Introduction to Biomolecules
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Lecture-29
Fatty Acid Catabolism (Part-2/2)

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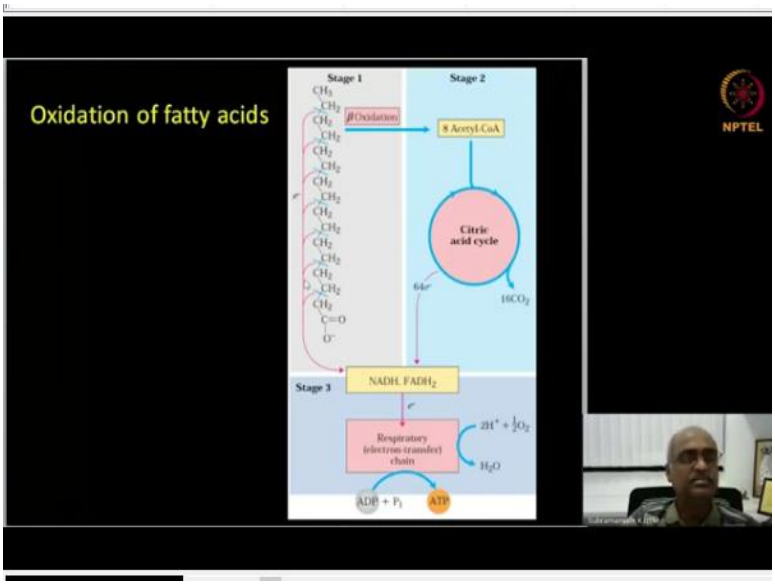

I will begin with answering your question. So, the reason you see the transporter only on the inner membrane and not on the outer membrane is because the outer membrane bound the enzyme carnitine acyltransferase, that enzyme is believed to transport when it actually transfers the acyl group to the carnitine. But the mechanism has not been fully worked out. So, the current thinking is that the enzyme releases the product into the inter membrane space.

I do not see any other question, so let us continue with our discussion on fatty acid oxidation. So, yesterday we saw how overall lipid digestion and mobilization from stored lipid results like lipid droplet and the connection of the endocrine system that is glucagon and epinephrine how they activate a protein kinase which phosphorylates perilipin and hormone sensitive lipase and mobilizing lipid all that we saw.

So, today what we are going to do is once the carnitine shuttle transports the fatty acids into the mitochondria. So, in the mitochondrial matrix is where the fatty acid is broken down 2 carbons at a time as shown in the cartoon here and since it like so in the conventional notation

so as per IUPAC this carbon will be 1, 2, 3, 4 and so on. But the conventional notation is this will be alpha, beta and gamma and so on.

But regardless of the length the last one is always called omega. So, when you say omega 3 unsaturated fatty acid body mean actually is double bond here, omega 1, 2, 3 and a double bond here. So, since this is the beta carbon and oxidizing this is what happens here and that is why it is called beta oxidation. So, we look at the individual steps of the beta oxidation.

So, essentially these 2 carbons will be broken up as acetyl-CoA and the carboxylic acid will be with this and then next these 2 and these 2 and so on. In 8 such cycles of reactions you will have this entire palmitic acid 16 carbon, fatty acid converted into 8 acetyl CoA molecules and this is stage 1 and the acetyl-CoA produced thus will enter into TCA cycle and get completely oxidized into carbon dioxide.

And the reducing equivalence will move to the third stage which we are already very familiar which is the electron transfer chain on the mitochondrial inner membrane. So, we will focus on this beta oxidation as the main thing today.

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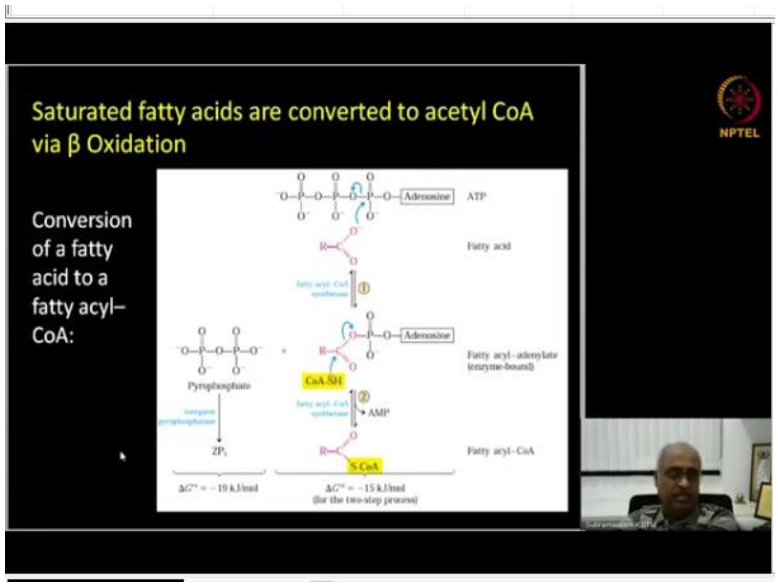

So, before that this we saw a little bit not in this detail but we saw this in last class as well, where I said the free fatty acid that is transported in the bloodstream by non-covalently binding to alb in when the fatty acid transporter transports them into the cytoplasm, where it is going to be oxidized for example muscle cells. The first thing is it gets activated by combining with coenzyme A fatty acyl CoA synthetase.

