Introduction to Biomolecules
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Lecture – 13
Lipids (Part 2/3)

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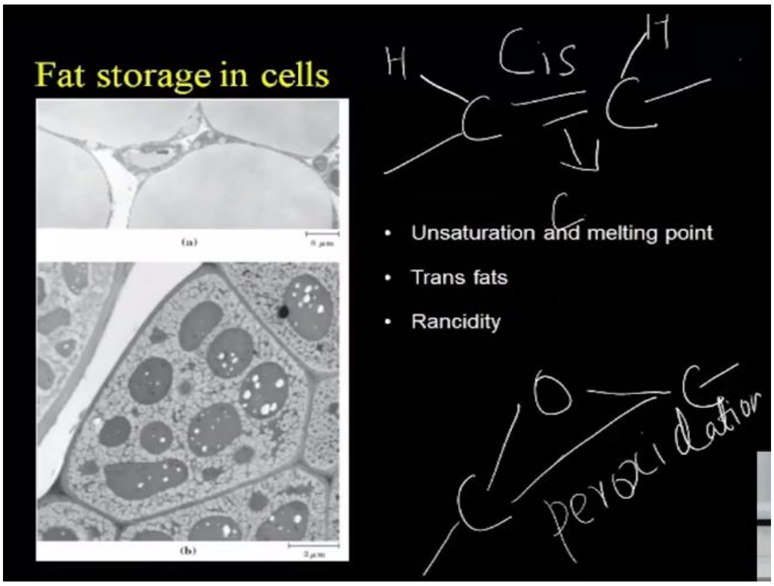

So, we will continue from the slide where we left in the last class that is triacylglycerol. So, I was explaining about the adipose tissue and adipocytes. So, these are 4 adipocytes filled with fat and then I showed you this is a cotyledon of a seedling. These are the seed leaves as soon as the seed germinates the two thick leaf-like structures, basically the seed that opens into two parts. So, these white areas are the lipid storage in them.

So, we need to learn three major points with respect to free fatty acids as well as the ester form with glycerol that is the triacylglycerol. So, they are in listed in bullet form. The first one is unsaturation and melting point. So, this is something we have yesterday considered that is when you have double bond in the aliphatic chain so that is what we call as unsaturation.

So, the degree of unsaturation reflects how many double bonds are there and that has a direct bearing on melting point as I told you in the previous class. The double bond prevents free rotation of between the two carbons that have the double bond and as a result or there is a fixed orientation of the chains on both sides of the double bond. And that interferes with compact packing and as a result fats having more double bonds in the side chains they usually are liquid at room temperature.

So that is why vegetable oils which have a lot of mono and polyunsaturated fatty acids they are liquid at room temperature. On the other hand, butter which has mostly saturated fats is solid at room temperature. So, in this context we need to consider one more point which is this degree of unsaturation also leads to lipid degradation and a process that we call as rancidity.

You may have noticed if you have stored oil particularly at room temperature not tightly capped for long time it starts to develop a foul smell. So, then you say this oil has gone bad and then you throw away and that smell the one that you call as oil has gone bad is technically known as the rancidity. This is primarily because what actually happens in these unsaturated fats is you know like if you have double bond let us say, so here you have carbon on either side.

So this double bond oftentimes becomes, I will draw here. It gets oxidized. So, this structure of one oxygen added between these two carbons this we call as lipid peroxidation. This again breaks down into aldehydes gates and carboxylic acid and so on. This breaking down into shorter portions due to oxidation, this peroxidation is what causes the property called rancidity. And this has a major consequence if it is the lipid chain of cell membrane.

So, then the cell membranes integrity is lost so therefore this is not something that is good for the integrity of cell membrane. So, to prevent this we have antioxidants in the lipid phase as well hydrophobic antioxidants, we will learn about them a little later. So, this free radical generation that happens, free radicals produced in other reactions can cause this peroxidation and this peroxidation can lead to breakdown of the membrane lipid as well as the breakdown products are reactive again.

So, this is for example it is easy for you to understand how this will break into an aldehyde. And so to prevent all of that you have antioxidants in the lipid phase as well so that is rancidity. And the second important point we need to consider here again is all this results from the double bond, the unsaturation. One the melting point goes down, then I told you about rancidity.

Then the third is the possibility of trans fat. So., this double bond here is a site for or cis and trans, you know geometrical isomerism. So, for example if the groups attached here so you could have that same group attached in trans orientation or on the other hand you could have both of them on the same orientation. Let us say two hydrogens attached and they could be on the same orientation or on the other orientation, so this would be cis.

So, this cis and trans possibility arises due to this double bond and the prevention of the rotation of these groups around this bond. And due to that you have these isomers possible and naturally occurring unsaturated fats are all cis isomers so that is what is normally found in our body. And these trans isomers are usually not hydrolyzed and metabolized in our body and they usually lead to buildup of fat deposition in our blood vessels.

Leading to high blood pressure and leading to atherosclerosis and other heart diseases. Atherosclerosis results from reduction in the luminal face of the blood vessels and therefore the blood flow is obstructed increasing the pressure required to push the blood and therefore the heart overworks and they eventually you have heart problem. And trans fats usually are a cause of this. So, therefore trans fats are not good for health.

And where do we get the trans fats normally from? There are two sources of trans fats. One cattle, you know like cow sort of animals their digestive system harbor bacteria that produce trans fats. So, therefore meat products as well as dairy products have trans fats that is one source. So, therefore you should not have too much of that, it is bad for health. And second source is people make saturated fat out of vegetable oils.

For example you try to reduce this double bond and therefore it is saturated fat and that is called a hydrogenation. So. vegetable oils usually are hydrogenated to produce artificial butter you would have heard the commercial name Dalda or vanaspati. So they are vegetable oils artificially saturated, the double bonds are reduced chemically in the factory and you get saturated fat. So, these have a historical reason.

At one point getting enough butter was not easy and butter was expensive therefore people wanted to make hydrogenated vegetable oil as a substitute for making sweets and other baked foods like bread, cookies and biscuits and so on. But in the process people realized they are more stable than a natural saturated fat and vegetable oils which have unsaturated fat and therefore the bakery items made using trans fats were stable for longer.

They could be stored longer without having the problem of rancidity that is one. Second people liked that texture, you know they are crispier. If you have cookies made using trans fat like vanaspati or Dalda, they are crispier and people liked the texture. For example if you go to a place like Delhi on the roadside where you have a famous samosa guy, he makes that samosa really crispy and tasty and nice and that is because he generously uses Dalda in the oil in which he fries the samosa.

And when you eat that you get a lot of trans fat and the trans fat is really deadly for health. You know as you get past middle age you often run into high blood pressure and obesity and atherosclerosis, cardiovascular disease all of that. So, the trans fat is a major cause. So the FDA recommendation or is I am not sure about what WHO says, FDA recommendation that is Food and Drug Administration of US their recommendation is that totally avoid trans fats.

