Biochemical Engineering

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Module No. # 01

Lecture No. # 22

Urea Cycle, Gluconeogenesis and Glyoxylate Cycle

Good morning students. In our earlier classes we have discussed very many cycles path way and we have also learnt that how respiratory process that catabolism is going on in any living system. Today, we will be learning another new pathways, pathway which is going on inside any living cell and it is playing a very important role as per as the living system is concerned. And that is called the urea cycle. And today I will start with this urea cycle followed by gluconeogenesis and it will be ended with glyoxylate path way.

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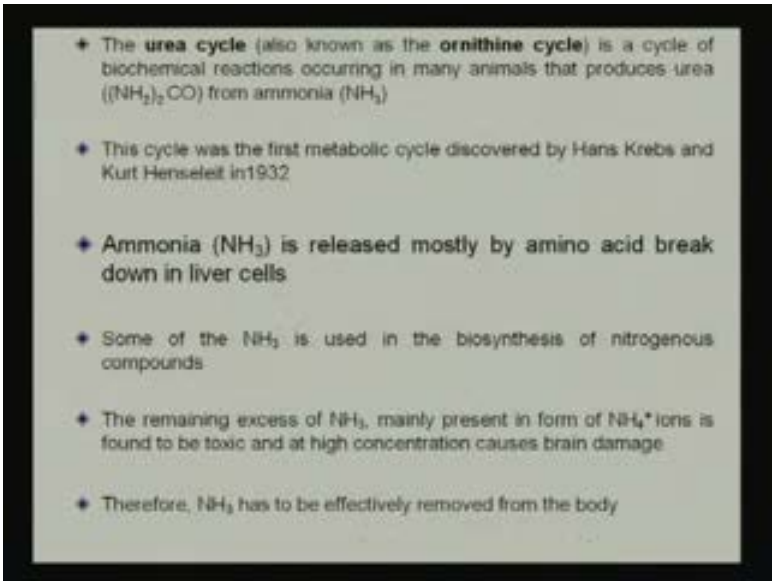

So, let us start with urea cycle. Now urea cycle is otherwise known as ornithine cycle. The biochemical reaction which is going on in every living cell including that animal being and that produces urea from ammonia. This cycle is the first metabolic cycle

discovered by Hans Krebs and Kurt Henseleit in the 1932. In this particular cycle what we will be learning? We will be seeing that how urea is being produced in the living system.

Now, ammonia which is released mostly by this living, by this amino acid is broken down in the liver. Some of this ammonia is used in the biosynthesis of nitrogenous compound and the remaining excess ammonia mainly present in the form of ammonium ion is found to be toxic and at high concentration in the living system if it starts getting accumulated. It has been seen that it causes brain damage. So, this particular bi product which is produced inside the cell is to be removed. And how it is removed? It is removed through this urea cycle.

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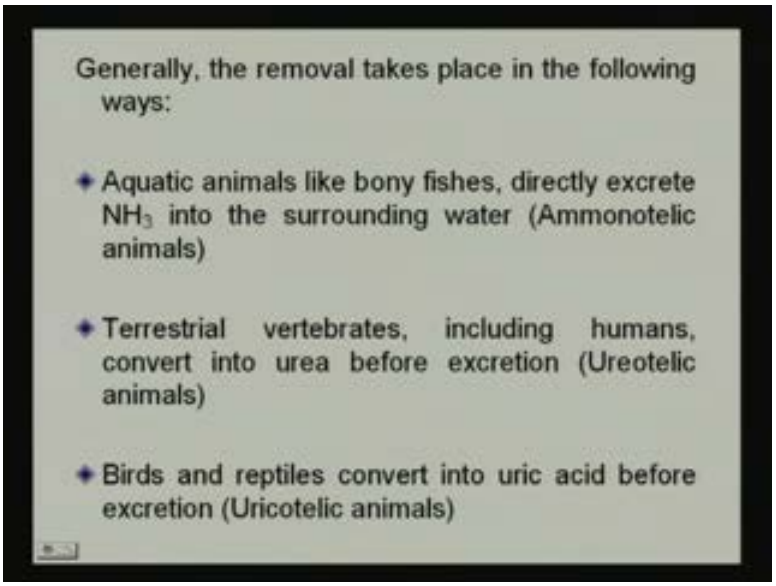

So, ammonia has to be effectively removed from the cell because of this toxic effect.

This removal of this ammonia takes place in the following way: Incase of aquatic animals, so I in the beginning only I have told you that in any living system this type of urea cycle is present. So, incase of the aquatic animal, mainly these bony fishes; it directly excretes ammonia into the surrounding water and this group of animals are called ammonotelic animals. That means this are these are the group of animal they are secreting ammonia directly to the surrounding and it is going out of the body system. Incase of terrestrial vertebrates, including human so incase of our system what we do? How we excrete? It is getting excreted in the form of urea and this is and these groups of

animals are called ureotelic animals. Incase of birds and reptiles where they convert this ammonia to uric acid before excretion and that group of animals are called uricotelic animals.

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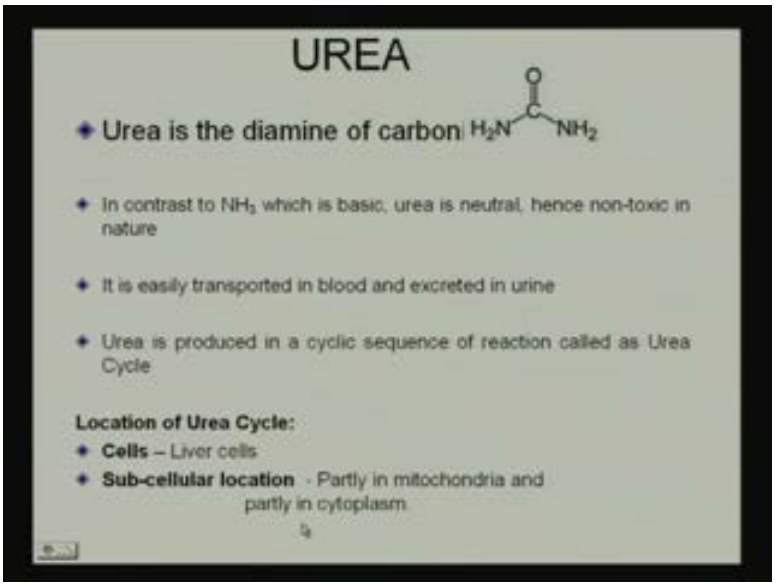

So, these are the different variations. So, what we have learnt? We have learnt that this ammonia can directly be released from the body. It may be converted to urea or it may be converted to uric acid to the surrounding environment and it is going out of the system. And when such type of metabolism and when such types of processes are going on inside the system, we are we are detoxifying our body from this toxic accumulation. Today, we will be learning how urea is being excreted from the system living system.

Now, if we see the structure of urea, it is the diamine of carbon, very simple structure that is two amino group here attached to this C double bar O. In contrast to ammonia, which is basic in nature urea is neutral and hence it is non toxic in nature. It is easily transported in blood and excreted in urine. Urea is produced in a cycle sequence of the reaction called as urea cycle. Its location if we see the location of this urea cycle then, in the lever cell and sub cellular location that is if we further classify then, we can find that it is partly taking place in the mitochondria and partly it is taking place in the cytoplasmic fluid of the cell. So, you just see incase of glycolytic process we have seen that glycolysis is taking place in the cytoplasmic fluid. Mitochondria is taking place in the, this TCA cycle is taking place in the mitochondria. But, you see this urea cycle

which is taking place in partly in the mitochondria and partly in the cytoplasmaic fluid. So, this is the particular cycle. Now, here if we see come in comparison to the other metabolic path ways, what we already learnt that glyocolotic pathway when I discussed I told you that this process is the ten steps process. In case of TCA cycle, I told that TCA cycle is the eight steps process. And in each step we have seen that the roles of precursors are immense. We cannot ignore.

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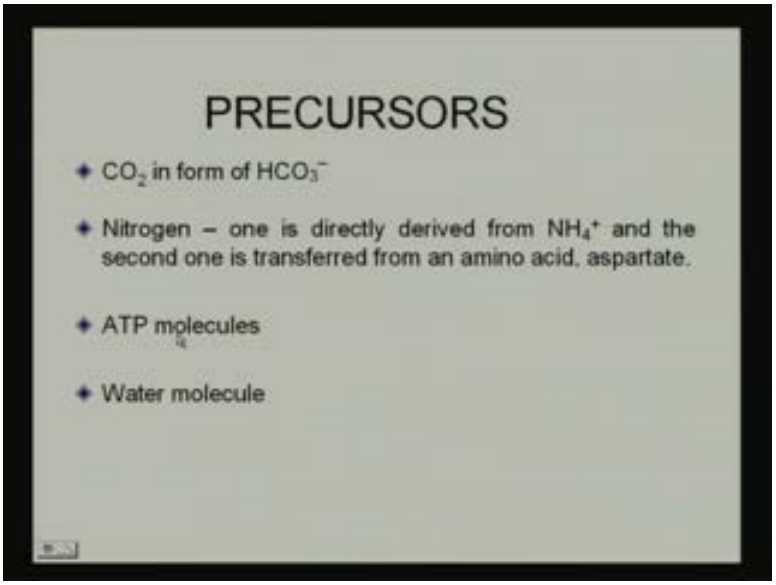

In this particular urea cycle also we have seen that precursors are playing a significant role in the five step process of urea cycle. Now, these precursors are carbon dioxide in the form of bicarbonate. This nitrogen, how nitrogen nitro groups are coming? One is directly derived from the ammonium that is N H 4 plus and second one is coming from the amino acid that is, the aspartate. ATP molecules are playing a significant role in this urea cycle. Incase of that respiratory process we have seen that how ATP molecules are generated when this catabolic process is going on in the living system. Here, we will be seeing that how ATP driven process is also simultaneously going on in the living system. And urea cycle is one of such example. Now here, ATP is needed to carry forward this reaction. Water molecule is also playing a significant role in urea cycle.

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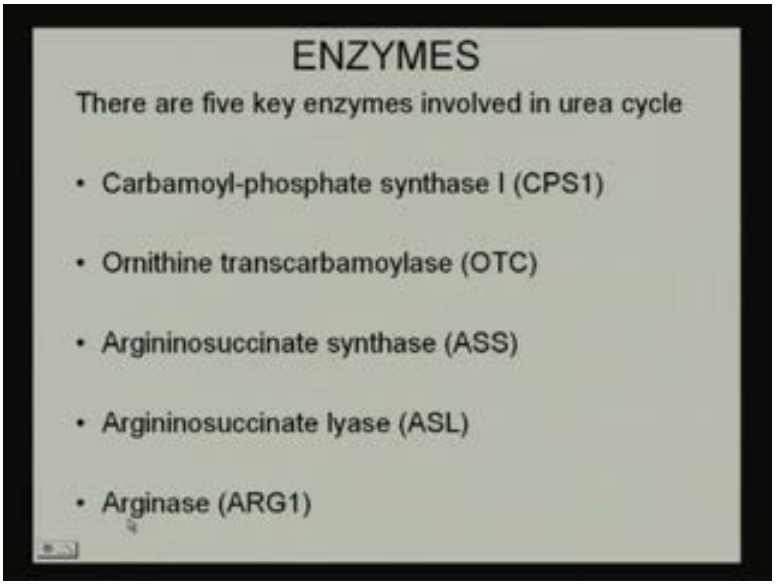

Now, as I have told you that urea cycle is a five step process and here different enzymes are playing very important role in this particular cycle. If we see the different enzymes we can find that carbamoyl phosphate synthetase one, ornithine transcarbamoylase, argininosuccinate synthetase, argininosuccinate synthase, argininosuccinate lyase and arginase enzymes are playing a vital role in this urea cycle.