And this fatty acyl CoA synthetase reaction is given into detail here. So, essentially it has 2 steps, the first step is the alpha phosphate of ATP combines with this carboxylic acid forming and mixed anhydride on the enzyme surface. So, this intermediate is on the enzyme. So, that is enabled by a nucleophilic attack on this phosphorus, remember this phosphorus will be positively charged due to the electronegativity of the oxygen and this dissociated hydroxyl group this therefore readily has a nucleophilic attack on this phosphorus and that is what leads to this anhydride formation.

So, remember the hydroxyl group on phosphoric acid is an acid group unlike the hydroxyl group on organic molecules where they are alcohols. So, therefore this linkage is an anhydride linkage and this once again I want to draw your attention on this carbonyl group that we learned long time ago. So, this carbon is going to be partially positively charged.

So, again a good nucleophilic attack by this thiol group leading to the formation of acyl CoA just like acetyl CoA that formed from pyruvate. So, and this anhydride formation releases this pyrophosphate which readily hydrolyzes and that again drives the reaction in this direction because of the stabilization by hydrolysis of one of the products formed from this reaction which is inorganic phosphate.

So, overall therefore this has a negative delta G. So, this is how first fatty acid is activated by combining with a good leaving group which is this thiol group here. So, this fatty acyl CoA synthetase is therefore an important enzyme a subjective regulation and there are many isozymes for this in different organisms so we do not get into those details. So, this fatty acyl CoA in this form is what the entry into the beta oxidation.

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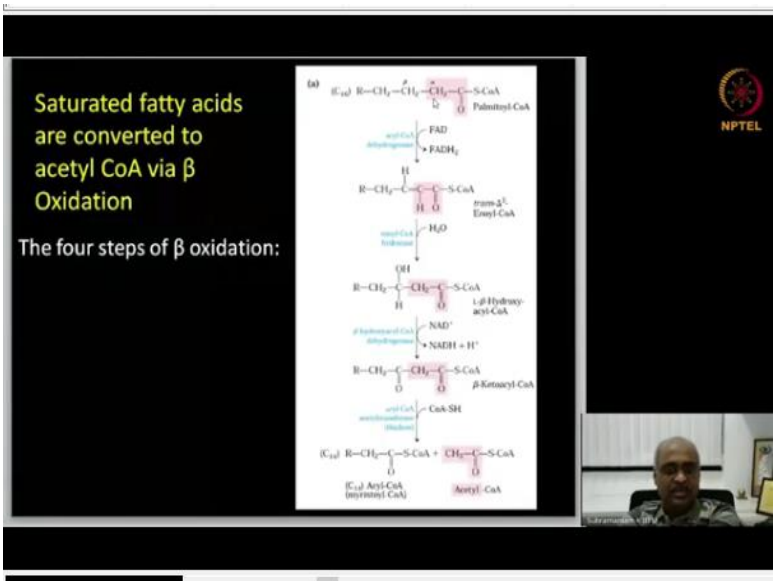

So, beta oxidation is extremely simple and very elegant mechanism of breaking down stable or carbon-carbon bond that we see here. So, the carbon-carbon bond, the methylene bonds in free fatty acids is very stable and that is cleaved by this beta oxidation scheme which actually is extremely easy for you to know simply because you have already encountered them in a different context.

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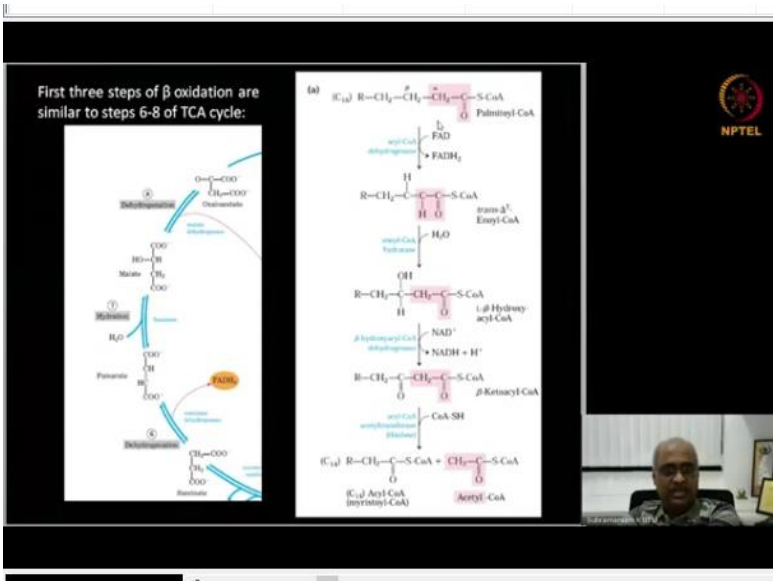

So, I put that also on the side, then this will become easy. So, this is part of the TCA cycle, the last 3 steps in the TCA cycle. So, the succinate formed by succinate CoA synthetase from alpha ketoglutarate we get succinyl CoA and from succinyl CoA we get the succinate and the succinate we already know that through membrane bound, this is remember in TCA cycle where everything else happens in the matrix.

This one reaction happens by the enzyme bound to the inner membrane and that directly transfers to the complex 3 instead of going via complex 1. So, this is actually complex 2 by itself and use this flavin nucleotide as the oxidizing agent here that gets reduced during this. So, essentially what is happening is between this alpha and beta carbon you have a double bond introduced by removal of hydrogen atom.