So you need to look at the wrapper or when you buy biscuits or cookie next time look at the wrapper whether it says trans fat 0. If it says trans fat 0 it is good, but it is not going to be very crispy, the biscuit might become quickly you know powdery but it is, it is a lot better for health. Similarly, when you buy bread read the label, make sure that it is trans fat 0 or if you go to a local bakery, a regular non-branded local bakery so they make everything using hydrogenated vegetable oil.

Because that is what makes their products smell good, feel good, taste good, store long all of that. So, remember trans fat. So this trans fat, rancidity, melting point all of them are directly due to the double bonds in the side chain of the acyl moiety in the triacylglycerol. So having covered these two topics, we will move on now.

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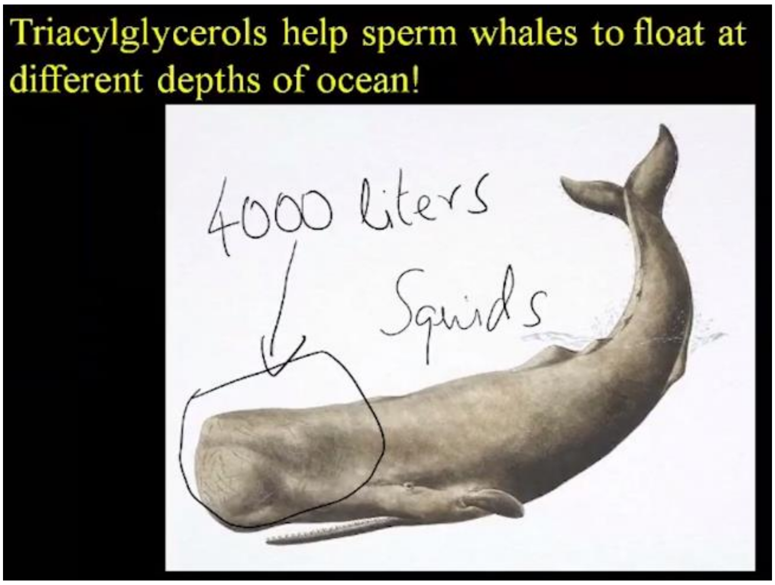

So another interesting story about triacylglycerol and this degree of unsaturation. So, yesterday I mentioned the difference between beef fat, I do not know how many of you have eaten beef or seen beef being cooked you will find like I have seen a patty that goes in making burger being grilled and then you will see lot of fat really melts and drips down and that has a longer chain fatty acid that is 18 carbon and 20 carbon, sorry it is 18 carbon stearic acid while butter has 16 carbon.

But both are saturated. So longer the chain higher the saturation then more solid that fat is. So, as a result beef fat is hard solid while butter is a soft solid. So, the difference here is only the length of the chain both are fully saturated otherwise. So, the point I want to make here is the length of the chain, the degree of unsaturation both are important. A mixture of them like you have varying lengths varying degrees of unsaturation.

All of that can give you is a mixture such that the melting point can vary a lot and as a result whether it is going to be denser or it is going to be less dense all of that is determined by these two factors that is length of the chain and the degree of unsaturation. So, shown here is a sperm whale, pay attention to its head. So, this is its mouth. So here is the eye and this is the portion a tank literally above the head in its head is done here.

But this portion is a tank that holds about 4000 liters of triacylglycerol, so remember the number 4000 liters of triacylglycerol here. So why is this whale storing so much fat there? That is primarily because its triacylglycerol has a happy mixture of the length and degree of unsaturation such that when it dives deeper from the surface, you know the surface is going to be warmer, the temperature is going to be warm.

It is surface or the air water interface it is going to be warmer and due to that this fat will be liquid. So, its density will be lower and it can neatly float on the surface, but when it dives deep, it dives as deep as 3000 meters, mostly about 1000 meters that even that is lot deeper like 1 kilometer from the surface of the ocean and at that depth you have schools of squid and squid is what this whale loves to eat.

Because at that depth it has no competition and as a result it dives and then just keeps quiet, wait for a school of squids to come by and then it eats them, it feeds on the squids which are found at that depth. So, when it dives that deep the water is denser there and it wants to wait there longer, so its buoyancy should be adjusted to the surrounding dense water and the way it does that is this becomes a gel, the triacylglycerol cools down because the temperature is cold.

So it cools and becomes a jelly solid mixture whose density matches the density of the surrounding ocean water and therefore it does not need to really spend a lot of energy to stay at that place floating. And when it dives back to the surface, then it becomes liquid and again its density goes down and it is in surface.

So, by exploiting this melting point difference that exists in the acyl moiety of the triacylglycerols this whale has developed an adaptation that allows it to stay float effortlessly at great depths. So, this is one of the interesting stories about triacylglycerol.

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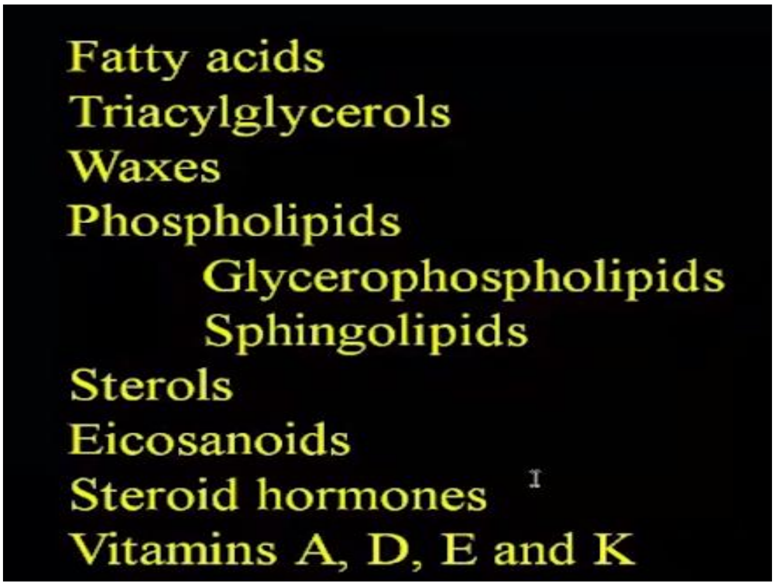

So next we will let us move on to the next lipid class which has waxes.

