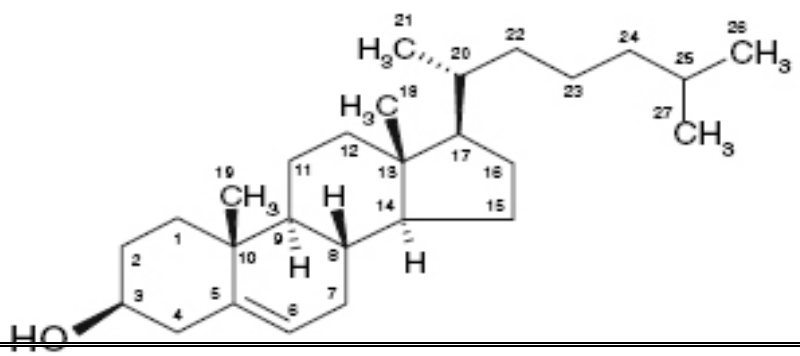


Isoprene

The nucleus


Steroid nucleus

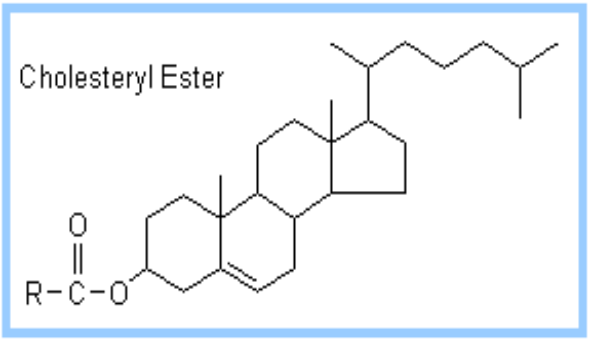
this structure is known as the steroid nucleus because all steroids have this nucleus, and this nucleus or all steroids are synthesized from 5 carbons known as isoprene,(5 and 5 = 10 and 5=15 and 5 =20 → 25 →30) 30 carbons can be modified by cutting some carbons ending with the most abundant steroid known as cholesterol which has **27** carbon molecules, notice it has the steroid nucleus and 10 other carbons extending from the chain and an amphipathic molecule, which is a molecule that has a hydrophilic and hydrophobic parts, also it has a hydroxyl group which is really important and we'll talk about it later.



Cholestrol,"the most common steroid :

Loay Zaghloul

From cholesterol we can derive other important steroid such as sex hormones like androgens (male hormones) estrogen and progesterone (female hormones), check the slides for their structure as they differ in minor groups here and there, but they have different functions though. Moreover, from cholesterol we can synthesize vitamins (mainly Vitamin D) the other vitamins which are A,E and K are made from isoprenoids, cholesterol can be used to synthesize bile acids which are amphipathic molecules synthesized in the gallbladder the main function of bile acids is to allow the body to absorb lipids, what the bile acids do in principle is breaking the large fatty droplets found in the intestines which were made because lipids are hydrophobic and they tend to cluster in hydrophilic environment, into smaller droplets, so they mix the fat in the hydrophilic environment now it's easy for intestinal cells to absorb these smaller molecules.



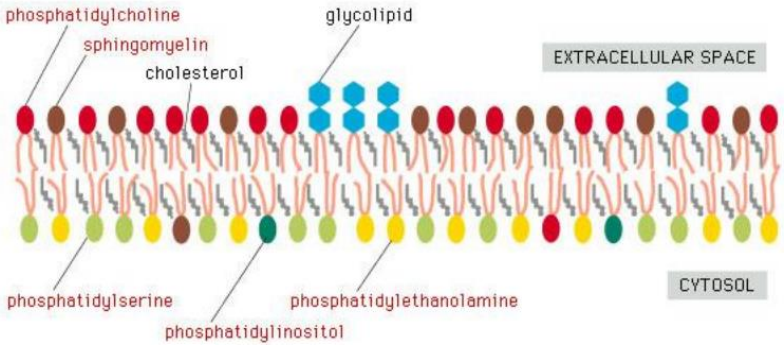
Cholesterol can be made more hydrophobic by attaching a fatty acid chain to the hydroxyl group forming a **cholesterol ester**, so overall you remove the hydrophilic group and add a hydrophobic group, making it more hydrophobic, here are some examples of cholesterol esters, here you have an attachment of 18 carbon fatty acid (cholesterol state) and the other is the attachment of 16 carbon fatty (cholesterol palmitate) .