So, that is why it is dehydrogenase and then you get double bond and then this is hydrated it is a hydration reaction so the enzyme can be called hydratase, where this and you have an this carbon getting oxidase, the beta carbon getting oxidized by forming a hydroxyl group there instead of the original hydrogen now it is a hydroxyl group and the other hydrogen of the water is with this when you reduce this double bond.

So, therefore this carbon is now oxidized, now at dehydrogenase malate dehydrogenase which uses NAD as a oxidizing agent here converts this into a keto group and that is how oxaloacetate is formed. The exactly 3 steps involving same co-enzymes and the first enzyme bound to the inner surface of the mitochondrial inner membrane is what happens in beta oxidation. So, now let us turn our attention to beta oxidation.

So, this is we are taking palmitoleic acid as the example here. So, palmitoleic acid as the name suggests is very rich in palm oil. So, this is a fully saturated 16 carbon fatty acid. So, this carbon and this carbon alpha and beta are equivalent to the succinates these 2 carbons. So, you have a dehydration reaction, so succinate dehydrogenase here instead of the substrate name being palmitoyl CoA dehydrogenase.

Generically for any free fatty acid it would be acyl CoA because this moiety is called acyl, the aliphatic chain with the carboxylic acid moiety is the acyl moiety. So, the substrate is acyl CoA and therefore it is acyl CoA dehydrogenase and it uses the same substrate oxidizing agent and the FAD gets reduced to FADH 2 and this directly enters into the electron transport chain via on an intermediate complex called ETF that we learned when we were looking at the electron transfer complexes.

So, if you remember there are multiple routes to get to complex 3, one is via the complex 1 to complex 3 via ubiquinone and then we had the succinate dehydrogenase and then the third was this fatty acid oxidation and fourth is actually glycerol phosphate from the outside

entering directly into complexity. That is what we saw when we learned about electron transfer chain.

So, here we are only focusing on the fatty acid oxidation. So, this enzyme does very similar reaction as the succinate dehydrogenase. So, you have a double bond here between alpha and beta. Now this is an enyl group so therefore it is called an enoyl CoA hydratase because it hydrates that molecule and in that process this beta carbon is oxidized instead of a hydrogen now you have a hydroxyl group.

So, that this is the reason why it is called beta oxidation. Then so this is equivalent to fumarase reaction. So, this is as we are calling fumarate hydratase. So, like that it is enoyl CoA hydratase. Now this is a beta hydroxy acyl CoA and dehydrogenase would be called beta hydroxy acyl CoA dehydrogenase. So, that uses NAD as the coenzyme exactly the same way as malate dehydrogenase converting into oxaloacetate.

So, you have got a beta-keto acid there and here again beta-keto acyl group. So, these 3 therefore are very similar to the TCA cycle. So, you introduce a double bond then you add water in the process one of the carbons that is the beta carbon it is oxidized to hydroxyl group then you have a dehydrogenation converting into a keto group. So, these are the 3 first steps of the beta oxidation.

So, the long chain fatty acid. So, these 3 exist in the mitochondrial inner membrane attached to the inner membrane on the inner phase of it as a tri-functional protein TFP it actually is a hetero octamer alpha 4 beta 4 hetero octamer because 2 types of subunits alpha and beta and 4 each therefore it is an hetero octamer and it ensures that all of this happened with no substrate leading from the enzyme surface.

So, therefore this is also an example of substrate channeling, but when the chain becomes shortened and when the free fatty acid chain is shorter like 12 carbon or below, then 3 different matrix enzymes that is present in mitochondrial matrix the same 3 functions but in 3 different enzymes, they catalyze further beta oxidation and the last step here is called commonly as thiolase.

But scientifically it is acyl CoA acetyl transferase because it is going to transfer this acetyl group. So, now you look at this carbon which had a very stable bond here now is actually bonded to 2 keto groups, one side it is this beta ketone on the other side it is the carboxylic acid ketone group. So, therefore this is going to be partially positively charged and this will have a carbon and an acidic character readily dissociating a hydrogen and the carbon ion getting resonant stabilized.

So, it is like a very good leaving group and it readily gets cleaved by this thiolase into acetyl-CoA. So, one more coenzyme A coming in and this is carried as acetyl CoA and you have 1 coenzyme A remaining attached with the free fatty acid which is now shorter by 2 carbons. Palmitoleic acid becomes myristoyl CoA or a 16 carbon free fatty acid becomes 14 carbon free fatty acid.

Now this can go through this cycle once more and then it becomes 12 and then 10 and so on and after 8 cycles you will have 8 acetyl CoA from 1 palmitoleic acid. So, this is what is beta oxidation.