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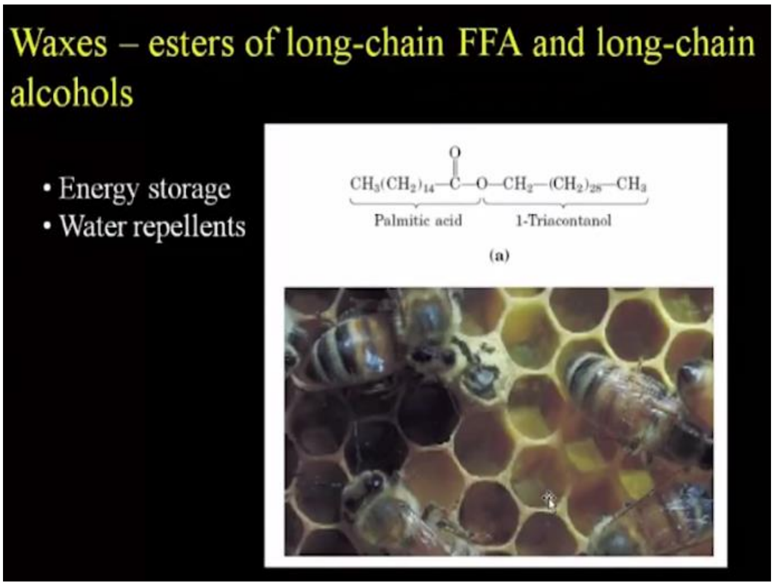

So, waxes as I told you at the introductory class so these are long chain free fatty acids in easter linkage with long chain fatty alcohols. These are CH 2 CH 2 CH 2 like in a long chain with an alcohol group and with that you have a free fatty acid like palmitic acid on a 16 carbon and hexadecenoic acid if you want to follow the systematic name. So that sort of an ester two long aliphatic chains, one has carboxylic group, another one has the alcohol group and the ester is nothing but wax.

So, you can see the usefulness of wax here in this image here. The honeybee nests this honeycomb structure it is made of wax. So, this is mainly is an energy storage like other lipids. Its primary function is actually water repellent. So, you would have seen many shiny leaves and the shininess of the leaves is due to a layer of waxes. Some of the micro photosynthetic ocean organisms called planktons they store much of their fuel in the form of waxes.

So that is about wax and the waxes are important. So, waxes are there even in sperm whale as well. And these are useful in cosmetic industry for preparing fragrances of many different varieties and for them these waxes are important. And due to that some of these organisms that produce these kinds of fats they are hunted down nearly to extinction, for example the sperm whale. A single whale gives you 4000 liters of fat and therefore people hunted these for getting lamp oil.

You know before fossil fuel, the petroleum was discovered, people were relying on these oils to light lamps particularly in the western world. So due to that these whales are now in endangered species, you know only very few exist now.

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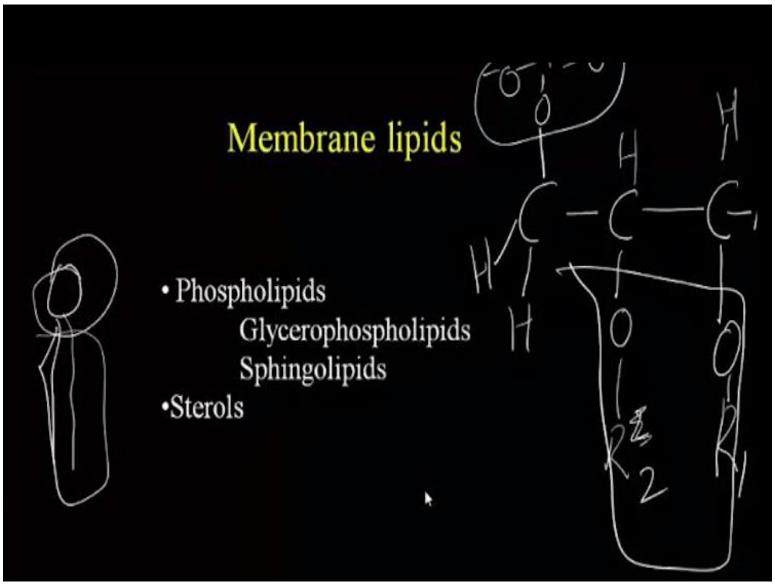

And the next class is a major one which is the phospholipids, membrane lipids. We already know about these phospholipids are the head group which is the glycerol where you can have hydrophilic moieties and two of the alcohol groups in glycerol can have acyl moieties with the free fatty acids and that is how you get this structure. So, this is the glycerol head group and these are the two acyl moieties that we draw.

So, essentially it is this structure. So here you have an acyl group, let me put as R2 and this as R1, so CH 2 OH. So here you can have a power group like for example you can have a phosphate group, the other one I am not writing this, it is going above the board. So this portion can have other hydrophilic groups attached and that is what is this the head group and these two chains here this is what your long chain here.

So, these are the phospholipids and the phospholipids are of two types. One is glycerophospholipid and the other one is sphingophospholipid. So, we look at both of these now.

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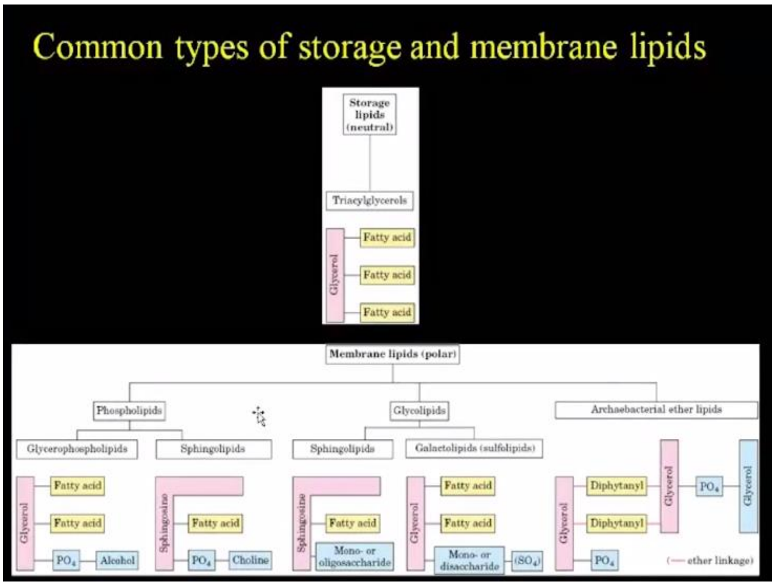

So **so** this triacylglycerol you are already familiar with, the storage lipid. Now we are looking at the membrane lipid because they are polar and one major group among them is the phospholipids and phospholipids there are two types. Glycerophospholipid, the structure that I just drew is glycerophospholipid and there is one more called sphingolipid that also can have phosphate group.

So, we will revisit the glycolipids later. So, let us first deal with the phospholipid and understand their structure and then come back to glycolipids.