One health problem of cholesterol is **atherosclerosis** which is basically the position of cholesterol in the artery, normal cholesterol level means normal blood flow, but when there is a higher level of cholesterol makes position of cholesterol to

atherosclerosis which leads to blocking of arteries and finally heart attacks.

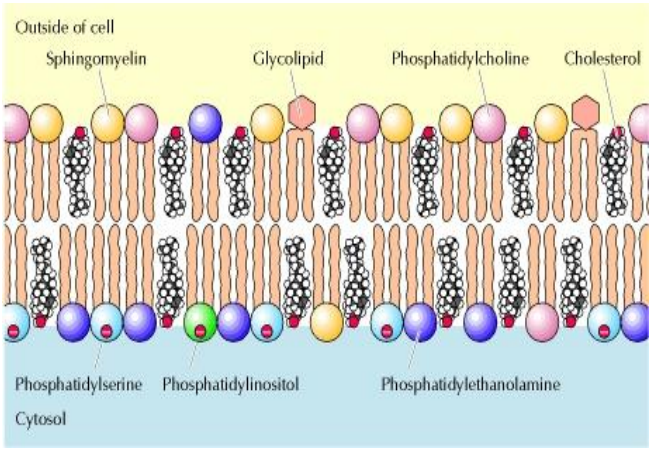
Cell membranes:

We said in previous lectures that there are 3 types of phospholipids : 1- micelles 2- liposomes 3- lipid bilayer, which has 2 layers of phospholipids and the phosphate head groups extending outside and to the inside clustering of fatty acid chains, now in this lipid bilayer the model in cells is known as **fluid mosaic model**, because it's not a lipid bilayers it's decorated with proteins and sugars, so it looks like mosaic, and its fluidic because it's dynamic it keeps on moving and flipping. Now this lipid bilayer contains lipids, proteins as well as carbohydrates. At different distributions, different cells have different amounts of lipids, proteins and carbohydrates and different types of proteins as well.



If you look closely upon the lipid bilayer in the cell, you can notice that the distribution of the phospholipids isn't distributed evenly in the outer leaflet (exposed extracellular matrix) and the inner leaflet (exposed to the cytoplasm) so for example in the outer leaflet we will have phosphotidylcholine, glycoprotein and sphingomyelin. And that makes sense because sphingomyelin is a protective sheath of nerve fiber so it should be exposed to the outside, also glycoproteins which are involved in cell-cell interaction and cell recognition, so they must exist outside and then we have the inner

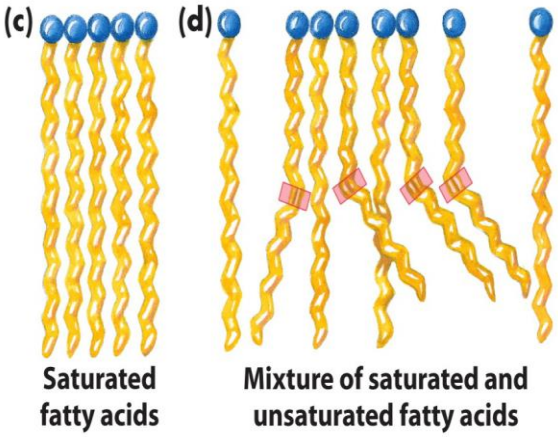
leaflet which has phosphotidylethanolamine, phosphotidylserine and phosphatidylinositol. And that makes sense again because phosphatidylinositol is involved in cell signaling (cleaved to produce 2 molecules diacid cholestrol and 3 phosphoinositol pi3 and these 2 molecules induce the release of calcium from inside the cell).



On the other hand, cholesterol is distributed evenly in both leaflets, so you'll have the same amount in both leaflets, if you compare different cells in animals, plants and prokaryotes, you will notice that animal cell membrane will be rigid compared to plant cells due to the presence of cholesterol, plant cells have something that is similar to cholesterol though, while prokaryotic cells have no cholesterol whatsoever so it's cell membrane is more fluidic.