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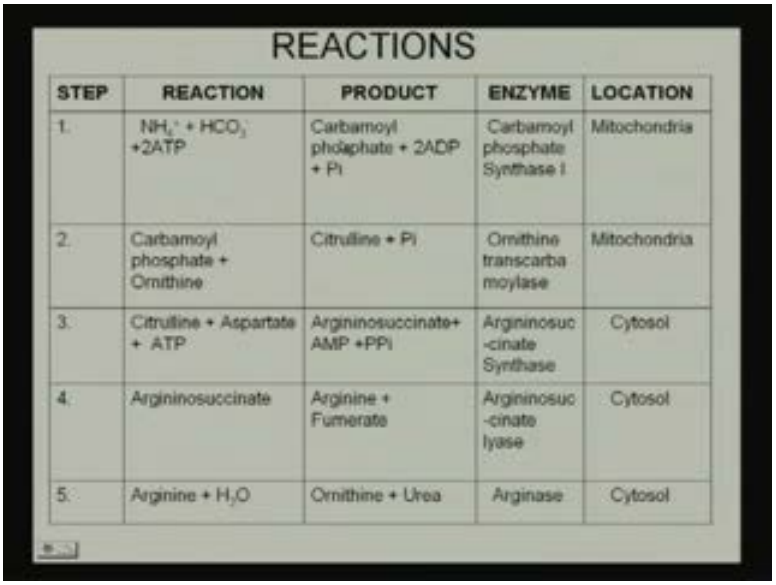

Now, at a glance if I give you the overview of this urea cycle then we can see that, initially this ammonium ion and bicarbonate in presences of two molecules of ATP is

produced carbamoyl phosphate. And this carbamoyl phosphate is the first product of urea cycle. This particular reaction is taking place in the presence of the enzyme called carbamoyl phosphate synthase one. This particular reaction when it is going on, it produces two molecules of ADP and inorganic phosphate. This particular step is going on inside the mitochondria of the cell. When we are coming to the second step, carbamoyl phosphate and ornithine which are already present in the mitochondria, it is producing citrulline and one inorganic phosphate in the presence of ornithine transcarbamoylase. And here this step also taking place in the mitochondria of the cell. As soon as citrulline is produced, citrulline is going out of this mitochondria and it is coming to the cytoplasmic fluid of the cell. And citrulline in presence of aspartate and one molecule of ATP is needed to go forward this reaction and it is producing argininosuccinate and one AMP and inorganic phosphate. In the presence of this enzyme argininosuccinate synthase and this reaction as I have mentioned that it is taking place in the cytoplasmic fluid of the cell. Argininosuccinate in the presence of argininosuccinate lyase this is the reaction when lytic process, breakdown process going on and it is once again forming this arginine and fumarate and it is taking place in the cytoplasmic fluid of the cell. Arginine in presence of water once again gets converted to ornithine and urea. Urea is going out of the system and ornithine from the cytoplasmic fluid is once again entering to the mitochondria to carry out this cycle. And this way continuously this cycle is going on inside any living system and urea is generated and going out of this living system.

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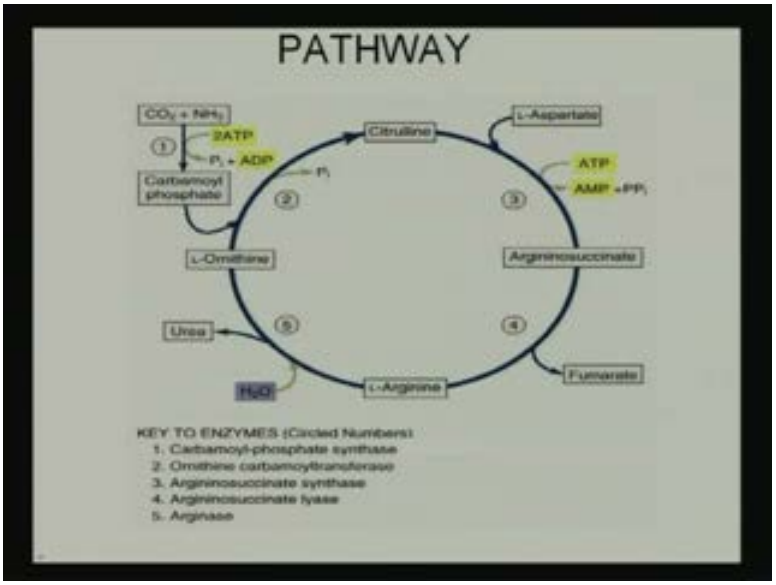

Now, I have told you the overview of this reaction. Actually how these reactions are going on? This is a very simple pathway and here as I have told you the overview and then we will come systematically each and every step and how this product and bi products are produced, we will also see and learn. See here this carbon dioxide and ammonia in presence of two molecules of ATP producing this ADP and P i and carbamoyl phosphate is produced. See this carbon dioxide which is donating this bicarbonate and this ammonia see here ammonia is there.

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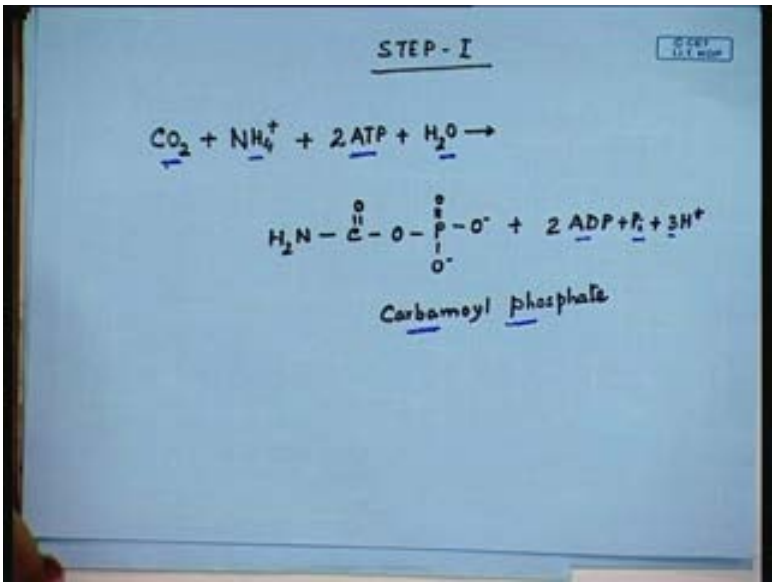

See this ammonia in the form of ammonium ion two molecules of ATP and one water molecule is yielding carbamoyl phosphate along with the production of 2 ADP P i and 3 hydrogen molecule. So, this is the first step of urea cycle.

Now here, you see carbamoyl phosphate synthase enzyme is playing a significant role in this conversion process. Now, when this is getting converted it is this carbamoyl phosphate is produced. This carbamoyl phosphate in presence of ornithine is converted to citrulline and the enzyme which is playing a significant role is the ornithine carbamoyl transferase. So here, you see this is producing this citrulline. This process up to this process it is going on in the mitochondria of the cell. Here, as soon as citrulline is produced, citrulline in presence of aspartate in and the enzyme argininosuccinate synthase is getting synthesized in presence of one molecule of ATP and producing argininosuccinate. Argininosuccinate when it is produced in the presence of the enzyme

argininosuccinate lyase is once again splitted into arginine and fumarate. This fumarate is I, we know that this fumarate is one of the bi product of TCA cycle. So, this fumarate is entering to the TCA cycle and this arginine which is another product of this particular cycle goes forward at in the presence of this enzyme arginase it releases this urea from it and another product ornithine. This ornithine is once again entering to this mitochondria of the cell.

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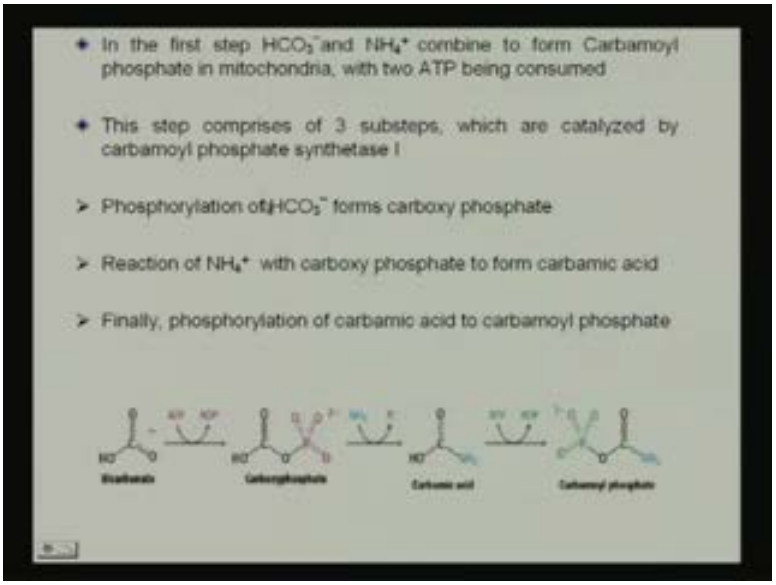

Now, let us come step wise to this particular reaction that how these reactions are going on and how the intermediate products and bi products are produced? In the first step we have learned that bicarbonate and ammonium ion combine to form cabamoyl phosphate.

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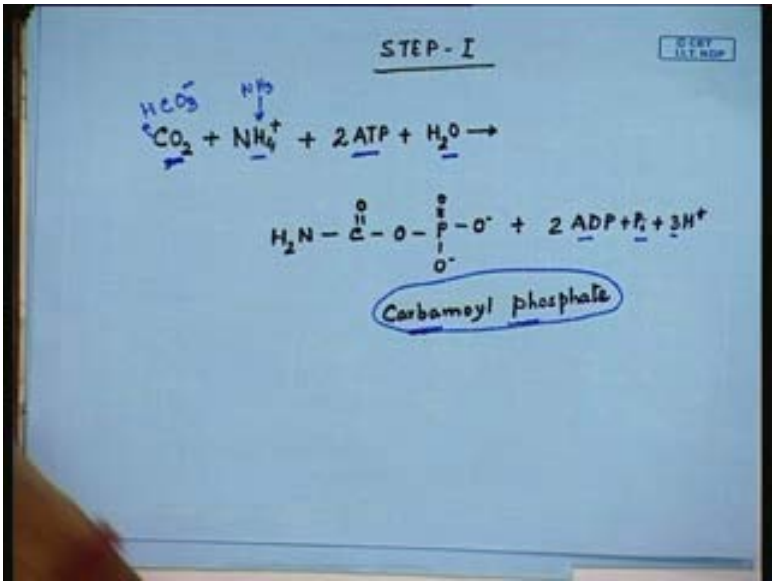

So, we have already learnt this carbamoyl phosphate formation where this bicarbonate that is H C O 3 minus which is contributed by this carbon dioxide and from this ammonia this ammonium ion is coming. So, these two products when they are coming, this bicarbonate you see, this is the bicarbonate and when ATP molecule I told you that two molecules of ATP are needed. This is two molecules of ATP. So, first molecule ATP is coming and it is donating its phosphate group and it is producing carboxyphosphate. You see this phosphate group is donated by this ATP and ADP production is there. That means this bicarbonate is getting converted to carboxyphosphate. Now here, when carboxyphosphate formation is there then ammonia in the form of ammonium ion is coming and playing a significant role. Now, this ammonia is coming and it is forming the carbamic acid. That means this carboxyphosphate now once again become this removal of phosphate group is taking place and it becomes carbamic acid. When this carbamic acid is formed, another molecule of ATP is coming and donating its phosphate to this carbamic acid and ultimately you see this carbamoyl phosphate is formed. You see this is the phosphate and this is the carbamoyl group and carbamoyl phosphate is produced which is the end product of this first step of urea cycle. Now, if we sum up then this step comprises the three sub steps where phosphorylation of bicarbonate forms the carboxyphosphate this is the first step. Reaction with ammonium ion with the carboxyphosphate to form carbamic acid this is the second step. And finally, once again this carbamic acid is getting phosphorylated. And finally, phosphorylation of carbamic acid to carbamoyl phosphate is taking place. So, we can see that this reaction what we

have seen that though it is showing a single step reaction but, in reality it is a complex reaction where three sub steps are needed, where bicarbonate is converted to caboxyphosphate. Caboxyphosphate is converted to carbamic acid and once again ultimately carbamoyl phosphate is produced.