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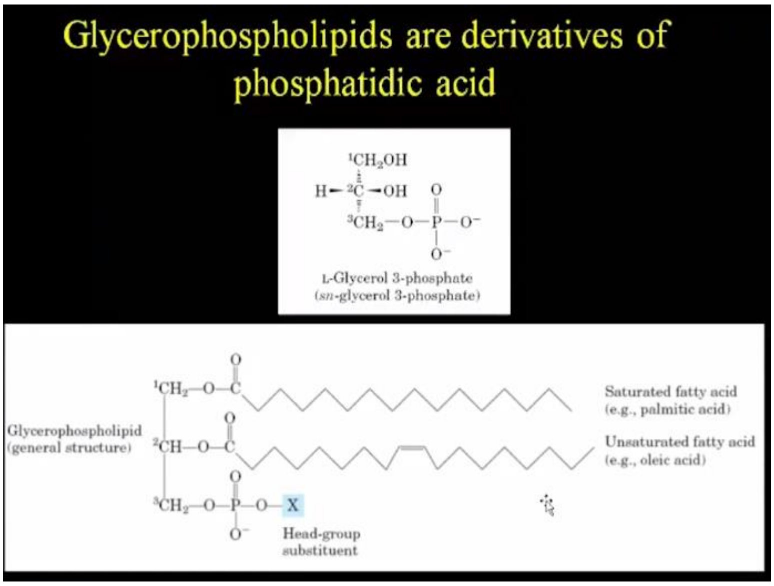

So the phospholipids; the first one is the glycerophospholipid. So here you have the glycerol CH 2 OH CH OH and then CH 2 OH. This is in ester bond with mineral acid phosphoric acid. So here you have two groups available for further attachment to other groups and this is the glycerol 3-phosphate. So, this is the third carbon. So, it is glycerol 3-phosphate. So, these two can have ester linkage with the fatty acids.

See here one shown with double bond and this phosphate group can be further derivatized with polar groups and that is what is the head substituent. This basic one where it is just the phosphoric acid is called phosphatidic acid, so written here phosphatidic acid. So phosphatidic acid is the simply diacylglycerol where the phosphate group is just the phosphate, nothing, no other group is added OH, OH.

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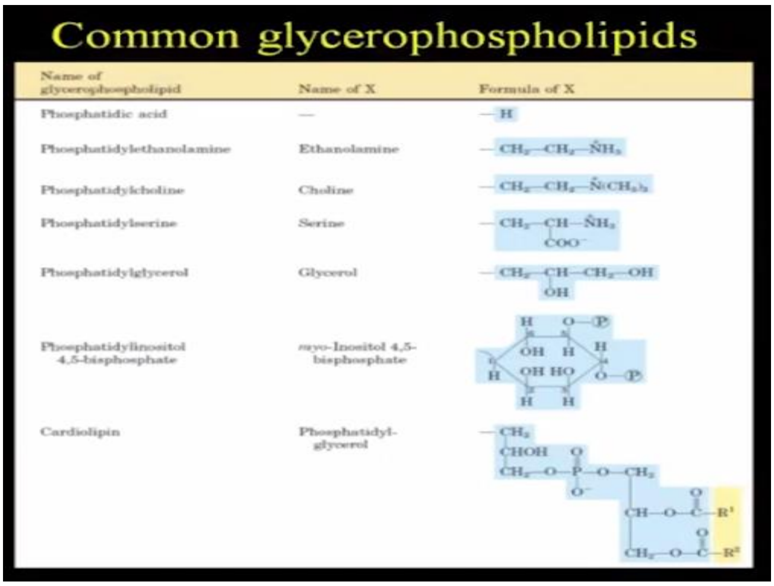

And it can have derivatives. So phosphatidic acid simply here hydrogen there. Then you can have an ethanolamine there or you can have a phosphatidylcholine, so this is very important in bile salts which is required for emulsifying fat in our food for digestion in the small intestine. So, these are part of the bile. So, for now you need not worry about it that we think when we go to fatty acid metabolism.

So, like this there are variety of groups, I am not going to read out each one of them. So you get the idea, so this group can have variety of polar substitutions and that forms the head group and these are the two tails. So that is how you have lipid bilayer. So, you have two leaflets there. So, you have head group on one side and then head group on the other side. So just to make sure nobody has confusion I will draw this again.

So, you have the two acyl groups and the head groups where in phosphatidic acid it is simply the phosphate and it could be derivatized. So, you have one leaflet like this and then you will have one more leaflet as well. So, therefore these hydrophobic groups face each other and therefore they have hydrophobic interactions and these polar groups face this could be the extracellular matrix outside of the cell and this could be cytoplasm cytosol.

So, both side it is aqueous environment and here is the hydrophobic. So, this is how the phospholipids form the cell membrane. So the next one, so these are glycerol derivative phospholipids therefore we call glycerophospholipids.

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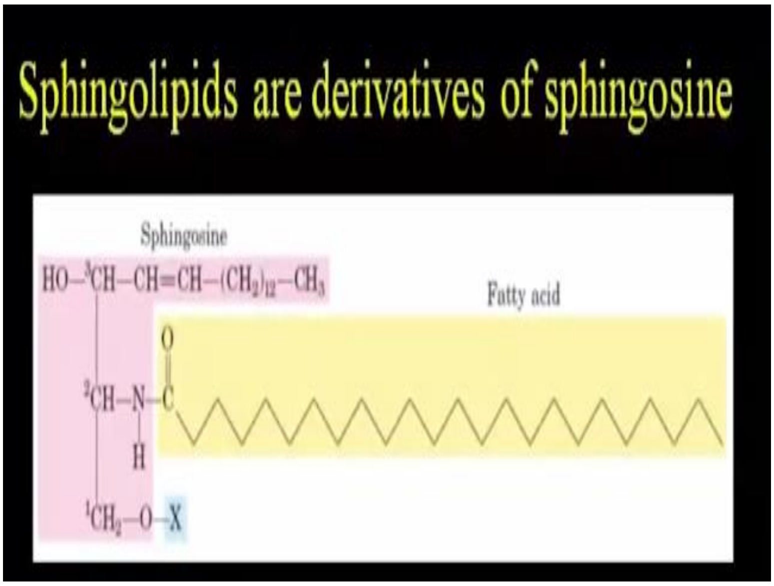

So, the next one is spingolipid where instead of glycerol it is the sphingosine. This pink color shaded one. So, sphingosine is the basic unit. So sphingosine as drawn here its first three carbons resemble glycerol's three carbons, but its side chain yes it is a long amino alcohol, so it has OH groups and then an amino group. It is a long chain amino alcohol having one double bond and in the second carbon you have the acyl moiety there.

And then this alcohol group can be derivatized with polar groups just like the glycerophospholipids. And when you have a phosphate group here and that becomes the basic sphingophospholipid and its name is ceramide.