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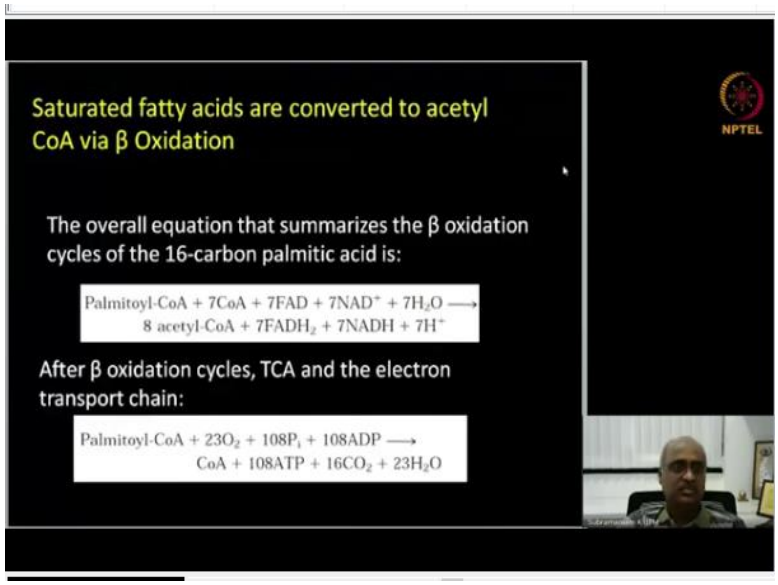

So, now let us take stock of the balance sheet here. So, overall equation therefore can be summarize this way, 1 palmitoleic acid, then 7 co-enzyme A and 7 FAD and 7 NAD, then 7 water molecule remember the hydration step produces 8 acetyl CoA and 7 FADH 2 7NADH . So, this will be the summary. But at the end of the entire oxidation that is this acetyl CoA produced here enters through the TCA cycle.

And then the electrons flow through the electron transport chain from these reducing equivalents produced here conserved in FADH 2 and NAD and at the end of all when oxygen molecules are converted into water and the acetyl-CoA carbons become carbon dioxide, this would be the balance. So, 1 palmitoyl CoA will consume 23 molecules of oxygen and 108 ADP molecules producing 108 ATP.

So, this is the net gain from 1 palmitoleic acid oxidation. So, the 16 carbons end up producing 108 ATP molecules and 16 carbon dioxides because you have 16 carbons so 16 carbon here as well and 23 molecules of water. This is very, very important. So, fatty acid oxidation actually generates water. So, our body does produce water from molecules that are not simply a hydration. So, from normal fatty acids you can actually generate water molecules. This becomes critical when we go to the next slide.

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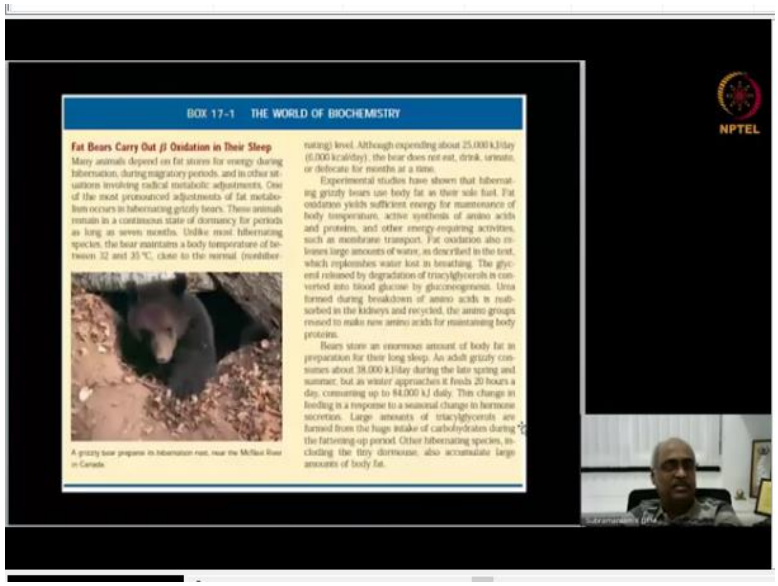

So, this is a box item as you can see it is coloured differently from the rest of the text. This is just connected to reality, so biochemistry is basically explaining the secrets of life instead of looking at yourself as a black box. Now you are able to see yourself as an amalgamation of molecules and what these molecules do in terms of energy storage, energy production and structures functions and so on.

So, this is an extra relation to everyday life. So, already the whole thing that we learn are all related to everyday life and this is to further illustrate that point. So, these animals here you see a grizzly bear, some grizzly bears live in northern part of North America. So, these are

large black bears. So, if you have seen our bears in western ghost these are like the bears in Western Ghats like black bears, ferry.

But these are really big, a single bear will be about 400 kilograms body weight and in northern part of north America like for example rocky mountains of Canada for 8 months of year it is frozen and serious winter and it does not get to eat, but remaining period particularly early spring and early summer it consumes a as you see here 38000 kilojoules a day equivalent of food primarily salmon the fish found in which come to fawn in the rivers there.

But as winter approaches like late summer and yearly autumn then it feeds about 20 hours a day consuming about 84000 kilojoules a day, what does it do with all of that? All of that are converted into triacylglycerols and stored under its skin subcutaneous fat; it stores a lot of it, because now for months nearly 8 months it is not going to get any food. So, it completely depends on beta oxidation.

So, it is going to remain dormant like that is why the title says sleep. So, while they are totally dormant what do they do during dormants? They do not eat, they do not drink, they do not go tired, they just stay still under some cave or some shelter. But by oxidizing fat that is stored this 84000 kilojoules eaten every day during the late summer and autumn, those fats are oxidized by beta oxidation.

That helps the bear to maintain normal body temperature 30 to 35 degrees outside frozen. So, it is able to maintain this because the beta oxidation gives you the required ATP to keep all metabolism going, protein synthesis is happening, all normal things going and I told you it does not drink water where does the water come from? It is these 23 molecules from every palmitoyl CoA.