Fluidity of membrane

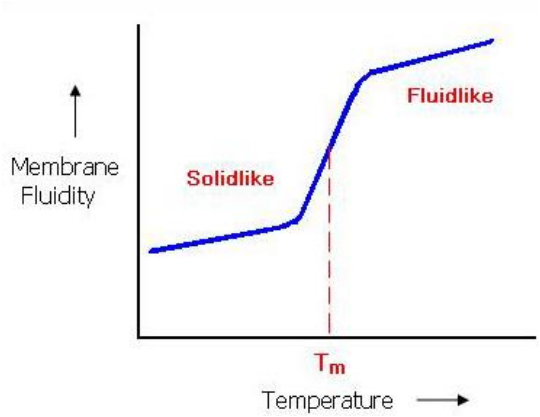
it's dependent upon several factors:



1- **Fatty acid chains:** Saturated = straight chains meaning they cluster together forming a very rigid structure, on the other hand if you have a fatty acid with cis bond, it will form a kink

which creates phases in the plasma membrane which allows for the movement of molecules in the plasma membrane and movement of the fatty acids themselves so these unsaturated fatty acids make the membrane fluidic.

2- **Temperature (external factor):** at low temperature you will have low kinetic energy, as a result these fatty acids will tend to be accumulating together very tightly, and so the membrane will be so rigid, if you increase the temperature gradually you also increase the kinetic energy of these molecules and electrons and these fatty acid chains will keep on moving so resulting in the formation of disordered fatty acids or disordered structure of plasma membrane, and there is a point called transition point or melting point that changes the structure of the membrane from solid like to fluid like state



3- **Cholesterol:** it interacts with the membrane where it has the hydrophobic part of cholesterol interacting with hydrophobic chains of fatty acids and the hydroxyl group we talked about earlier interacting with the phospholipid head group of fatty acids or phospholipids. The effect of cholesterol on membrane fluidity, it actually has opposite effects depending on temperature, at low temperature there is low kinetic energy and the fatty acid chains tend to cluster together but cholesterol being between these chains it prevents the accumulation and the packing of the fatty acid chains keeping the membrane structure fluidic. On the other, hand at high temperature when the kinetic energy is really high fatty acids

keep on moving they can collide with each other resulting in the collapse of the membrane, in order to prevent the collapse of the membrane and collision of fatty acid chains, you have cholesterol in the middle preventing them from hitting each other. **So it stabilizes the membrane**.

If you look at people in the Eskimo you will find that they have very high amount of blood cholesterol, yet they have low rate of atherosclerosis and heart attacks, the reason for that is because they eat fish, and fish has omega fatty acids (3, 6 and 9) as a result the membrane of these people is full of unsaturated fatty acids, and that's why their membranes are fluidic at these low temperatures and that's why they don't get atherosclerosis.

There are different type of membrane proteins:

1-integral which integrates into the membrane
2-periphral exists at the cell's surface
3-proteins that are integral but the part that goes into the membrane is not a protein or peptide part but it's rather a lipid molecule that is attached to the protein itself.

Peripheral proteins are loosely attached to the membrane and they can be easily removed by adding a detergent, and these proteins are either associated with phospholipids head groups or with other integral proteins.

If you look at the integral membrane proteins they have different structure or different mechanisms which they can insert themselves into the membrane, and if they insert themselves into the membrane they would have 2ndry structure which is either alpha-helix or beta-sheaths, alpha-helix mainly exists in

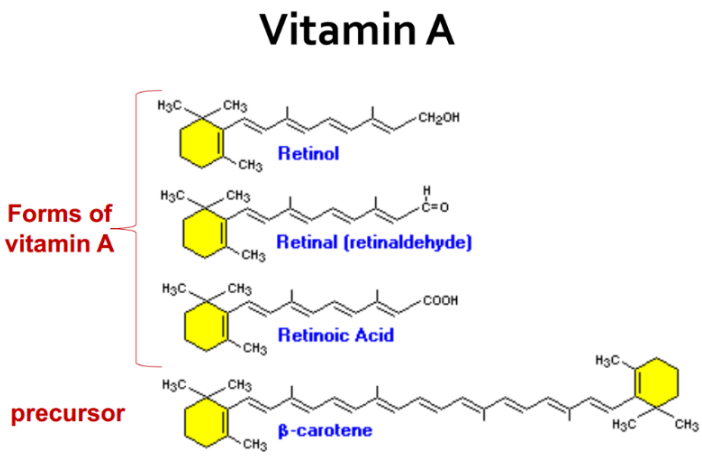
eukaryotic cells while beta-sheaths mainly exist in prokaryotic cells, the reason why the transmembrane domain the part which integrates into the plasma membrane is an alpha helix or beta sheath is to minimize the interactions between the amino acids with the fatty acid chains, because you want to separate them from each other as much as possible because amino acids may have hydrogen bond donors and acceptors so they can be polar and fatty acid chains are hydrophobic so to minimize interactions they have these shapes, some proteins can form channels so they can go in and out the membrane and they are known as multipass proteins.