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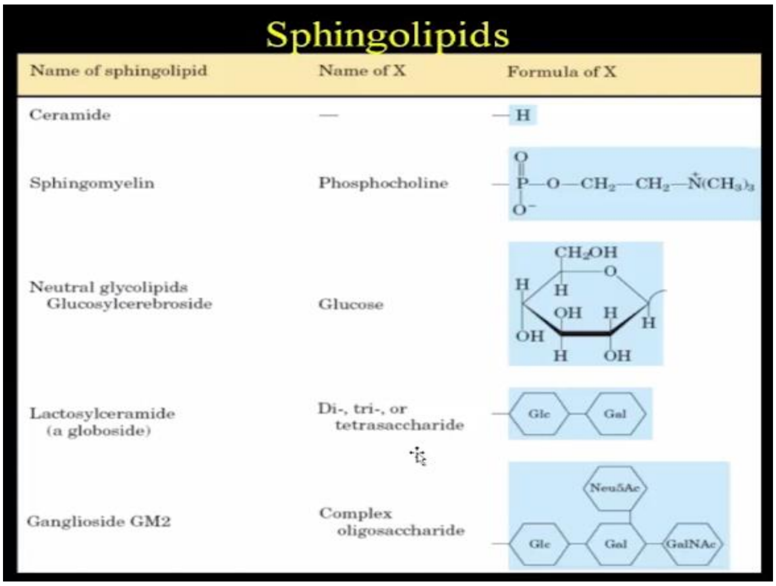

Shown here ceramide. And to that if you have phosphocholine attached then it is sphingomyelin. This is what covers the long axons of our neurons and insulates them electrically and it insulates against heat as well. So primary insulation that is electric so that that is what is the sphingomyelin. It is present in the myelin sheath and that is why we call myelin.

This sphingo itself has an interesting history to it because the person who discovered this molecule could not understand what it actually does and what is its important function. So, therefore he thought it is mystery like sphinx in Egyptian civilization and therefore he called them sphingolipids. They are mysterious like sphings. And so that is sphingomyelin and then you can have one glucose alone.

So ceramide is just this OH group and when you have instead of phosphocholine this sphingomyelin. And if you have only one glucose attached to the OH cerebroside. Instead of glucose if you have lactose like galactose glucose, then it becomes a globoside. And when you have multiple sugars oligosaccharides, then you have a ganglioside and there are varieties of gangliosides.

So, again I am not going to bother you with all the individual names of these substituents, but you need to have this main idea sphingolipids have sphingosine base and then their amino group have a long fatty acid chain attached and therefore it will be the hydrophobic part, hydrophobic tails, and then one of the alcohol groups can be derivatized. So, without any derivative it is ceramide, then you have various derivatives.

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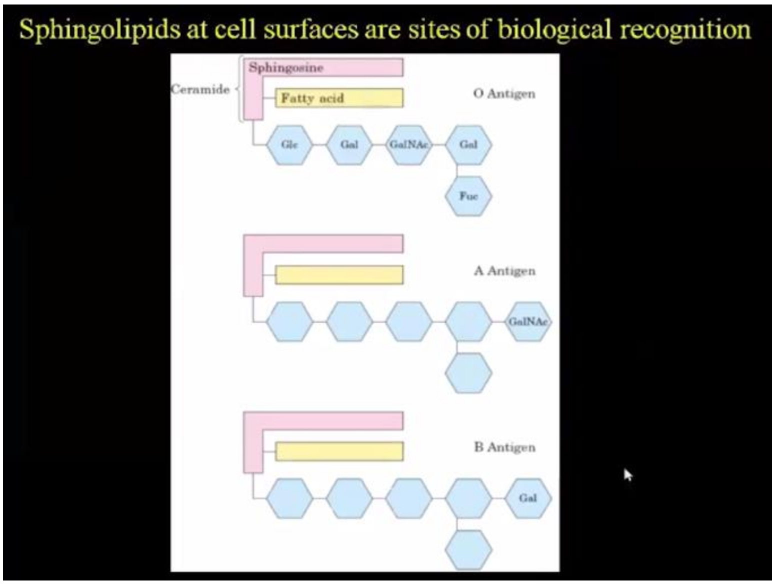

So now an important aspect of sphingolipids is shown in this slide that is our blood groups. So, given that this will be the tail in the membrane and this will be on the surface you know the head group this is polar. So here if you have this sequence this particular oligosaccharide glucose, galactose, N-acetyl galactosamine, galactose and fucose then that is recognized. You remember these are address tags, sugar code we learned yesterday.

And this structure when it is present on the cell surface that is O antigen in our blood cells and you attach one N-acetyl galactosamine to this galactose, you are A group. So, antibody specifically bind to this that do not recognize this. And instead of N-acetyl galactosamine you have just galactose that is B antigen. So, this is the biochemical basis of A, B, O blood group.

So, if you have an AB b blood group, then your cell surface RBC surface has both these sphingolipids. So, sphingolipids are the antigens A, B and O. So, they are important for biological recognition. So we are done with the phospholipids. So I think we kind of, yes we glossed over or we ignored this particular group. I will spend one minute on this.

So, instead of these phospho groups in the glycerophospholipid you can have sugar moiety directly added into this alcohol group of glycerol and when you have them, they become the galactolipids and usually remember we have learned the carbohydrates, monosaccharides can have or acid groups like carboxyl groups, sulfate group attached and usually they are sulfated mono and disaccharides and that is galactolipid.

Then you have this sphingolipid, instead of the phosphate group you could have an oligosaccharide attached and they are the sphingoglycolipids. So, this is phospholipid group where the phosphate becomes part of it and here oligosaccharide is the one that is hydrophilic group and therefore these are glycolipids. So, you have two types of membrane lipids, one is the phospholipid and another one is the glycolipids.

So do not worry about this, this is too much for an introductory group. So, introductory biochemistry class I am going to ignore these archaebacterial specific lipids because I am sure already you are going to complain that we are learning a lot of molecular structure.

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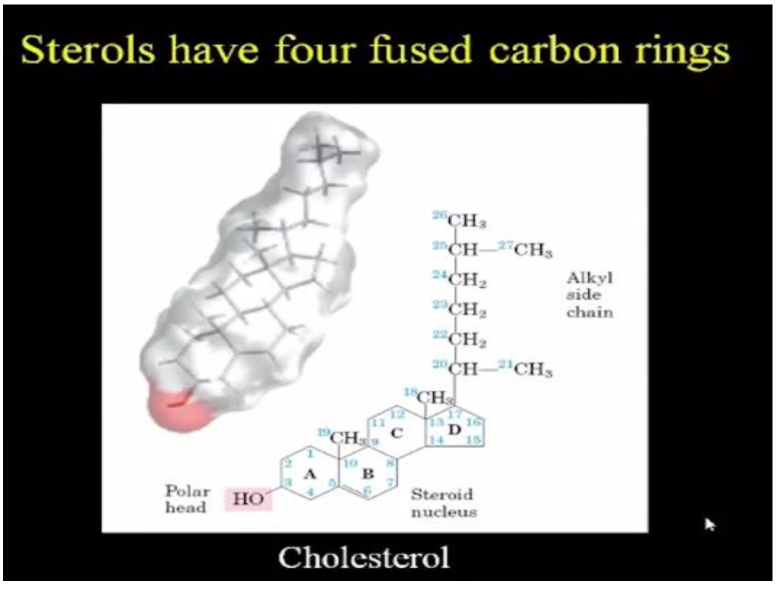

So, the next is something that we cannot ignore like the way we ignore the archaebacterial specific lipids. Sterols are very important. Cholesterol is one of the main components of our biomembranes. It is important to determine the fluidity in addition to the unsaturation in the fatty acid moiety of the phospholipids, presence of cholesterol in the membrane is also important for membranes unique dynamics.