And that is what provides its water. What does it do for glucose? It is you need glucose for the brain or if glucose is not their ketone bodies. So, these come from these triacylglycerols. Blood glucose, it is generated via gluconeogenesis and the amino acid catabolism leading to production of urea since it does not eat any new food and all stored is triacylglycerols the nitrogen of the urea is efficiently recycled into making new amino acids.

So, what I am trying to say here in this elaborate story is that solely using triacylglycerol and efficiently recycling nitrogen, it is able to have the entire metabolism of the body going normal using triacylglycerols alone. So, that is what they do and they lose a lot of weight by the time the spring comes and the cycle goes on. So, this is an interesting story about beta oxidation.

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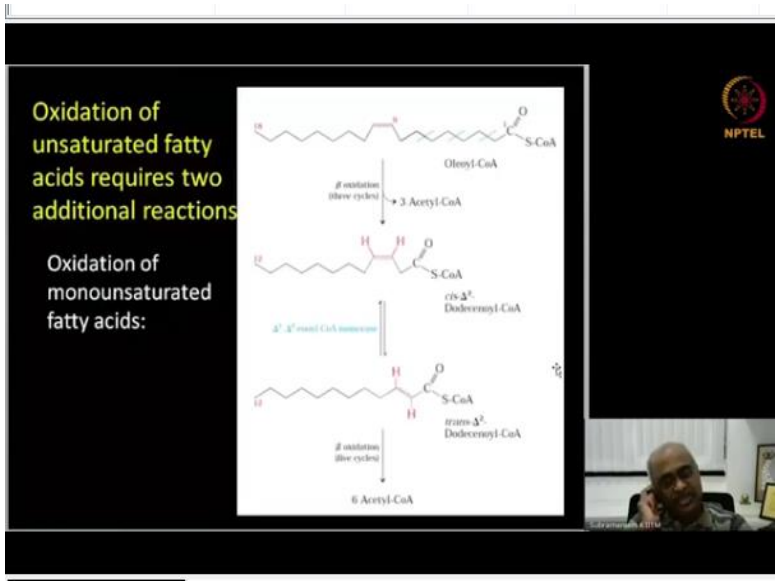

So, now so far so good the palmettoic acid had 16 carbon, so I could chop it in 2 carbon at a time and the final one also was 2, what if there were extra like instead of 16 it was 17 what do we do? One and the second if there is a double bond and we know that the naturally occurring double bonds in free fatty acids as well as in the ester form in triacylglycerol they all are cis as shown here.

But in beta oxidation conveniently I ignored a couple of points that is this double bond is trans that is what this dehydrogenase does and this enoyl CoA hydrates is very specific for this trans substrate, if it is cis it is not going to work. So, that poses a problem. These 2, 1 if I have odd carbon what do I do and second if I have cis double bond what do I do?

So, those fatty acid oxidations require 2 additional steps and for the one that has only double bond but still even carbon as you see here oleic acid, oleoyl CoA. So, here this cis needs to be converted into trans and that is done by an isomerase. So, it will undergo the normal beta oxidation and when it comes to this which will not be a good substrate for the enoyl CoA hydratase.

An enoyl CoA isomerase, so these indicate the positions of the double bonds converts that into a trans double bond and then beta oxidation continues. So, this is to take care of the cis double bonds that naturally occur and this is where an isomerase an additional enzyme is required.

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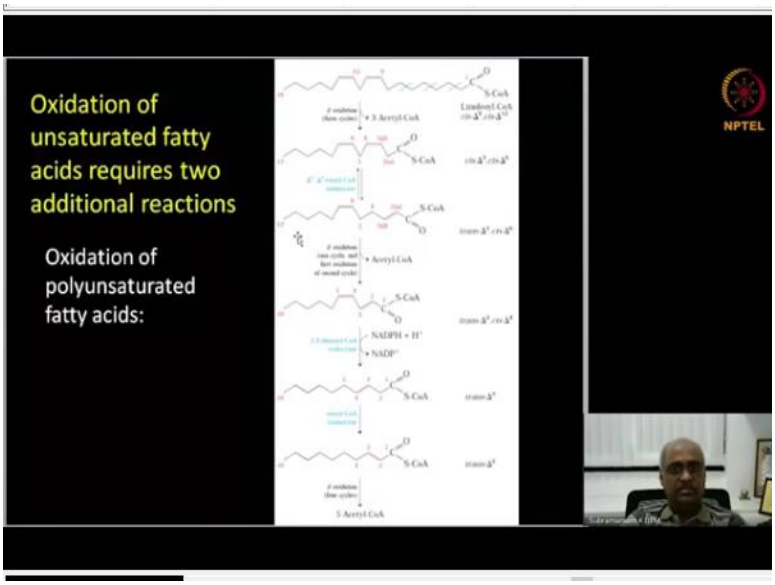

So, if you have this sort of a situation where you have a polyunsaturated fatty acids. So, you need one more enzyme. So, monounsaturated simply 1 isomerase is good enough then the rest it can continue. So, if you have a polyunsaturated I will just blow this up a bit. So, I am sure you can see the first part. So, linoleic acid, linoleic acid has 2 double bonds and linolenic acid 3 double bonds or arachidonic acids 4 double bonds, we would not get into all of that, we just need to know examples of how they are handled.

So, here you have 2 double bonds like this between carbon 9, 10 and 12 and 13. And these are cis; all naturally occurring double bonds in fatty acids are all cis double bonds. That is why at the beginning I told you this hydrogenation which produces trans double bonds while saturating actually the double bonds as a byproduct, they are a problem nutritionally bad for health.