The lipid anchor proteins are basically proteins where there is an attachment of fatty acid chain to the protein and this fatty acid chain integrates into the membrane and it attaches the protein to the membrane itself, and there are different types of lipid molecules that can attach proteins to the membrane and they include myristate which binds to amide-bond, other 4 bind via thioester- bond or thio-ether linkage which is used to bind prenyl groups.

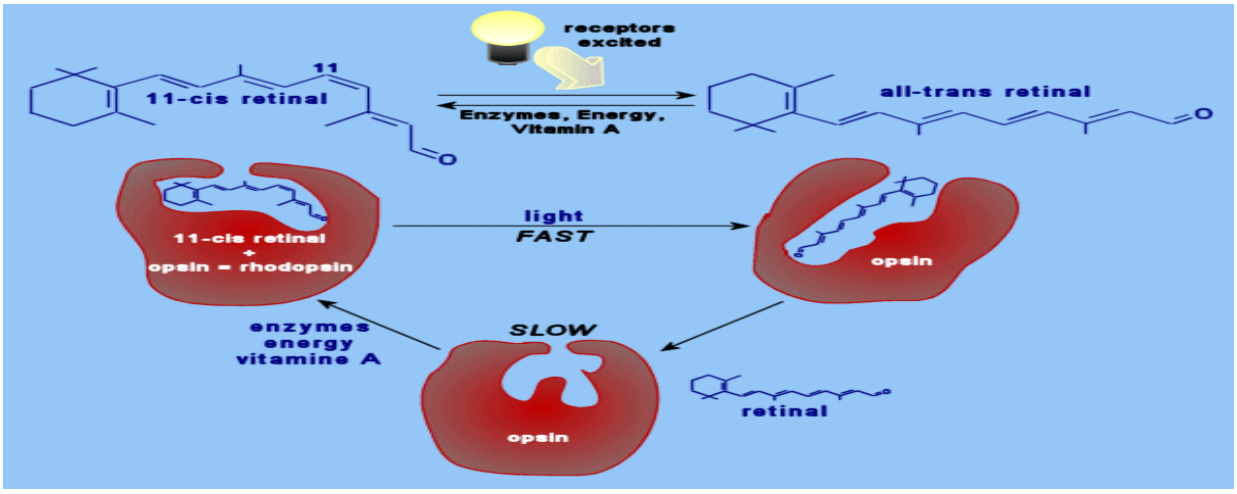
The doctor talked about the cancer drug; RAS,it causes killing of cancer cells in laboratory then worked on animal cells, but when it came to humans it failed, it had no effect on human cancer. No one knows why that happened.

Vitamins:

there are vitamins that are lipophilic because they are mainly hydrophobic, vitamins A, D, K and E.



Vitamin D is synthesized from cholesterol, while A, K and E are from isoprenes.
These are the different forms of vitamin A retinol(hydroxyl group) retinal(aldehyde group) retinoic acid(carboxylic acid group) they are derived from B-Carotene (carrots), vitamin A have different functions, we'll talk about one of them, which is **11-cis retinal**, it is vitamin A but it has a Cis double bond at position number 11, it has a kink to it, it binds to a protein called opsin just like we have globin binding to heme we have hemoglobin, we have opsin binding to vitamin A 11-cis retinal we have a protein called rhodopsin, rhodopsin = 11-cis retinal + opsin, now this protein is found in visual cells called Rod cells,