And the cholesterol is a main example of a class of lipids called sterols and the basic structure of sterol is the presence of these four rings. This is cyclopentanophenanthrene ring. So these three benzene rings attached in this fashion is what we call as the phenanthrene and this is cyclopentanophenanthrene. And to that you might have a side long alkyl side chain as seen in cholesterol and some may not have this and these groups will vary from sterol to sterol.

This is the specific structure of cholesterol. So, you have a polar head already an OH, this is the polar group and you can have more polar moieties attached via this hydroxyl group here. And cholesterol is also important storage sterol and it is also the precursor for the formation of many steroid hormones that we will see in the next slide. And the cholesterol is also added to a peptide like signaling molecule.

Which you probably will learn in cell signaling as part of cell biology class or much later if you take developmental biology elective and there I will talk about cholesterol modified signaling molecule that is critical for many developmental processes. So, now let us look at the steroid hormones.

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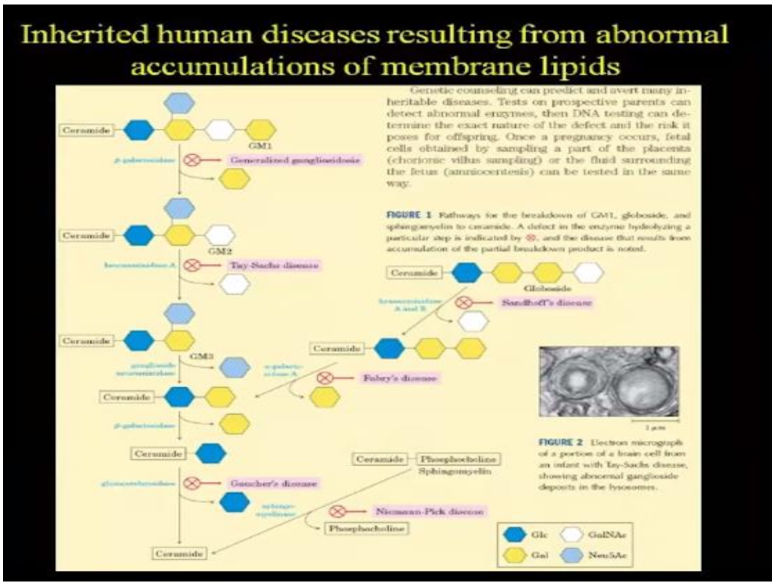

Okay before that there is one important side note that we need to learn. So, these oligosaccharides that you find in phospholipids and sphingolipids, so here this picture is showing primarily sphingolipids or only sphingolipid here, yeah it is all sphingolipids. Ceramide in one side and then here you have the globoside, sphingomyelin. So here the breakdown of specific polysaccharides or specific carbohydrate sugar moiety from this long chain is catalyzed by specific enzymes.

For example from this ganglioside, remember ceramide with the oligosaccharide is what we learned as ganglioside you have a beta galactosidase enzyme that removes this particular sugar. And if this enzyme is not present, suppose someone has a genetic mutation and as a result they do not produce this enzyme then they cannot hydrolyze this and that leads to a disease called the generalized gangliosidosis.

And similarly, another pathway where you have problem the next step actually you have Tay-Sachs disease and so on. At each step if that particular enzyme is mutated you have a particular disease because of the failure to metabolize these molecules. And if someone in a family is known to have this disease, then you can diagnose in the offspring by taking amniotic fluid.

You know the fluid that cushions the developing embryo and look for whether that mutation is there or not in that amniotic fluid, the cells present there one can culture and find out whether that mutation is there. Then accordingly you can counsel them, a process called the genetic counseling. So, the main point here is there are many inborn errors in metabolism, meaning genetic mutation so it is there you know in birth itself and they cause problems in lipid metabolism leading to human diseases.

So, these are in general called inborn errors in metabolism, meaning they are already there when you are born and these are errors in metabolism, metabolism fails in this process. And since this is based on DNA sequence, it can be diagnosed and genetic counseling can be used to counsel the people about going ahead with the given pregnancy or marrying that person is right thing or not given your genetic consolation and so on.

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So this is kind of setting the stage for our next transition of lipid functions which is lipids function as signals. They are not simply compact storage of energy or compartmentalization as we see in cell membrane. They can act as signaling molecules and they can be co-factors in enzyme-catalyzed reactions and they are pigmented as well which are very important. So, we will go ahead and look at them what they do in each one of these authors.

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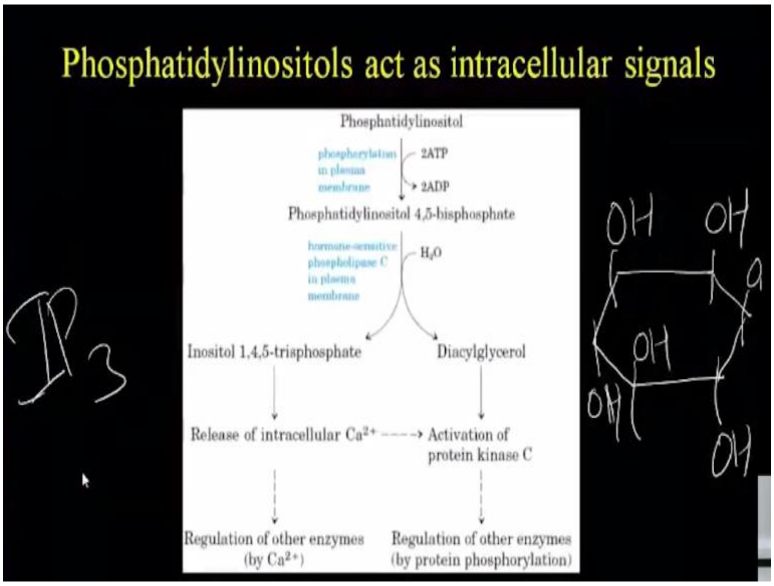

First, we are going to look at as signaling molecule. Phosphatidylinositol, we know phosphatidic acid right, glycerol having two acyl groups and the third alcohol group has phosphate and that is phosphatidic acid. If that phosphate has this sugar alcohol inositol, so inositol it is like glucose structure it is just that as OH everywhere. I am ignoring the hydrogen in the interest of time and then an OH here and then an OH here.

So, this is inositol. It is a sugar alcohol. You do not have CH 2 OH here, then otherwise it is like any other hexose and when that is attached to phosphatidic acid that is phosphatidylinositol. And this is a membrane lipid and this could be further phosphorylated leading to what is called phosphatidylinositol 4, 5-bisphosphate. So you need to understand the difference in biochemistry between biphosphate, bisphosphate, trisphosphate as written here versus triphosphate.