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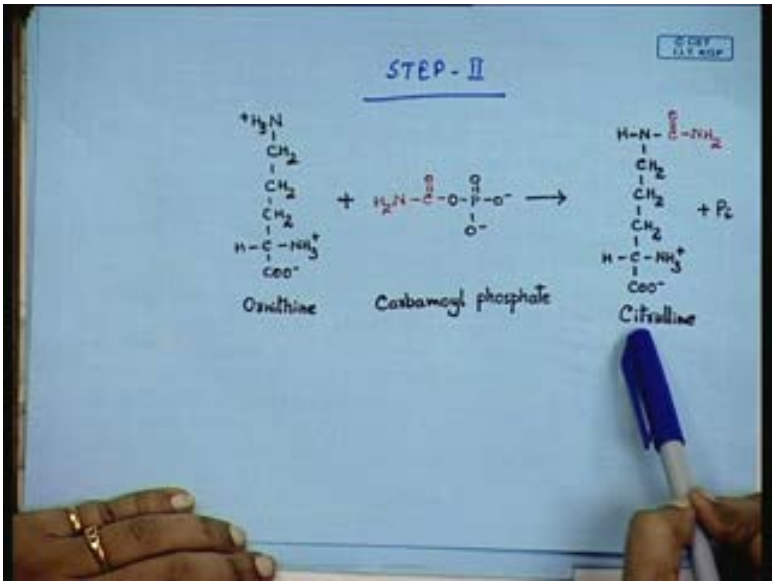

Now, when this carbamoyl phosphate is production is over then this second step, this is the second step. In this step two what is happening? This carbamoyl phosphate is reacting with the ornithine. See this is the ornithine which is there in mitochondria is coming in contact with this carbamoyl phosphate and it is producing the citrulline.

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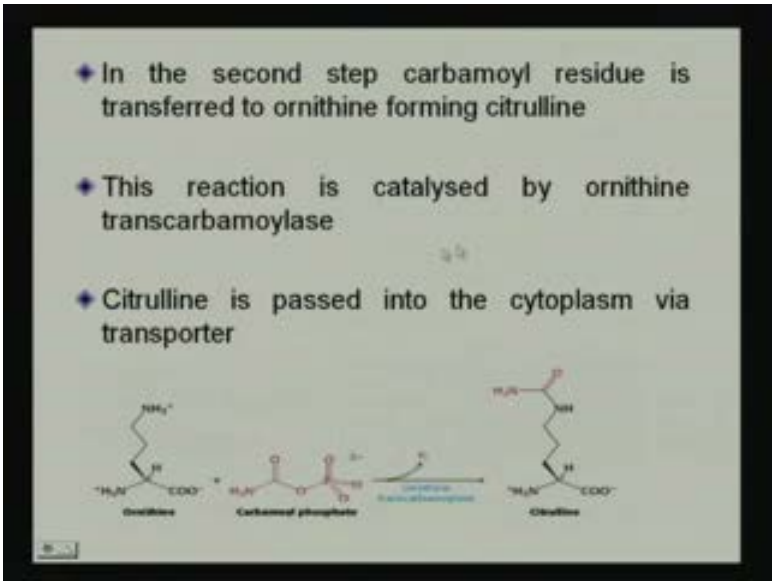

Now here, in the second step carbamoyl residue is transferred to ornithine forming citrulline. That means this is a carbamoyl residue. These carbamoyl residues are getting transferred to this ornithine group and this ultimate result is the formation of citrulline. This reaction is catalysed by ornithine transcarbamoylase enzyme. Citrulline is passed into the cytoplasm via the transporter, the transport system which is there.

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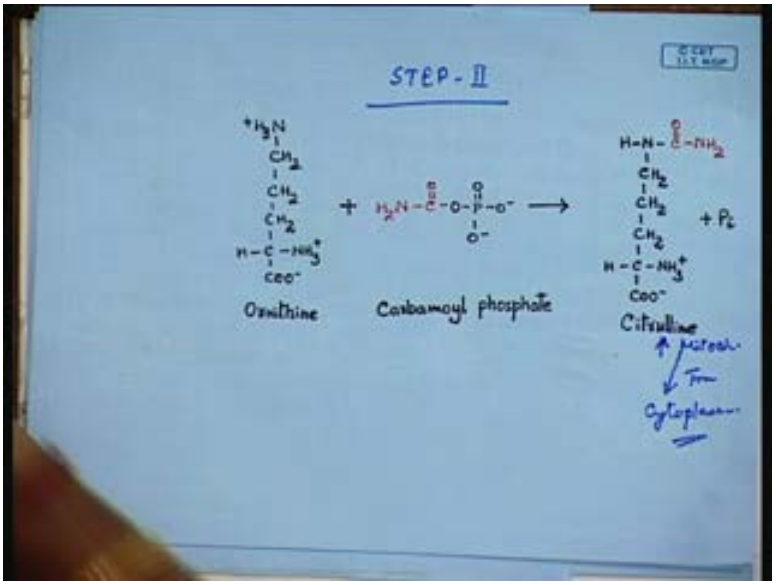

The citrulline, now also this citrulline which is produced is in the mitochondria of the cell and this citrulline is now coming through transporter to the cytoplasmic fluid of the

cell, now this transportation of this citrulline is taking place. So, in this step what we have seen? We have seen that carbamoyl phosphate this this carbamoyl group is being transferred to ornithine and citrulline is formed.

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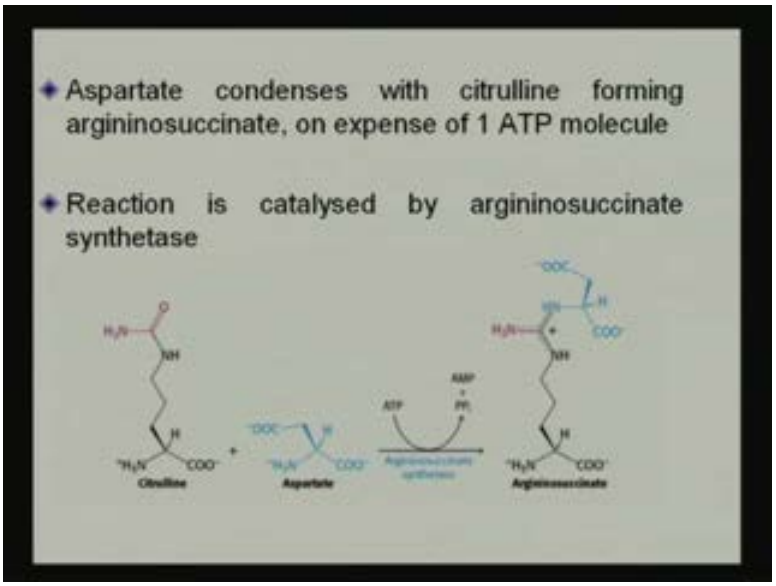

Now, in the next step what is there? That aspartate is condenses with this citrulline forming argininosuccinate.

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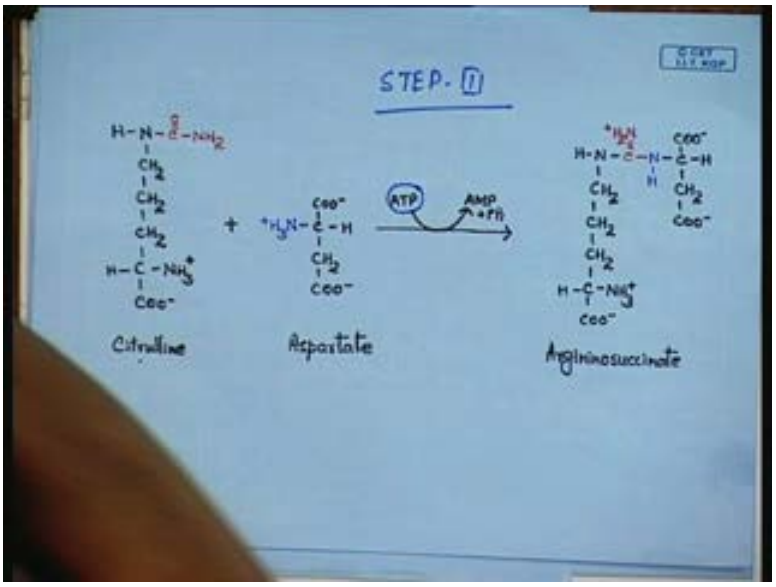

Now, if we see this citrulline which is the end product of the second step. In the step three what is happening? This citrulline in presence of aspartate that condensation

reaction is going on in presence of one molecule of ATP which is producing one AMP and inorganic phosphate and argininosuccinate is produced. This reaction is catalysed by argininosuccinate synthetase enzyme. Now, here we can see that here this transfer of this group is taking place and amino group of the this aspartate is going and getting binded and the new group is getting connected with the citrulline producing argininosuccinate. This is the condensation reaction.

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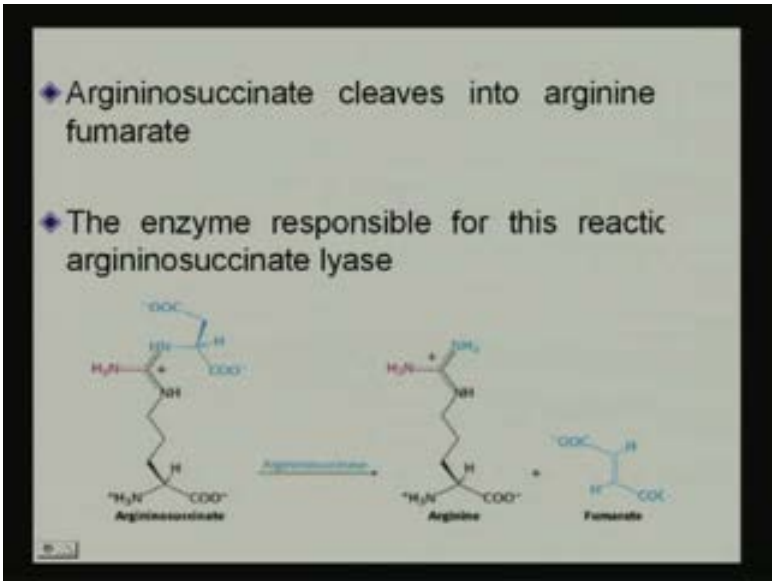

Argininosuccinate in the next step is getting cleaved. Now, this argininosuccinate is once again producing this separating this arginine from the fumarate.