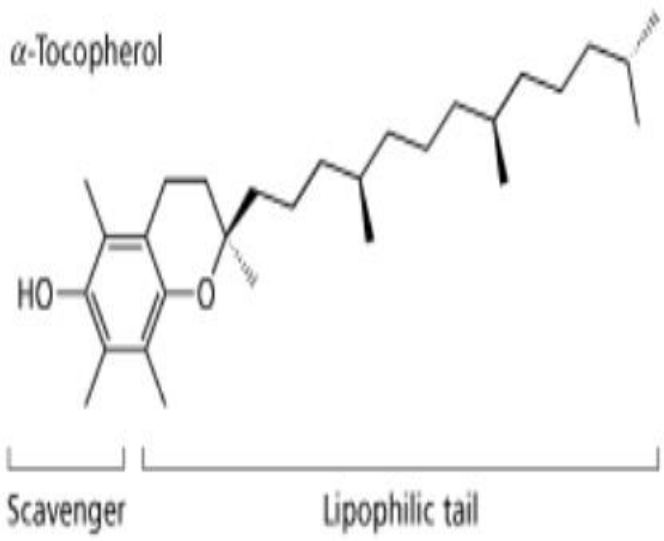


they are in our eyes they are responsible for absorbing light and allowing us to see.

The way they absorb light is the following, light hits 11-cis retinal and it changes its structure from the cis orientation to the trans orientation so it becomes a molecules known as All-trans retinal, remember when he told us about hemoglobin has this heme as a dome like-structure, which becomes straight or flat and it changes the structure of whole the protein, secondary, tertiary and quaternary structure, now the same thing happens here, when you have 11-cis retinal changing to all-trans retinal it changes the structure of the whole protein the whole rhodopsin protein allowing for the protein to send a signal inside the cell, telling the cell there is light, we'll talk about the mechanism later on in one of the modular systems. The plasma membrane of the rod cells is viscous because it has a lot of proteins compared to lipids and this allows movement of molecules inside the membrane.

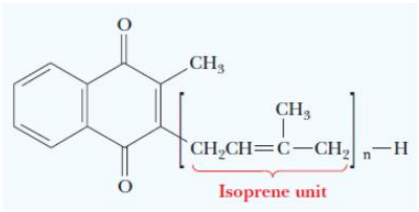
Vitamin D is synthesized from cholesterol starting in skin in a molecule known as 7-dehydrocholestrol with light changes structure to cholecalciferol by breaking a ring of the 4 cholesterol ringed structure (check slides) then in the liver hydroxylation to 25-hydroxyvitamin D3 then in the kidney further hydroxylation to 1,25-dihydroxyvitamin D3 (2 hydroxyl groups) which is the active form of vitamin D, YOU ARE NOT REQUIRED TO KNOW THE STRUCTURE. But if he brings the structure and he asks if this is cholesterol, vitamin A, E, K or D you should tell that it's vitamin D.

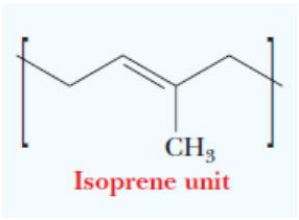
Vitamin E is an anti-oxidant, it removes the harmful effects of free-radicals and reactive oxygen species by donating an electron to them, to the right is the structure of vitamin E, it has a lipophilic tail, and 2 ring structures, the hydroxyl group is the active part which donates electrons, so it donates an

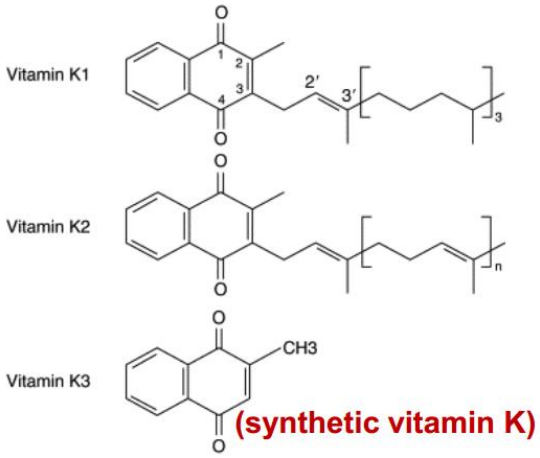


electron to a free-radical, we have the lipophilic tail for 2 reasons, first to be able to attach vitamin E to the cell membrane, because that's where it should be to protect the cell membrane against free-radicals and the second reason is to help dissolve vitamin E in fatty tissue like adipose tissue.