So, here what actually happens is then first beta oxidation goes on as far as it can go, then end up producing a situation like this. So, you after this cleavage you end up having this 9th position actually becomes the third carbon. And you have a double bond between third and fourth. So, normally for beta oxidation you need the double bond between second and third. So, here it is in the wrong place and in addition wrong orientation and that is taken care by 2

enzymes, one is this isomerase which switches this double bond to this position and trans as well.

So, then it can proceed now. And after it goes through then you need another enzyme which is a reductase. So, shown here, so what this reductase does is it reduces one of the double bonds and repositions the other one such that these 2 double bonds like delta 2, delta 4 now becomes a delta 3 trans and then another isomerase converts that into 2 and 3. So, the combined action of an isomerase and reductase ends up producing the right orientation of the double bond.

So, that this polyunsaturated fatty acid can be fully oxidized by beta oxidation. So, once again if it is monounsaturated just the cis needs to be converted to trans and further you need an isomerase and if it is multiple double bonds then the double bonds can be at the wrong position between wrong carbons and therefore a reductase is required to reduce a double bond and this reductase not only reduces the double bond it also repositions.

Like for example it is not reducing 4 to 5 or 2 to 3, instead one of the double bond is reduced but then the resulting single double bond is between 3 and 4. So, you need to pay attention to this. So, it is not a typographical error here. So and then an isomerase repositions again from 3, 4 to 2 and 2. So, these 2 enzymes make those substrates suitable for beta oxidation.

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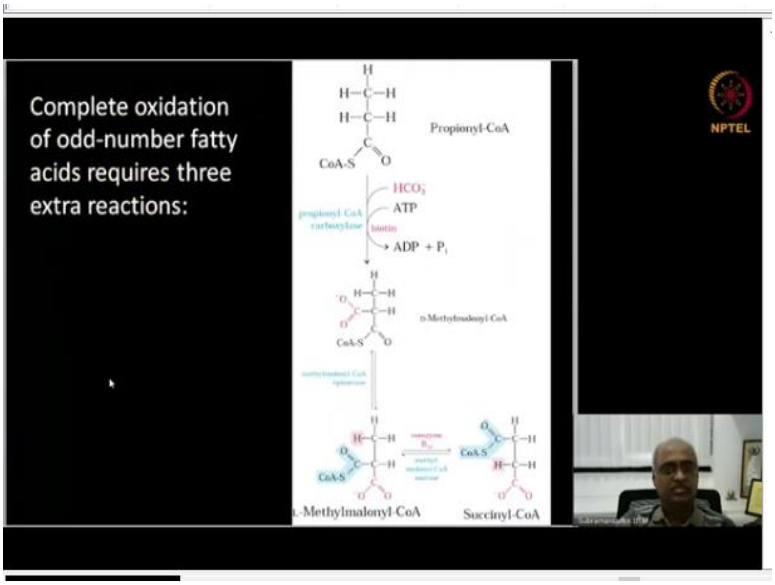

So, now let us move on to a situation where we have odd-number fatty acids. So, this is what I began prematurely. So, the first we dealt with mono unsaturation that is how to handle cis

double bonds, second we handled multiple double bonds. The third is if I have an odd carbon what do I do? So, like for example instead of 16, it is 17 or 15, then at the end of the last cycle you will end up with the 3 carbon coenzyme A acyl CoA.

So, that will be propionyl CoA, this propionyl CoA how this is oxidized is a very interesting story. So, this is where you are going to see the most complex of molecules that you are so far seen only acting as a cofactor here. So, let us see how this happens? So, here this carbon gets oxidized by combining with the carboxylic acid group, like pyruvate carboxylase producing oxaloacetate in gluconeogenesis that we learned earlier.

So, there I told you biotin acts as the cofactor. So, the activated carbon dioxide in the form of carbonic acid is the one from where carbon dioxide is transferred to biotin and biotin we also learned it as one of the biological tethers, it can move from one active site to the other active site and this very similar reaction to pyruvate carboxylase, this propionyl CoA carboxylase produces what is called the methylmalonyl CoA.

So, this structure is malonyl CoA, the 2 carboxylic acid joined by a acetyl group, so that is the malonyl CoA and then you have methyl group attached to it. So, it is methylmalonyl CoA and this is not a substrate for the very important enzyme that we are going to look at instead L version only is a good substrate. So, this is the D and the L version is produced by an epimerase methylmalonyl CoA epimerase.

So, remember epimers means isomers but not mirror images methylmalonyl CoA epimerase basically switches this carbon, this group and this group orientation, such that it becomes L-methylmalonyl CoA and here these 2 shaded groups exchange places. So, this is an example of this kind of an alkyl group getting swapped for a hydrogen reactions. So, such reactions happen and this is a good example of that and that swapping happens without this hydrogen ever leaving into the medium which is full of protons.

So, this very hydrogen gets attached to this carbon while this entire moiety sometimes simply an alkyl group. So, here it is a substituted group swapped to this. So, this is done by an enzyme called methylmalonyl CoA mutase. So, the end of product is like you have CH 2 CH 2 both sides you have the carboxylic acid which is nothing but succinic acid and with this coenzyme A it is succinyl CoA and we know succinyl CoA enters into TCA cycle, from

succinyl CoA we will get succinic acid and fumarate which we just saw. So, this is a intermediate of the TCA cycle and it gets into TCA cycle.