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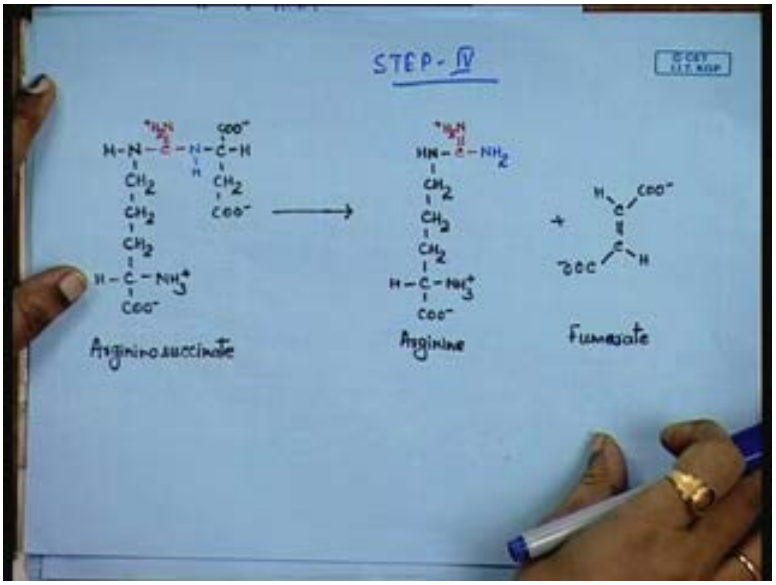

Now, you see here this it is that step four. In the next step what is happening? This argininosuccinate in the presence of lyase enzyme argininosuccinate lyase it breaks this bonding and you see here this arginine it is one amino acid arginine. See here this amine groups are getting separated and fumarate which is one of the bi product of TCA cycle is being released and this fumarate can enter to the TCA cycle for subsequent utilization.

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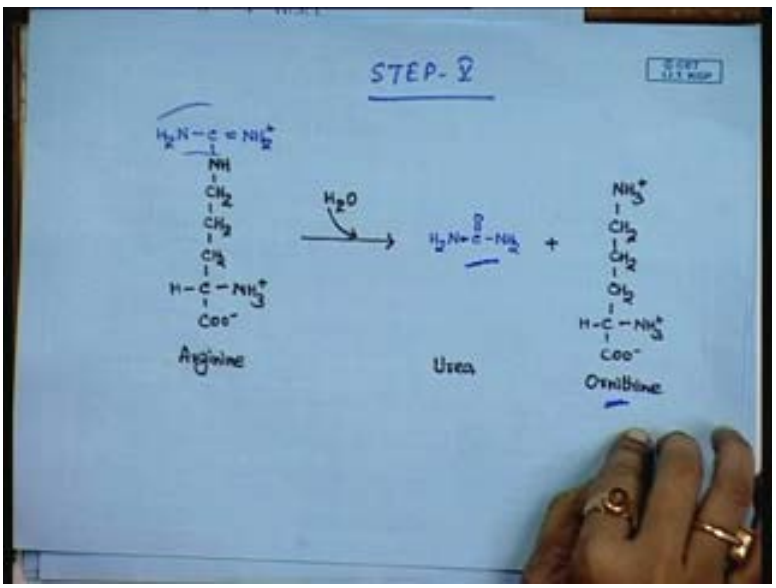

And in the last step what is happening? In step five what is happening? This arginine in the presence of the enzyme arginase is getting converted to urea and ornithine. The

hydrolysis of arginine generates urea at ornithine. Now, see here this group is being separated and urea is produced and ornithine is once again going and entering to the mitochondria for urea cycle.

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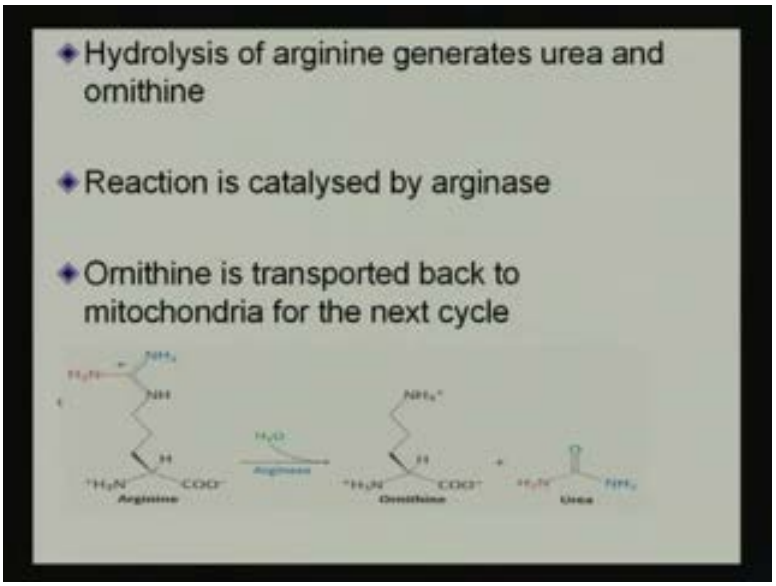

This reaction is catalysed by this arginase inside. Ornithine is transported back to mitochondria for the next cell cycle.

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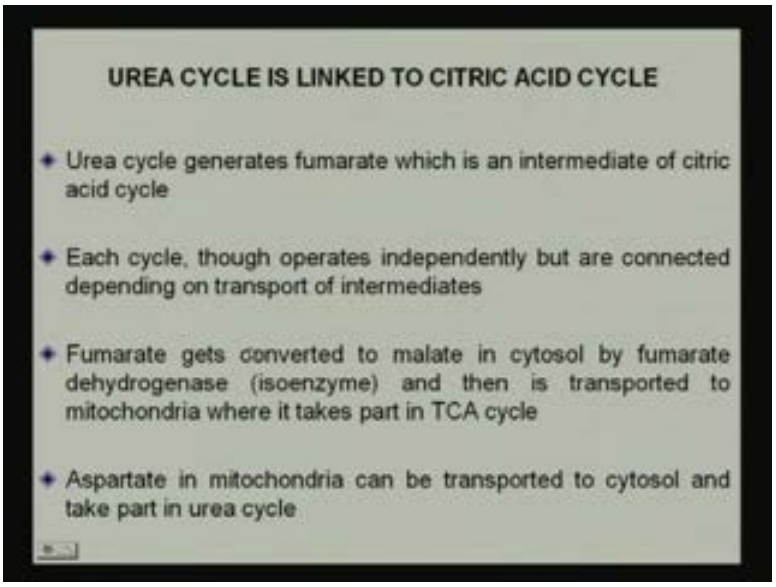

Now if we see this urea cycle, it can be linked with the citric acid cycle. As I have already mentioned you, that urea cycle during this urea cycle we have seen the

generation of fumarate which is one of the intermediate of TCA cycle. Each cycle though operates independently but, are connected depending on the transport of intermediates. Fumarate get gets converted to malate in cytosol by fumarate dehydrogenase that is one of the isoenzyme and then it is transported to mitochondria where it takes part in that TCA cycle. So, in the mitochondria this fumarate takes part for citric acid cycle. Aspartate in mitochondria can be transported to cytosol and it takes part in the urea cycle.

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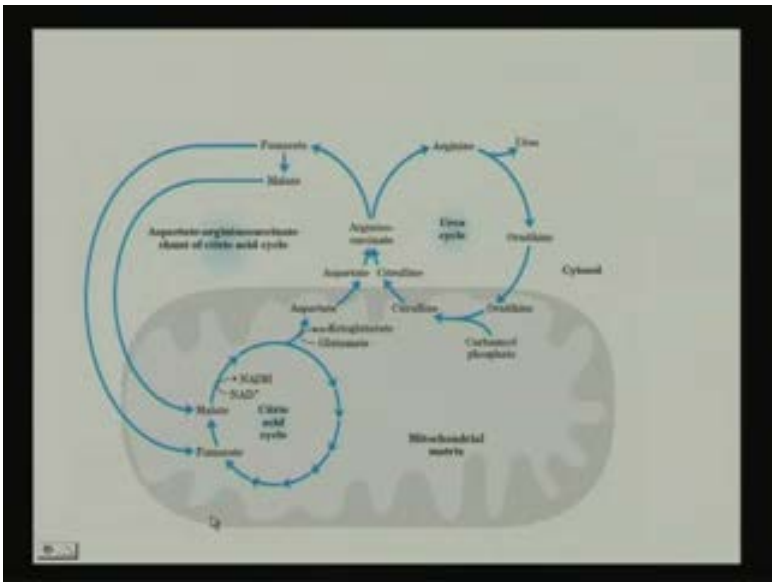

Now here, whatever I have told if I sum up then, we can find that you see here carbamoyl phosphate in the presence of ornithine is producing citrulline. As soon as citrulline see this is the cell and this is the mitochondria and this is the cytoplasmic fluid. So, citrulline is produced. Citrulline is getting transported out of this mitochondria to the cytoplasmic fluid. This citrulline is now producing argininosuccinate. Argininosuccinate when it is cleaved it is producing arginine and fumarate. So, this fumarate is entering to this TCA cycle back to this mitochondria. Fumarate may get converted to malate and this malate can once again come and enter to this TCA cycle. And this particular reaction we can tell that aspartate argininosuccinate shunt for citric acid cycle which is a bypass reaction. And here this arginine which is produced is releasing urea and ornithine. And ornithine is transported into mitochondria and this urea cycle is getting completed and this is all about this urea.

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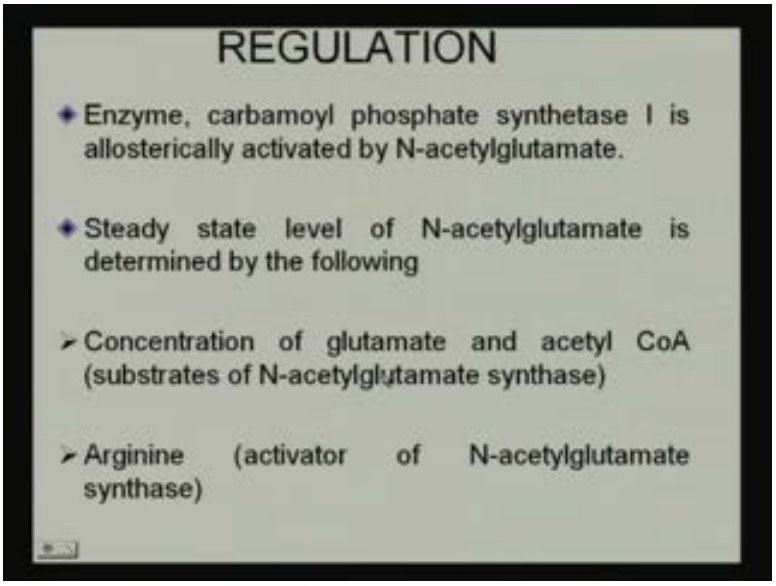

Now, coming to this regulation; the enzyme carbamoyl phosphate synthetase one is allosterically activated by N-acetylglutamate. This one of the very important product which is controlling the activity of carbamoyl phosphate synthetase one. Steady state level of N-acetylglutamate is determined by the following: that is the concentration of glutamate and acetyl coA that is one way and another is the arginine; which is considered to be the activator of N-acetylglutamate synthase enzyme. So, these are the two important regulators. If we see this acetyl coA and glutamate we can find that in the cell acetyl coA is produced with fatty acid oxidation and beta oxidation.