So, here for example 1, 4, 5-triphosphate means this particular hydroxyl group was an in ester linkage with the phosphate of the glycerol. And in addition, you have in the fourth position a phosphate attached and a fifth position a phosphate attached. So, three different alcohol groups having the phosphate that is trisphosphate. If you have two of them then it is bisphosphate.

Instead you have a phosphate attached to one of them and to that phosphate you have another phosphate and another phosphate as you see in ATP that is triphosphate. Three phosphates attached in tandem to one alcohol group, so that is triphosphate. So, this is how tri and tris differentiate the different structures. Tris means three different alcohols having monophosphates, tri means one alcohol group having three phosphates.

So, this inositol 4, 5-bisphosphate you know which is made on the membrane, the membrane phosphatidylinositol, the inositol moiety can be phosphorylated twice by transferring from ATP. So, this will be ATP phosphatidylinositol phosphotransferase that will be the name based on whatever we learnt about naming enzymes. Remember the enzyme commissions 4-digit names.

And this molecule produced in response to extracellular signals that bind to specific receptors on the membrane can be hydrolyzed to produce, so once in the phosphatidic acid if you remove the phosphate out then it is simply diacylglycerol. So that is going to be part of the membrane because of the acyl groups. While this inositol that is hydrolyzed the phosphatidic acid’s phosphate now remains with the first carbon of inositol.

So you produce inositol 1, 4, 5-tris phosphate or very affectionately signaling people call it as IP 3. So this IP 3 is the major intracellular signaling molecule. So, this is produced by extracellular signals that interact with the membrane bound receptors leading to inositol phosphorylation and hydrolysis to release the inositol trisphosphate. This moves within this cytoplasm and releases stored calcium.

For example, endoplasmic reticulum and the calcium released in conjunction with the diacylglycerol activates protein kinase C which is an enzyme that phosphorylates' proteins. Remember covalent modification of proteins can activate or inactivate them. We saw the phosphorylase being activated by phosphorylation and that phosphorylated phosphorylase being inactivated by removing the phosphate group.

So, by phosphorylating downstream target proteins this protein kinase C modulates activity within the cell. So that is how the extracellular signal is transduced by the production of intracellular signaling molecule IP 3. So, this is one way by which lipids act as signaling molecules.

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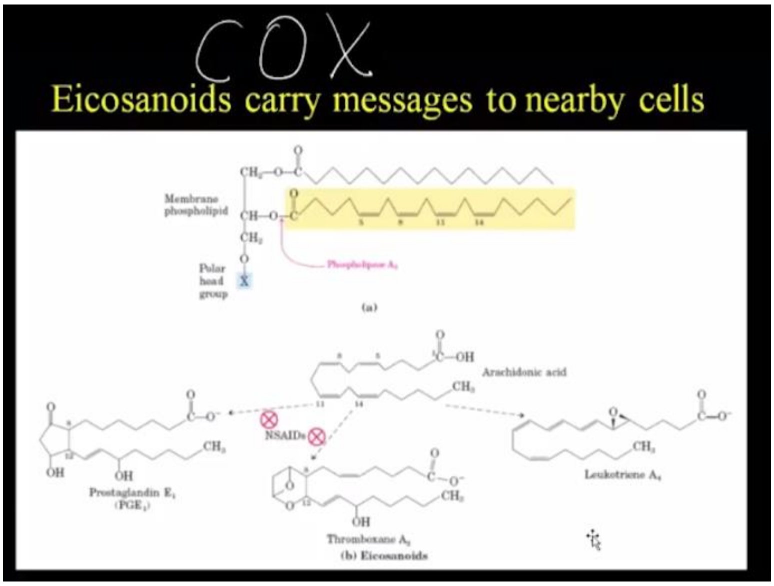

So next is a major class of signaling molecules prostaglandins, thromboxanes, and leukotrienes. The discovery of prostaglandins was considered so significant that the discovery has won Nobel prize for having discovered prostaglandins. So, these were first isolated from prostate gland and that is why the name prostaglandin, but they are produced by other tissues as well. So now let us get to them from what is familiar to us.

So, we already know this structure diacylglycerol group and with this polar head group. So, I glossed over or I did not even talk about these enzymes called lipases, they are named based on which bond here, you know they cleave here, cleave here, cleave here, cleave here they have their names a1, a2, b, c and so on. So, you do not need to worry about it. In this particular example, here you have the fatty acid chain with the four double bonds.

And this is arachidonic acid, 20 carbon fatty acid with the four unsaturated bonds and this is released from the membrane in response to signals and this shown in a hairpin shape here for convenience of moving to the next step. This is the free arachidonic acid, it is a carboxylic acid with four double bonds and there is an enzyme called cyclooxygenase or affectionately COX.

So it is basically cyclooxygenase because it cyclizes this structure. This linear structure by this bond formation here becomes a cyclical structure and that is a prostaglandin. There are many derivatives that is what is indicated by E1 here. So, I am not going to get into those details, not necessary here. And this is how biosynthesis of prostaglandin takes place. And a different modification your thromboxane and then another one leukotriene, so this is not cyclical.

So here you have this peroxide kind of structure here. So, these are three molecules produced from this 20 carbon fatty acid that is where the name comes from eicosanoids, eico standing for 20 carbon. Deco means 10 and eico is 20. So, these three together are called eicosanoids. Now let us look at individually each one of these three what they actually do and probably we will stop there today.

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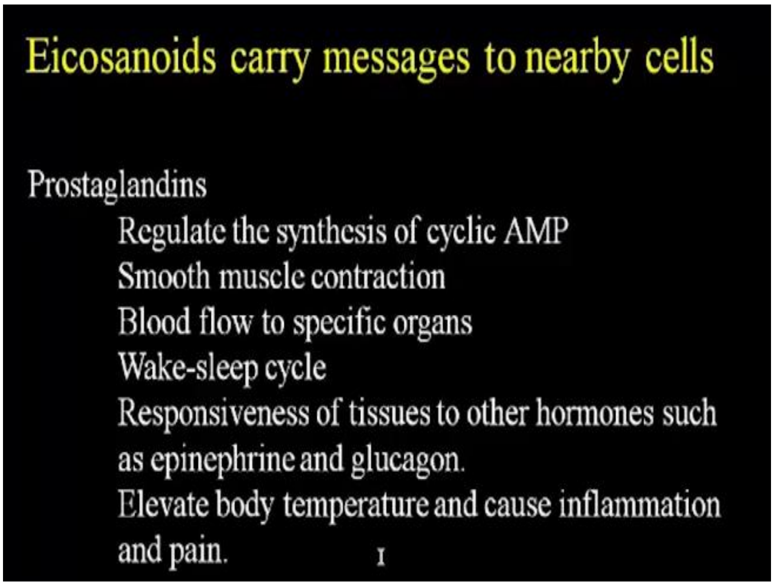

So prostaglandins they regulate the synthesis of cyclic AMP. So, this is an internal phosphate linkage between two hydroxyl groups two alcohol groups of the ribose, a single phosphate. Remember the phosphate has H 3 PO 4. You have three acid groups there, so it can actually make three ester bonds and the cyclic AMP has only two ester bonds between the third carbon and the second carbon of the ribose and that is what is cyclic adenosine monophosphate.