This is how this 3 carbon carboxylic acid that ends up after beta oxidation as the last molecule if it is a odd chain odd number fatty acid. So, essentially a carbon is carboxylated by a biotin containing enzyme and then that the intramolecular rearrangement generates that into succinyl CoA. So, this is what happens and this swapping hydrogen with an alkyl group between 2 adjacent carbons by this mutase requires another vitamin B complex.

So, I think last time I told whatever we saw is the last vitamin B we are going to see, but I forgot about this and I also forgot about a metal cofactor a new metal, the last one we saw was molybdenum in nitrogenase complex. So, today we are going to see one more vitamin and one more metal. But the chemistry of this reaction is too complex for an introductory course. So, I am not going to get into it. And even this structure like all these structures here will memorize but not the B 12 structure that I am going to show you in the next slide.

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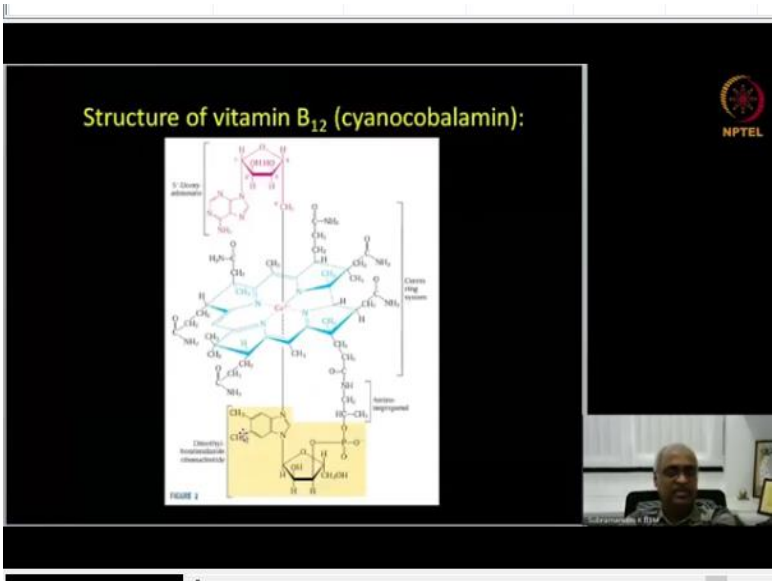

So, this is a B 12 in all its glory. So, it is not very difficult, it is possible to remember this structure I am not dragging but I had this in my exam and I reproduced it got full marks with no errors. So, essentially you have a porphyrin like ring system. So, the same 4 nitrogens instead of magnesium or ion you have a cobalt and the cobalt is coordinated with these 4 nitrogens as well as with these 2 moieties which are familiar to us.

This is an adenosine in our ribose, so deoxyadenosine you have and other side a similar looking molecule dimethylbenzimidazole, ribonucleotide and then you have these side chains. So, this swing system is called core in ring system and this ring system is what that enzyme mutase uses for swapping a hydrogen with an alkyl group and how that swapping happens and how cobalt plays a role in it that I am not going to get into the details of it, because this is not a full biochemistry course.

So, we will leave that type out. Even this molecule I am just showing it for the purpose of making you see how complex molecules are built from very few elements in the biological system. So, you do not need to memorize this structure. This is just to appreciate its beauty.

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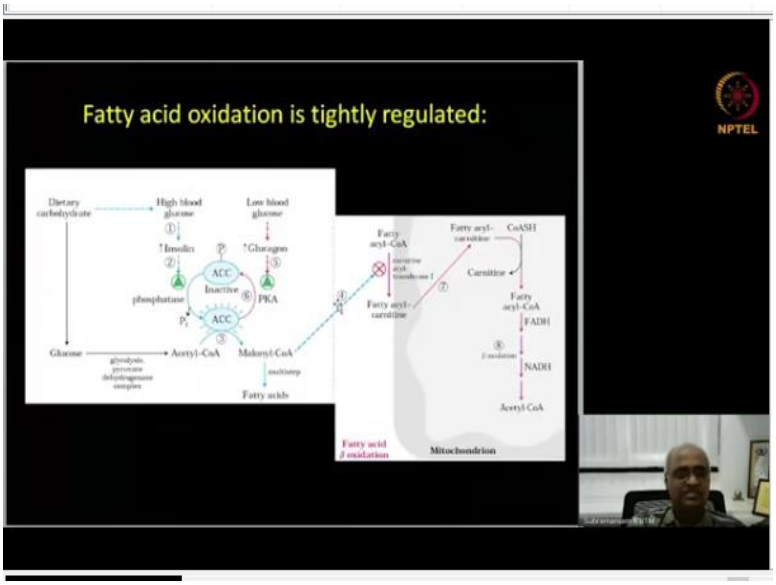

So, the last part of today's discussion is the obvious thing that a fatty acid oxidation kind of reaction must be tightly regulated and that is what we are going to see here. Do not even look at the slide for a minute I will just tell you that just. So, essentially if you have a lot of glucose available then you do not want to mobilize the lipid from the lipid storage. So, when glucose is available you want to inhibit beta oxidation.

And instead you want to promote fatty acid synthesis; we will learn that tomorrow fatty acid synthesis. Today we have broken up a fatty acid all the way to carbon dioxide. Tomorrow we will put them together to make a fatty acid. So, when you have a lot of glucose you do not want beta oxidation and you want fatty acid synthesis. So, this is the main point and now we know hormones are involved in the glucose regulation.