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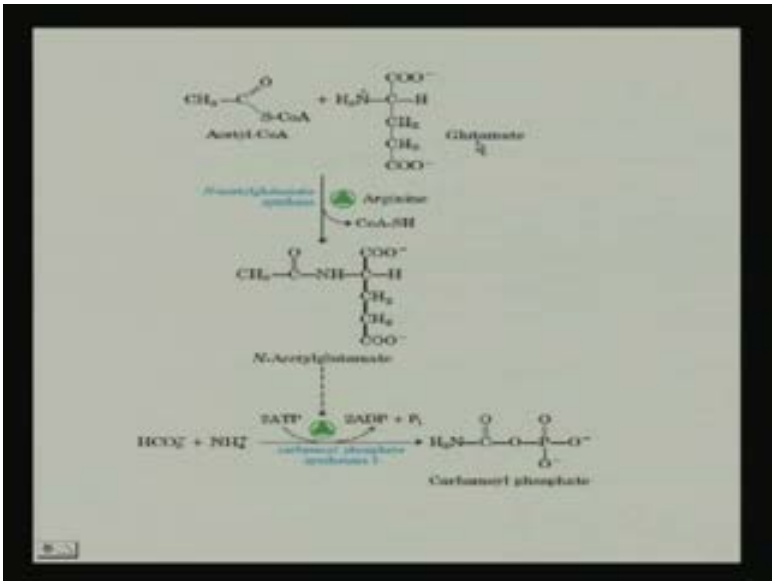

So there here, we can get acetyl coA and glutamate is one of the amino acid which present in the cell is undergoing reaction with inside with the help of the enzyme in acetylglutamate synthase and it is producing the enzyme called N-acetylglutamate. This N acetylglutamate and here arginine is also playing an important role to catalyze this reaction. Now, this N-acetylglutamate is playing a significant role as it is the regulatory enzyme for carbamoyl phosphate synthetase one. Now, this product undergoes several unknown reaction and ultimately it is coming and it is just activating this enzyme and this bicarbonate and ammonia in the presence of this enzyme is getting converted to carbamoyl phosphate which is the initial product to start the urea cycle. And this way this N-acetylglutamate is controlling this or accelerating the rate of carbamoyl phosphate production in the cell.

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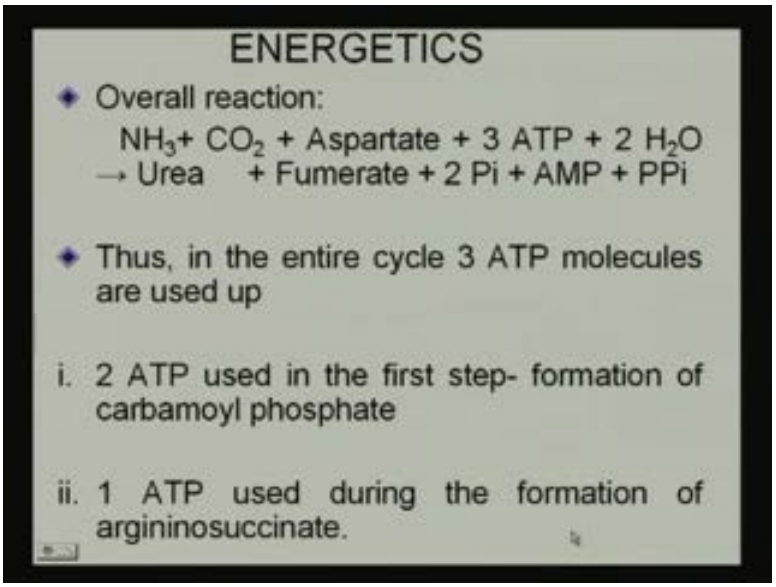

Now if we see the energetic, then we can find that ammonia, carbon dioxide, aspartate three molecules of ATP 2 molecules of water gives rise to urea fumerate. Two molecules of inorganic phosphate, AMP and pyrophosphate and thus in the entire cycle we can find that ATP, 3 molecules of ATP are used up. It is needed to carry forward this reaction. Two molecules of ATP is being used in the first step and one molecule of ATP is used during the formation of argininosuccinate and that is here it is the energy driven process.

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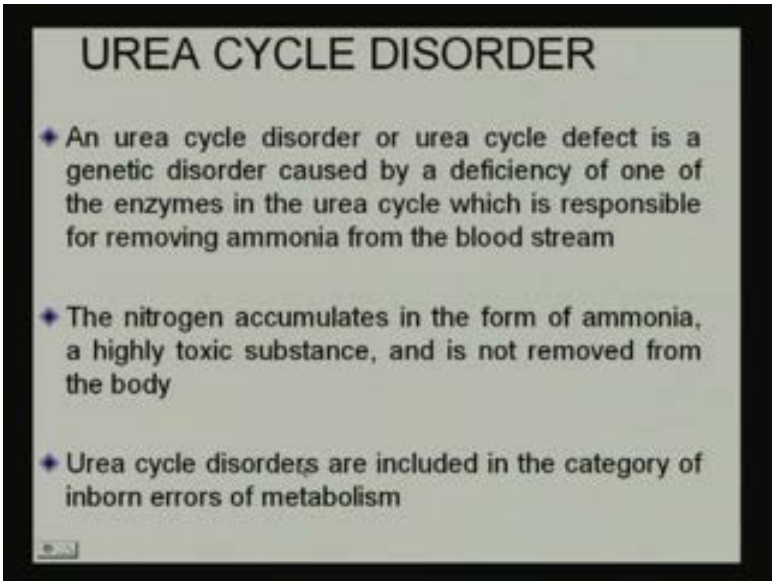

Now if we see the urea cycle disorder, then we can find that an urea cycle disorder or urea cycle defect is the genetic disorder caused by a deficiency of one of the enzymes in the urea cycle which is responsible for removing the ammonia from the blood stream. That means here with the defect that accumulation of toxic substances in the form of ammonia is there inside the living system. The nitrogen accumulates in the form of ammonia, a highly toxic substance and is not removed from the body. Urea cycle disorders are included in the category of inborn errors of metabolism.

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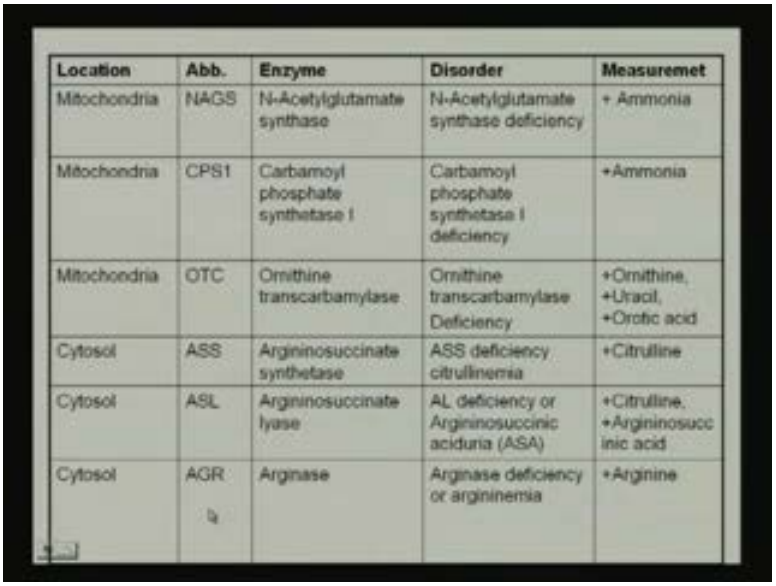

Location	Abb.	Enzyme	Disorder	Measuremet
Mitochondria	NAGS	N-Acetylglutamate synthase	N-Acetylglutamate synthase deficiency	+ Ammonia
Mitochondria	CPS1	Carbamoyl phosphate synthetase I	Carbamoyl phosphate synthetase I deficiency	+Ammonia
Mitochondria	OTC	Ornithine transcarbamylase	Ornithine transcarbamylase Deficiency	+Ornithine, +Uracil, +Orotic acid
Cytosol	ASS	Argininosuccinate synthetase	ASS deficiency citrullinemia	+Citrulline
Cytosol	ASL	Argininosuccinate lyase	AL deficiency or Argininosuccinic aciduria (ASA)	+Citrulline, +Argininosuccinic acid
Cytosol	AGR	Arginase	Arginase deficiency or argininemia	+Arginine

Now how to know? It can be this disorder can be recognized by very many ways. We can measure some of the end product in the plant and as I have, we have already learnt that this urea cycle is taking place either in the mitochondria or in the cytoplasm partly in the mitochondria and partly in the cytoplasm. So, here what is there if this N-acetylglutamate synthase enzyme is not there, then it is called N-acetylglutamate synthase deficiency. If this deficiency is there then ammonia concentration in a blood is going up. Carbamoyl phosphate synthase one and if this particular enzyme is not there then also it is called carbamoyl phosphate synthase one deficiency. And here also this ammonia concentration is going up. Ornithine transcarbamylase, this is another enzyme and if that disorder is there then we are calling ornithine transcarbamylase deficiency and here it is resulting in the higher concentration of ornithine urea orotic acid in the blood. In the cytoplasmic, when we are considering the cytoplasmic enzymes then argininosuccinate synthetase enzyme and if it is not there its deficiency is called citrullinemia. And here citrulline concentration in the blood is getting up. Argininosuccinate lyase if not there it if it is deficient then it is called A L deficiency or argininosuccinate acid urea deficiency. And here, citrulline argininosuccinate acid concentration in the living system is going up. If arginase enzyme is deficient, arginase enzyme is not there that is called argininemia. And here arginine concentration in the body is going up.

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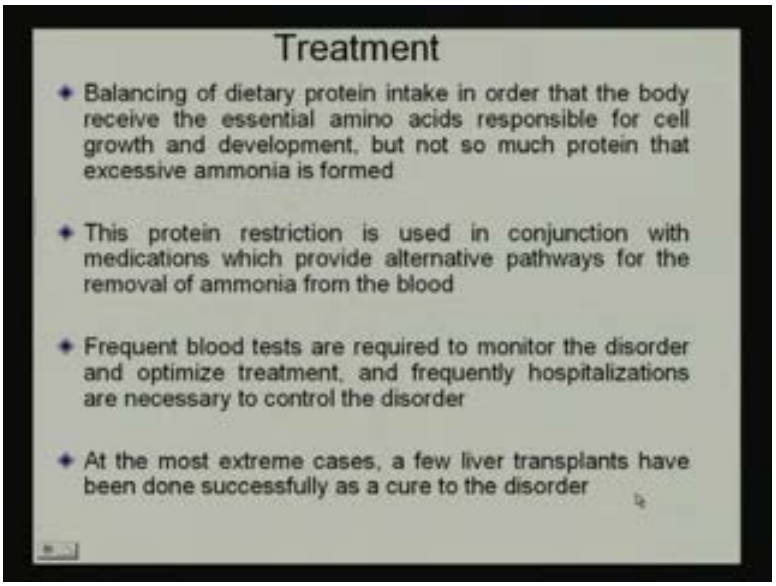

Now to treat such type of patients; for treatment what we are, we have we have to do by we are doing here the patient who are suffering from such type of diseases we have to give a controlled diet where this protein intake should be minimum, where because there should not be much protein that that can generate excessive ammonia which is formed out of this protein molecules. This protein restriction is used in conjunction with the medication which provides alternative pathways for the removal of ammonia from the blood. Frequent blood testing are required to monitor the disorder. Optimize treatment and frequently hospitalizations are necessary to control these disorders. At the most the extreme cases a few liver transplantation has been taken place successfully to cure this disorder.

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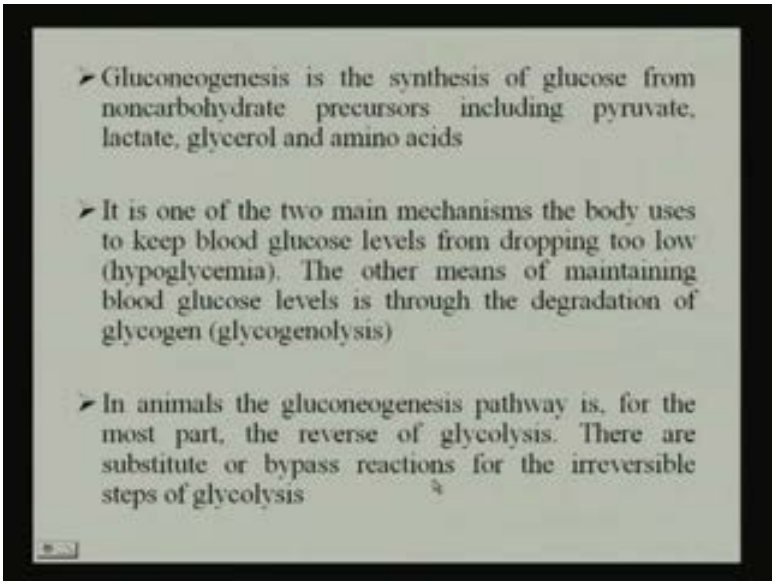

Now, if we come to this particular disorder and if we see this urea cycle we can find that these amino acids are playing a significant role in this particular cell cycle, in this urea cycle.