So, this is an important second messenger intracellular like IP 3. I introduced word here second messenger, right. So, I will explain that. You are already kind of familiar in the context of IP 3. The extracellular signal coming from somewhere else and binding to the cell surface receptor is the primary messenger, so you can call that as first messenger. In response to that internally in the cytoplasm you produce molecules like cyclic AMP or IP 3.

And they are the second messengers because they are still messengers. They have to go and tell someone to do an activity like for a protein kinase that needs to modify something to change their activity. So that is where this idea of second messenger comes from. So, the cyclic AMP is an important second messenger regulating variety of processes. Therefore, prostaglandins regulating the synthesis of cyclic AMP has influence on regulating many processes.

One a primary one being smooth muscle contraction. So, this smooth muscle contraction is the primary reason you have menstrual cramps. So, the prostaglandins are the hormones that stimulate the smooth muscle to push out the air follicle out and similarly during childbirth the very same thing the prostaglandins induce the smooth muscle contraction to push the fetus out and prostaglandins therefore play a very important role.

And they regulate blood flow to specific organs, again that comes from smooth muscle contraction. Blood vessels are smooth muscle and whether you are going to dilate it or constrict it is determining the blood flow and that is directly controlled by prostaglandins. In addition to this role on smooth muscle contraction, they are also important for wake-sleep cycle, responsiveness of tissues to other hormones such as epinephrine, glucagon.

You are not going to learn about them, so do not even worry about it. So, they are hormones regulating processes in the body and the body temperature elevation when you have inflammation and pain. So, if you have an inflammation and pain due to some infection and you want to control that you block prostaglandin. So temporarily you are relieved from the pain and inflammation and that is exactly what happens when you block the COX enzyme here.

You see this red cross circle here. So this is an inhibitor, remember enzyme inhibitors we have a learned. The most famous enzyme inhibitor is aspirin, you know acetylsalicylic acid the most common painkiller that people take and the aspirin blocks this COX and as a result of prostaglandin production is reduced, and due to that inflammation and pain is temporarily relieved. And these are non-steroid anti-inflammatory drugs and that is why they are called NSAID.

What it indicates that there are steroid class of anti-inflammatory as well. So, we will learn about them later, but for now the focus is NSAID which is aspirin. The main example is aspirin which blocks this enzyme, as a result you do not make prostaglandin and as a result you do not have pain and inflammation and it controls fever as well.

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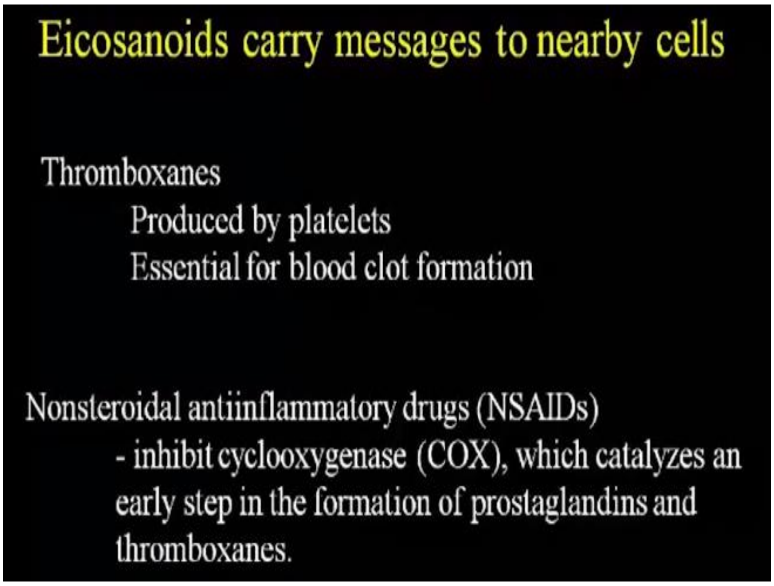

So, the next one is thromboxane. This is produced by platelets. These are like fragments of cells present in our blood and they are important for blood clotting and that is induced by thromboxanes. And so this I talked about NSAID already.

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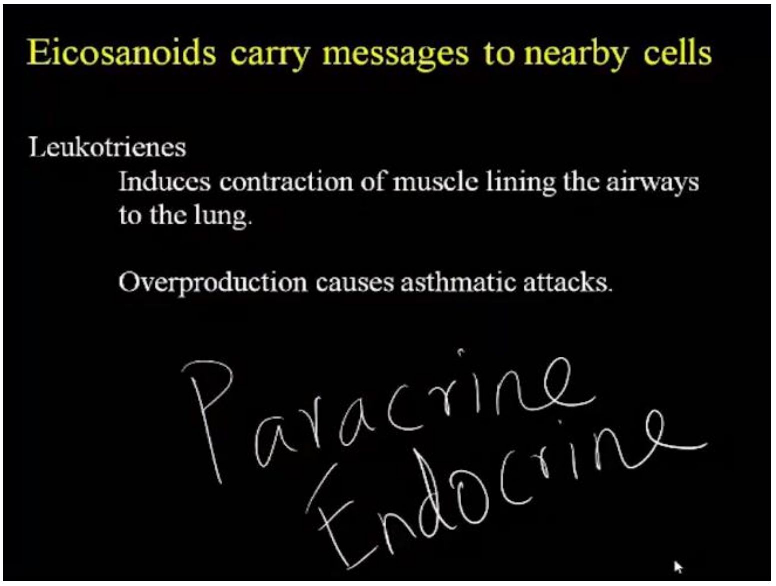

So, the third one is the leukotrienes. So, leukotrienes are involved in contraction of muscle linings of the airways of the lung. So as a result, too much leukotriene means constriction of airways and therefore you do not breathe well and that is the cause for asthma. So, some allergens like pollens can stimulate overproduction of leukotriene and the overproduction of leukotriene leads to contraction of the airway muscles.

The muscles that help in breathing they are pushed to the contracted mode and as a result you are unable to breathe well and that is what is asthmatic attack. So then anti-inflammatory drugs focus on preventing production of these signaling molecules and therefore these issues do not happen. So, these eicosanoids they all work in nearby cells from where they are produced and as a result they are called paracrine signals.

The molecules that travel long distance like insulin or epinephrine, glucagon written in the previous slide they travel from one organ to other organs a distance via bloodstream and they are called endocrine. So, we will learn probably a little bit about insulin later and otherwise we are not learning endocrinology as part of biochemistry. So, the paracrine molecules work nearby the area where they are produced. So, these eicosanoids are paracrine signals.

So, with this I will stop here today. Then tomorrow we will continue to co-factors, how lipids function as cofactors and how lipid derived pigments are important metabolism. So those aspects will cover in on Monday.