For example excess glucose like you had a several bread in the morning or a lot of idlis in the morning. So, you had a lot of carbohydrates. So, you have high blood glucose that triggers insulin. Insulin is an anabolism promoting hormone, meaning it promotes biosynthesis of molecules and gets stored. So, therefore blood glucose level is brought down. How is it brought down? The glucose is essentially converted into fatty acids and triacylglycerol and taken away from blood.

So, the blood glucose level is brought to normal level and so that is what insulin does. So, now let us follow the path of insulin. So, this high blood glucose triggers insulin secretion by the beta cells of the eyelids of langerhans in pancreas. Yesterday we were talking about glucagon and I told it is produced by alpha cells. And this insulin produced from the pancreas activates a phosphatase which dephosphorylates this enzyme acetyl CoA carboxylase, we have not encountered this, do not worry, we will learn about it tomorrow.

So, this is the first step in fatty acid biosynthesis, acetyl-CoA is going to get carboxylated to make malonyl CoA. Remember we saw that already. So, the malonyl CoA is right here. So, this will be the CH 3 CO that would have been the acetyl-CoA, here you have a carboxyl group added. So, it is malonyl CoA. So, this is methylmalonyl CoA. So, do not worry about that. So, it will be COOH CH 2 CO and coenzyme A.

So, that is what is malonyl CoA. So, this acetyl CoA, malonyl CoA is by carboxylating this acetyl group. So, that enzyme is this ACC acetyl CoA carboxylase. So, this is a key enzyme because this malonyl CoA can only go and become fatty acids. So, converting acetyl CoA to malonyl CoA means you have a lot of acetyl CoA and lot of glucose and you do not want to break any free fatty acids and you want to make the excess glucose that is coming in you want to convert it to fatty acids and store it and that is the only condition in which you will make acetyl-CoA to malonyl CoA transition.

And therefore this enzyme which is a committed step, this is committed to fatty acid biosynthesis that is subject to regulation and here the regulation is phosphorylation, dephosphorylation. So, this is covalent modification of the enzyme, a post-translational regulation. So, the activate form is the dephosphorylated form and that is stimulated by insulin.

So, insulin activates this phosphatase which converts this phosphorylated inactive ACC to activate ACC. So, this is the one important regulation and this malonyl CoA the next important regulation is this malonyl CoA, remember this carnitine shuttle is the rate limiting step in beta oxidation, because this transport into mitochondria is what is the rate limiting state, that is the slowest in the entire beta oxidation sequence.

So, that is subject to regulation. So, when you have excess malonyl CoA that inhibits fatty acyl CoA transport into the mitochondria. Because you have so much carbohydrate available that you are actually making fatty acid why would you take it into mitochondria? Mitochondria is not a storage depo, it is an oxidizing place, it is a powerhouse where things are burnt. So, you need to store in the cytoplasm.

So, therefore this malonyl CoA inhibits this carnitine acyl transferase. Therefore free fatty acids are not transported into the mitochondria. So, these are the 2 important steps in blocking beta oxidation and this happens after a good happy carbohydrate rich breakfast let us say. Now you have not eaten, drunk tea or coffee, no snacks, nothing for the last 4 or 5 hours and blood glucose level goes down due to continuous activity of this.

And that triggers the alpha cells to produce glucagon and what does glucagon do? We saw yesterday, it will bind to the receptor, activate cyclic AMP production and cyclic AMP will activate protein kinase A, and this protein kinase A yesterday we saw will phosphorylate the perilipin and make the lipid droplet lipids accessible for the lipase which is also activated by PKA.

So, this PKA is going to mobilize the fat out of the fat storage one thing, second it inactivates this ACC. So, you do not convert the acetyl-CoA to malonyl CoA and in absence of malonyl CoA this mobilized lipids by the other actions of PKA that we saw yesterday is going to act allow this inhibition is lost, we do not have malonyl CoA. So, therefore nothing inhibiting this (()) (45:50).

That is going to allow the transport of fatty acyl CoA free fatty acids into mitochondria for beta oxidation. Once into mitochondria you are not coming out alive as a free fatty acid, you are going to be broken into carbon dioxide. So, that is why this becomes key. So, this is how high blood glucose and low blood glucose by regulating the production of these 2 hormones

and controlling this activity by covalent modification like phosphorylation or dephosphorylation control the fatty acid synthesis and fatty acid oxidation.

What I really want you to focus your attention after having understood this part is the connection between carbohydrate and the fat. If you think I only eat butter, I never take sugar or I only eat sugar and rice and wheat, I do not eat fat, why am I becoming obese? So, look at this picture you understand that. Carbohydrates are nothing but fats, fats are nothing but carbohydrates.

Because they are all interconnected, from glucose you get acetyl CoA, from butter also you get acetyl CoA, and acetyl-CoA you can go into mitochondria and lipids after producing acetyl CoA is produced mitochondria but free fatty acids go into mitochondria get oxidized to make ATP. So, this is how carbohydrate metabolism and lipid metabolism are connected. Excess fatty acids or excess carbohydrate they are at the end of the day are all same. So, this completes our understanding of beta oxidation plus how it is regulated. So, I will stop here, tomorrow we will continue with the fatty acid biosynthesis. So, any questions?