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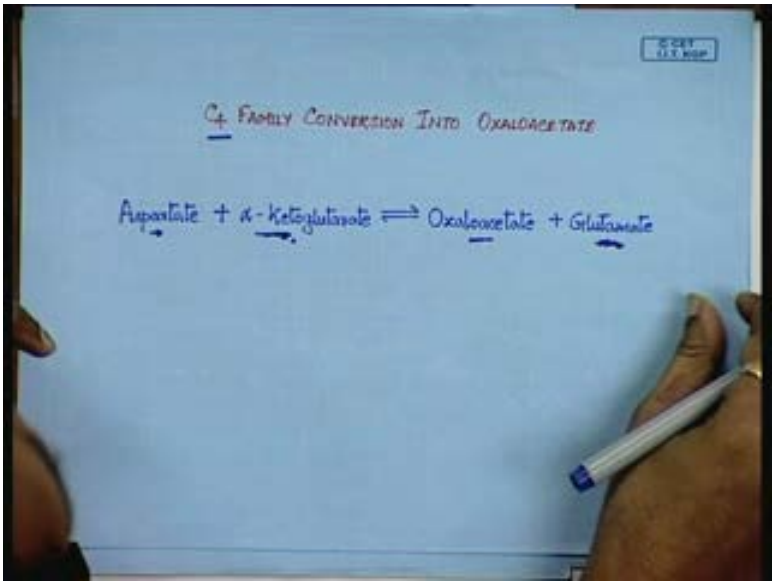

And if we see the different families; that is C 4 family conversion into oxaloacetate and if we see we have seen that in Nacetylglutamate is playing a significant role in operating this carbamoyl phosphor phosphate synthetase one. So, that enzyme which is there that glutamate is playing a significant role. So, if we see inside the cell how we can tell this aspartate and alpha ketoglutarate aspartate is the amino acid? And alpha ketoglutarate is one of the intermediate products of the TCA cycle? When they undergo some reaction they produce oxaloacetate and this glutamate which is playing a significant role in that supplying that N-acetylglutamate formation.

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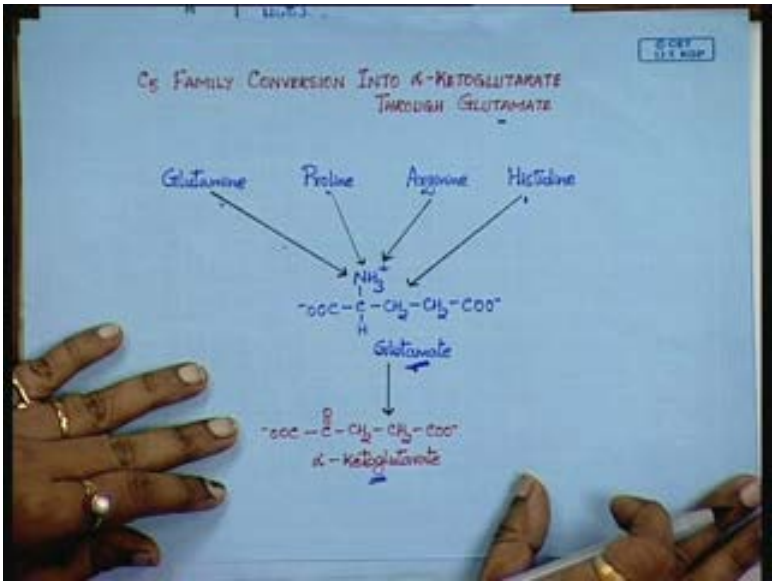

If we see that C 5 family conversion into alpha ketoglutarate through gluatamate, we can find that glutamine, proline, arginine, histidine they all are amino acids. They are converting to converted back to glutamate. When glutamate is there, glutamate is getting converted to alpha ketoglutarate and this is this way this alpha ketoglutarate and glutamate is playing a significant role to operate this urea cycle.

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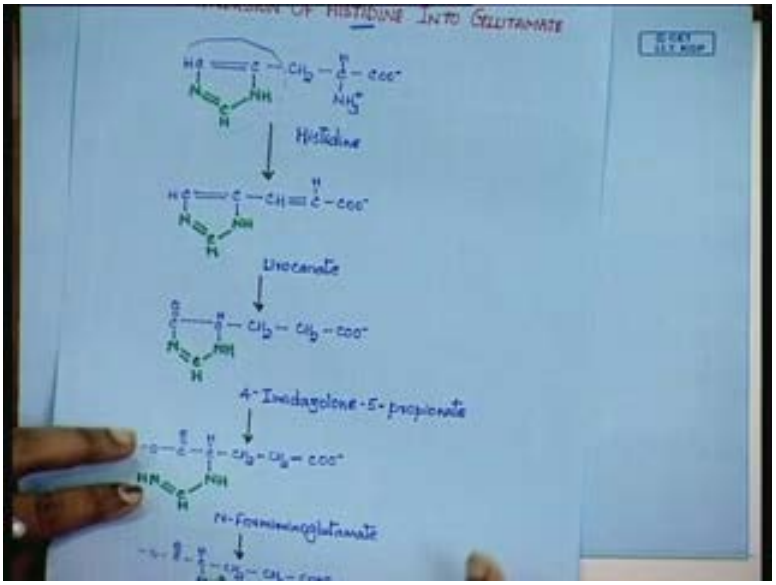

Now coming to this another important amino acid which is also playing a significant role in this particular glutarate production, we can find that this conversion of histidine into glutamate. Histidine is also another important amino acid which is present in any living system and it has got one imidazolium group. And this imidazolium group is present in histidine which makes it unique from any other amino acids and where it under goes some reaction ultimately we can find that, this glutamate is produced from this histidine molecule. And this way this glutamate concentration in the cell is being maintained by very many pathways from where this urea cycle or the intermediate this glutamate which is one of the important intermediate for this urea cycle operation. And this way this urea cycle is being operated inside any living system.

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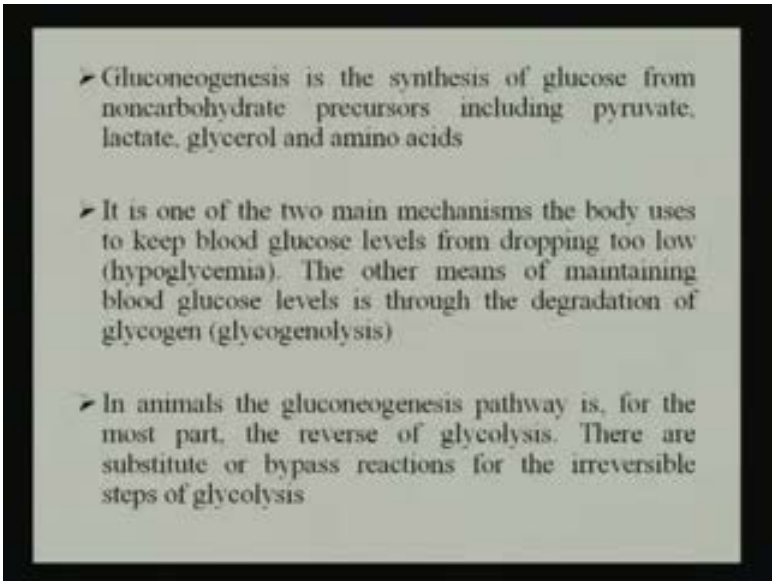

Now, coming to another topic that is the gluconeogenesis. Now here in my earlier class I have already discussed the synthesis of glucose that glucose is being produced. And I have told that how glucose to glycogen and glycogen to glucose production is taking place. are Or this type of conversion that excess glucose is there it is converted to glycogen body is in need of glucose glycogen is broken down to this glucose molecules and this way this glucose generation is there from this carbohydral moieties. That I have already discussed in my last class. But, today I will be discussing that another pathway that how glucose can also be produced from non carbohydrate source.

Now see, that gluconeogenesis is the synthesis of glucose from the non carbohydrate precursors that is pyruvate lactate glycerol and amino acids. So here, we can see that not only this carbohydrate but, the non carbohydrates are also playing a significant role as far as this glucose production inside the cell is concerned. It is one of the two main mechanism the body uses to keep blood glucose level from dropping too low. That is when blood glucose is dropping down it is called hypoglycemia. The other means of maintaining blood glucose level is through the degradation of glycogen. What I have already discussed and how glycogen is being chopped broken down to glucose that we have already learnt. Now, today we will be learning that from non carbohydrates source how glucose is being generated. In animals the gluconeogenesis pathway is for the most part the reverse of glycolysis. There are substitute or bypass reactions for the irreversible steps of glycolysis. Sometimes what we have learnt in glycolysis? Glucose is converted

to pyruvate. But, we can say here that pyruvate is one of the precursors for gluconeogenesis. So, from pyruvate when glucose is produced, it is just opposite to that of this glycolytic process. But, in actuality it is not totally like that. Because some of the reactions which are taking place and which are non reversible irreversible in nature those type of reactions are bypassed in gluconeogenesis.

Now, let us learn that what are those bypass reactions which are there in gluconeogenesis. Now here, as I have told that pyruvate to glucose is the gluconeogenesis.

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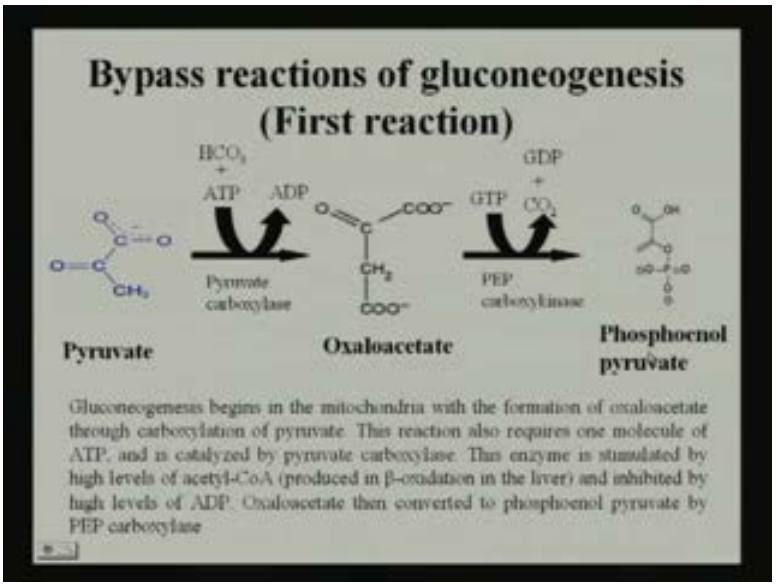

Now, if we start from the end product of the glycolysis that is pyruvate. Now, pyruvate in presence of pyruvate in in in the presence of the enzyme pyruvate carboxylase and one molecule of ATP is being required and this bicarbonate is needed to convert this thing to ADP. Now, gluconeogenesis begins in the mitochondria with the formation of oxaloacetate through carboxylation of pyruvate. This reaction also requires one molecule of ATP and is catalyzed by pyruvate carboxylase. This enzyme is stimulated by high level of acetyl coA that is, production in beta oxidation in the lever and inhibited by high level of ADP. Oxaloacetate then converted to phosphoenol pyruvate by the enzyme phosphoenol pyruvate carboxylase. So, pyruvate is getting converted to oxaloacetate. Oxaloacetate is then in the presence of carboxykinase enzyme. This enzyme is converting this oxaloacetate to phosphoenol pyruvate. And one molecule of GTP is

converting converted back to GDP and one molecule of carbon dioxide is being produced in this particular reaction. That means this is the decarboxylation reaction which is going on while conversion of oxaloacetate to phosphoenol pyruvate.