Finally, vitamin K, bicyclic, it's made from isoprene units, here there are 2 naturally occurring vitamin K1 and K2 and K3 is the synthetic vitamin K, the 2 ketone groups are the active part of it.







Dedications: abo z3'ayar, abo 3adal, el colonel, abo 3beidat, simsim, ellauzi, abo sharkas, abol masameer, abol karkash, smadi, abo khraisat, wbagi il shabab, sadeegna Marwan and (; last but not least tab, caps lock and shift

Sec 1,2,3 :

Sheet #3 → Dr. Nafeth Sec 1,2,3 → First paragraph

The correction is: "When the PH becomes = 9 :

- 50% of the amino group will be deprotonated "thus has a net charge of (-1)" , and 50% are protonated "has a net charge of (Zero)"

The wrong sentence was: zero, +1

Sheet #3 → Dr. Nafeth Sec 1,2,3 → The quiz →

Q.2

At PH = 9, 50% of the molecules will have a net charge of +1 and 50% will have a net charge of zero, thus the net charge of the solution is 0.5

Q.3

At PH = 8, The carboxylic group will be deprotonated, while 50% of the solution amino acids will have the SH group protonated with a net charge of zero and 50% will have it deprotonated with a net charge of -1 . Thus at PH = 8 the net charge of the solution will be -0.5

Sheet #7 → Dr. Nafeth Sec 1,2,3 → Page 4 → Paragraph 3

"We have several amino acids with Nitrogen in their side chains like: ..., **Glutamine**" **instead of Glutamate**

Sheet #8 → Dr. Nafeth Sec 1,2,3 → The quiz

Q.5 the answer is B instead of E

Q.7 C- almost entirely of alpha helix*

Sheet #10 → Dr. Mamoun Sec 1,2,3 → Page 10 → The paragraph talking about Sucrose:

The correction is: "α-D-gucopyranosyl-(1->2)- β-D-fructofuranose".

The wrong name was: "α-D-gucopyranosyl-(1->4)- β-D-fructofuranose"

Sheet #11 → Dr. Mamoun Sec 1,2,3 → Page 12 → The last paragraph:

The correction is: "a person with a blood type **AB** can get blood from any other type of blood"

The wrong sentence was: "a person with a blood type **A or B** can get blood from any other type of blood"

Sheet #12 → Dr. Mamoun Sec 1,2,3 → Page 3 → Lipid functions:

The mistake was in point #1 in considering **(Glycogen & Starch)** as **lipids** instead of **carbohydrates**.

Sec 4,5,6 :

Sheet #1 →Dr. Mamoun sec 4,5 6 → has 3 mistakes
And here are the details :

Sheet #1 → Dr. Mamoun Sec 4,5,6 → 1st page → 19th & 20th lines →
"Note: because amino acid has a carboxylic group (WITH +VE CHARGE) and amino group (**WITH -VE CHARGE**)..."
That's wrong and must be:
"Note: because amino acid has a carboxylic group (WITH -VE CHARGE) and amino group (**WITH +VE CHARGE**)..."

Sheet #1 → Dr. Mamoun Sec 4,5,6 → 5th page → under the title : Nonpolar, aliphatic amino acids → subtitle : 3-leucine →
"Put a methylene group (**CH3**) ..."
That's wrong and must be:
"Put a methylene group (**CH2**) .."

Sheet #1 → Dr. Mamoun Sec 4,5,6 → 7th page → under the title : Polar amino acids and the subtitle : 3- threonine → 7th line →
"*threonine and valine >> threonine looks like valine except: **one of the H in CH3 (valine) is replaced by OH in threonine**."
That's wrong and must be:
"*threonine and valine >> threonine looks like valine except that: **the omega carbon with the 3 H atoms attached to it (CH3) in (valine) is replaced by OH in threonine.**"

Sheet #7 → Dr. Mamoun Sec 4,5,6 → Page 4 → Paragraph 2 →
The correction is: "The other one is present in helix **E**".
The wrong sentence was: "The other one is present in helix **H**".

** You can find these corrected mistakes on facebook on this hashtag:
#corrected_sheets

Good Luck Doctors ☺