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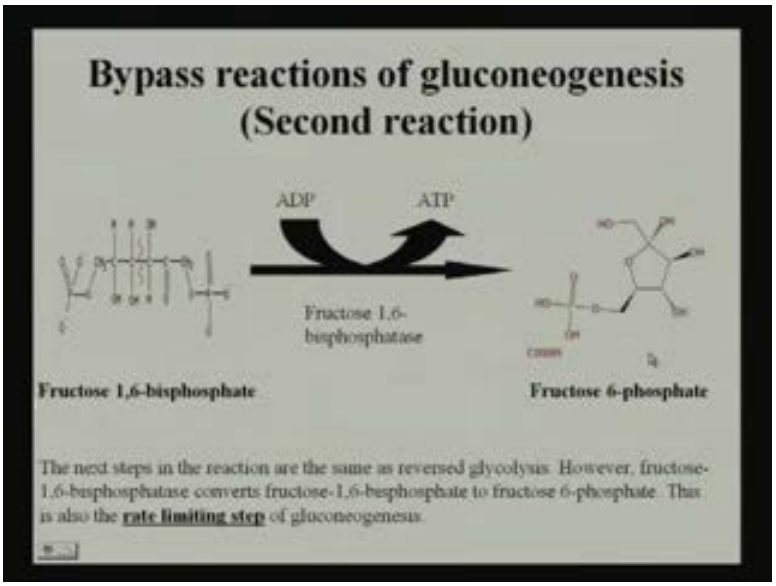

This is first step that is the bypass which is not there in case of glycolytic process. In the second reaction, if we see the second bypass reaction of gluconeogenesis then, we can find that fructose 1 6-bisphosphate. In the presence of this enzyme fructose 1 6-bisphosphatase is converting converted back to ADP to ATP. That means from this first phosphate that first carbon of this fructose which is phosphorylated, this dephosphorylation is going on and from the first carbon, phosphate group is being taken up and ADP is ADP to ATP formation is taking place and fructose 6-phosphate is produced. This particular step is also otherwise is known as rate limiting step of gluconeogenesis.

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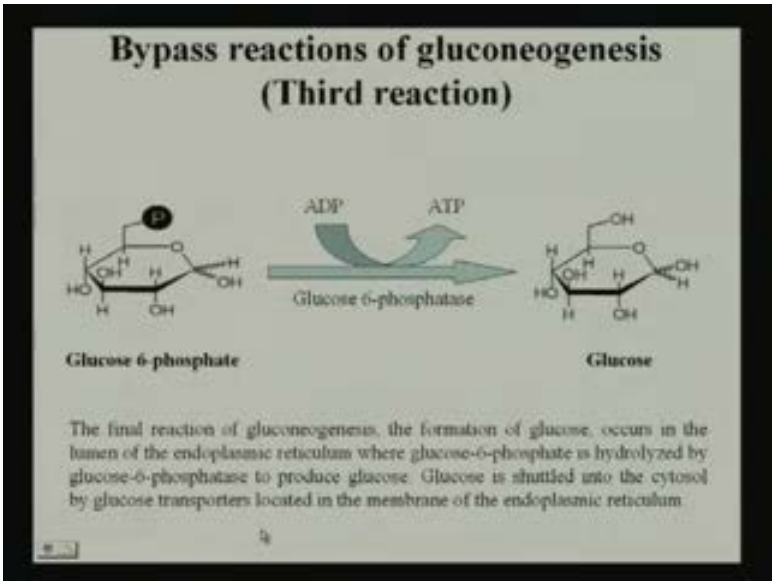

In the another bypass reaction, where we can see that glucose 6-phosphate is once again dephosphorylated and it is converted back to glucose in the presence of this enzyme glucose six phosphate. Here also, we can find that this molecule of ADP with the uptake of this this phosphate group is converted back to ATP. Now, the final reaction of gluconeogenesis is the formation of glucose which occurs in the lumen of the endoplasmic reticulum where glucose 6-phosphate is getting hydrolyzed by this glucose 6-phosphtase inside and glucose is being produced as final resultant product. Glucose is shuttled into the cytoplasm by glucose transporters located in the membrane of the endoplasmic reticulum.

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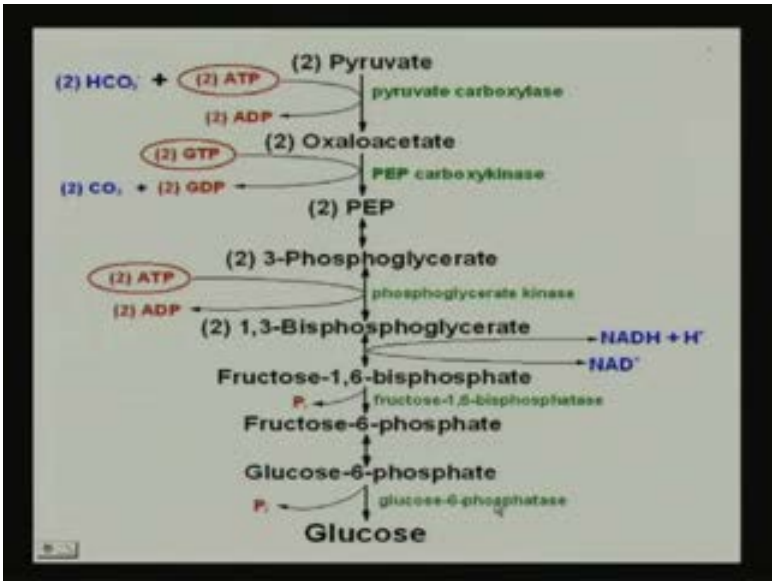

And this is the bypass reactions and remaining that the other reactions which are there inside this are same as that of this glycolytic process. So, if we see this reversal of this particular this particular reaction we can find that this pyruvate is getting converted to glucose and here is this bypass reaction. And these bypass reactions are different from that of this normal conventional reaction.

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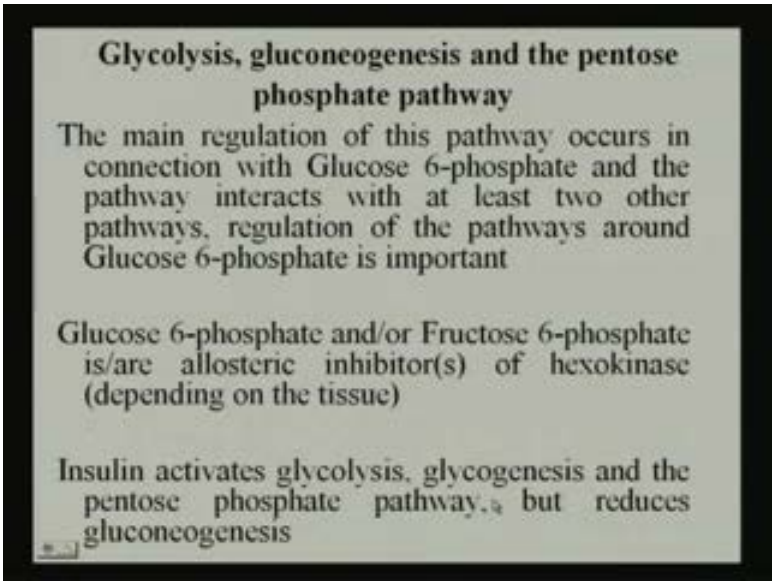

Now if we see the glycolysis, gluconeogenesis and the pentose phosphate pathway; the main regulation of this pathway occur in connection with this glucose 6-phosphate and

this pathway interacts with atleast two other pathways. Regulation of the pathways around glucose six phosphate is important. Glucose six phosphate and or fructose 6-phosphate are allosteric inhibitors of hexokinase that is depending upon or glucokinase that is the depending upon the tissue. Insulin activates glcolysis, glycogensis and the pentose phosphate pathway but, reduces gluconeogenesis.

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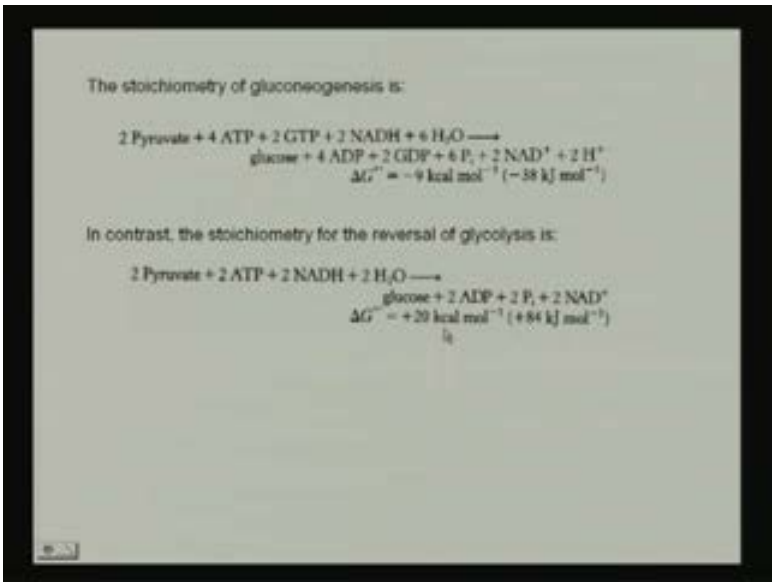

And these are the some of this differences and similarities. If we see the stoichiometry of gluconeogenesis then we can find that, 2-pyruvate from 2-pyruvate one molecule of glucose is being produced and this reaction is thermodynamically this thermodynamically this is possible and feasible. In contrast, the stoichiometry of this reversal of glycolysis is thermodynamically unfavorable reaction where delta g is coming, the positive eighty four kilo joule per mole. So here also, pyruvate is getting converted to glucose.

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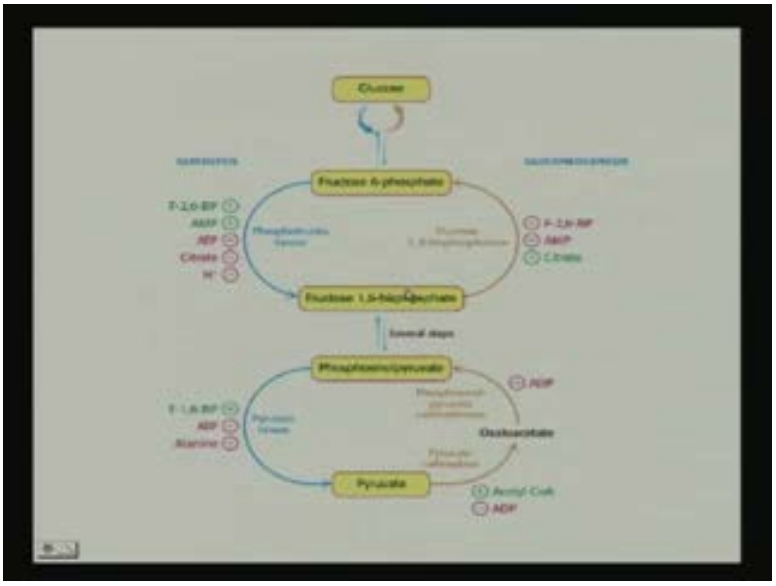

So this isthese are some of the differences in gluconeogenesis and glycolytic process. So, these are this bypass reaction this fructose 6-phosphate to this glucose formation fructose 1 6- bisphosphate. Here this is one of this reaction phosphoenol pyruvate is another bypass reaction and this glucose formation is the third step which is not similar to that of glycolytic process. And here are the dissimilarities of gluconeogenesis and glycolytic process.

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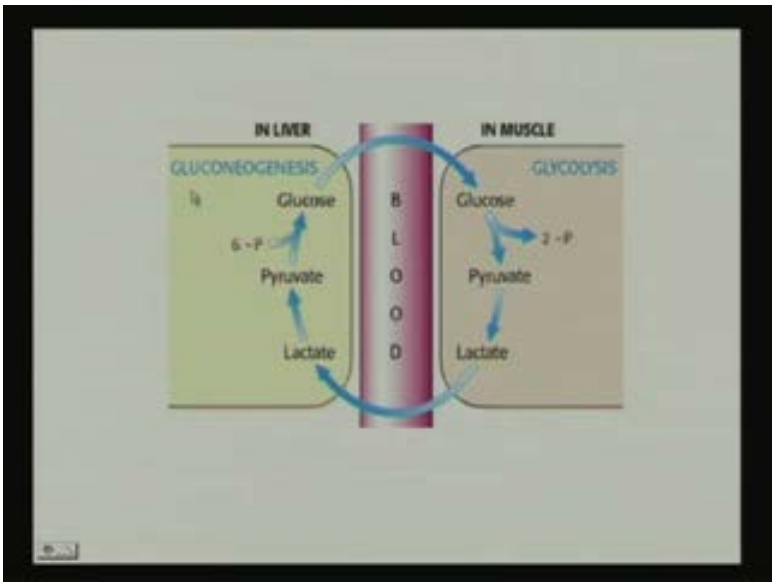

If we see that gluconeogenesis is taking place in the lever and in the muscle glycolysis is taking place now glucose is getting converted to pyruvate to lactate. And then this lactate is being enter to this lever cell and from lactate to pyruvate and pyruvate to once again glucose is produced in the process through the process of gluconeogenesis.

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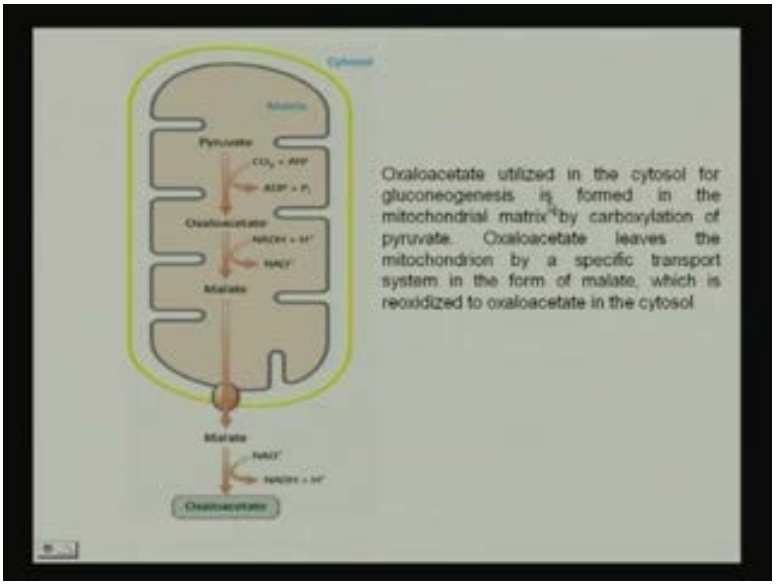

And this glucose is once again coming to this once again coming to the muscle cell of the body. Oxaloacetate utilizes the cytosol of this gluconeogenesis. Cytosol for gluconeogenesis is formed in the mitochondrial matrix by carboxylation of pyruvate. Oxaloacetate leaves the mitochondria by a specific transport system in the form of malate which is reoxidized and oxaloacetate is formed in the cytosol.

So, this is the pyruvate pyruvate to oxaloacetate to malate and once again this malate is coming to the cytoplasmic fluid and malate to oxaloacetate is produced and this way mitochondria and the cytosol these reactions are going on.

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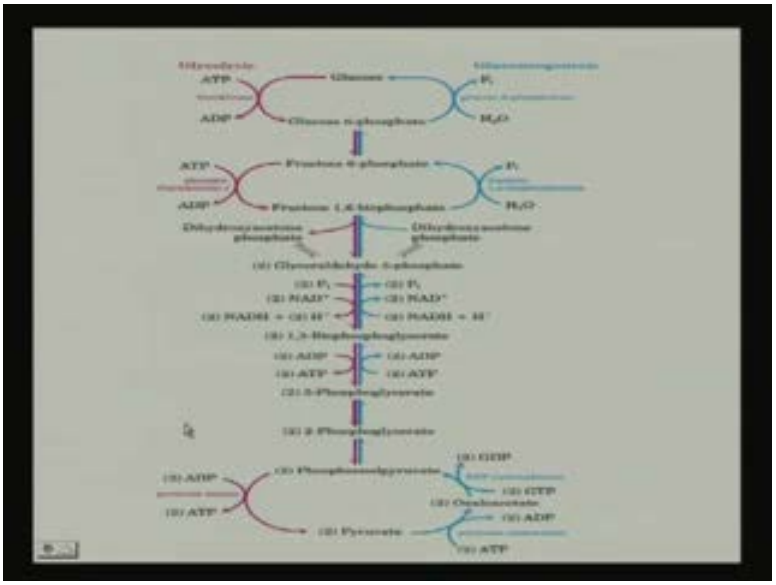

This is as I have already discussed. This is the reversal of this glycolytic and gluconeogenesis process. Now, if we see the similarities and dissimilarities of this glycolysis and this gluconeogenesis, we can find that here three enzymes which are participating in the glycolysis process is different from that of this gluconeogenesis.

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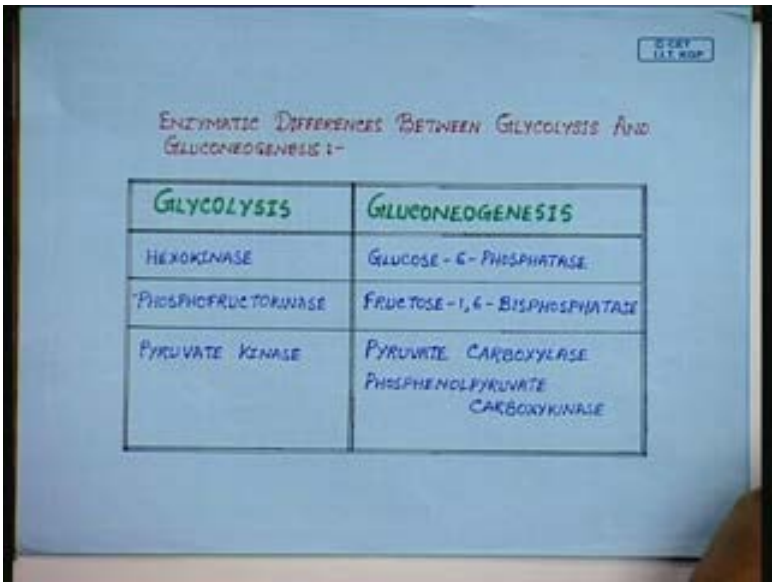

Hexokinase here it is in glycolytic process, here glucose 6-phosphatase phosphofructokinase fructose 1 6-bisphosphatase and pyruvate kinase. This pyruvate carboxylase or phosphenolpyruvate carboxykinase these are the enzymes.

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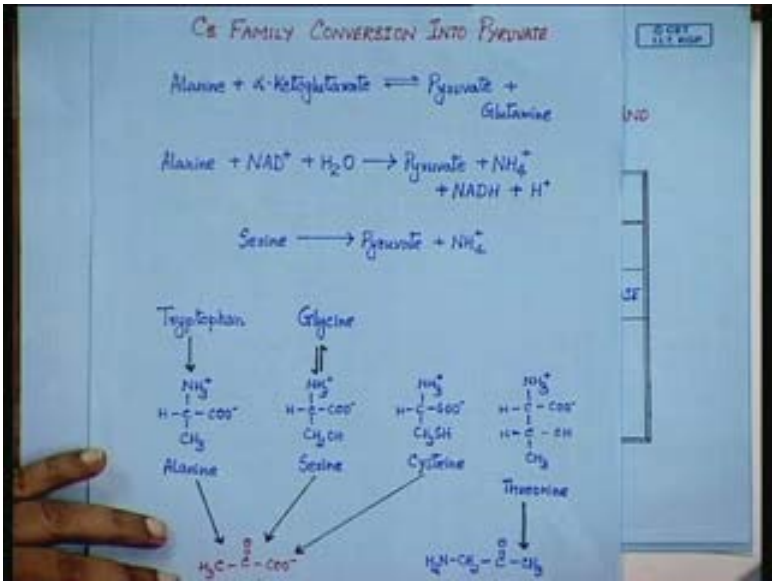

And if we see the C 5 family conversion to this pyruvate, we can find that alanine and alpha ketoglutarate is producing this pyruvate. This pyruvate can also be produced from this amino acid. Different amino acids like alanine serine tryptophan glycine and ultimately with this cysteine threonine and amino acetone are there. And ultimately you can see this pyruvate is produced and this pyruvate, from this pyruvate once again this gluconeogenesis, that glucose generation may also take place in the liver cell of the body.

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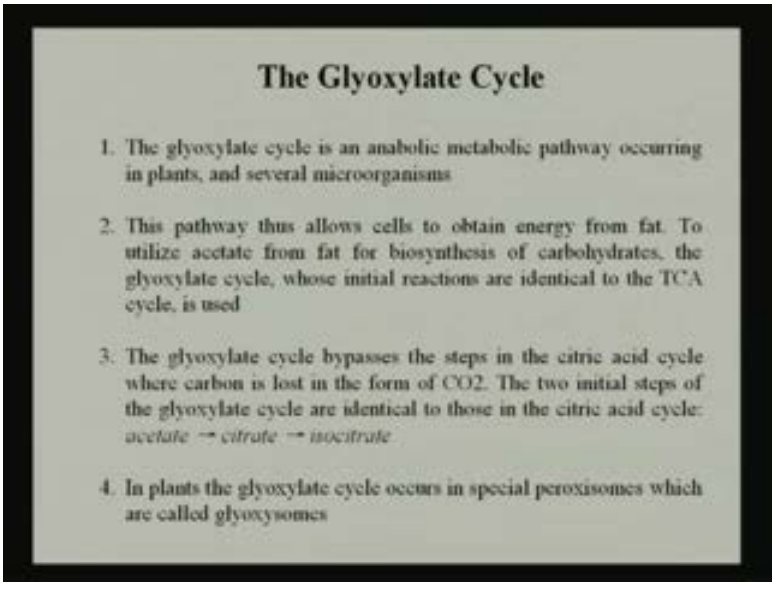

Now coming to this last this another cycle that is, the glyoxylate cycle glyoxylate cycle is an anabolic pathway which is occurring in the plant and several microorganism. This pathway thus allows the cell to obtain energy from the fat. It utilizes acetate from fat for biosynthesis of carbohydrates, the glyoxylate cycle whose initial reactions are identical to that of this TCA cycle. So here, we can find that this acetate is getting converted to citrate, citrate to isocitrate and then isocitrate that other reactions which are there which is forming this succinate and glyoxylate which is entering once again to this particular cycle.

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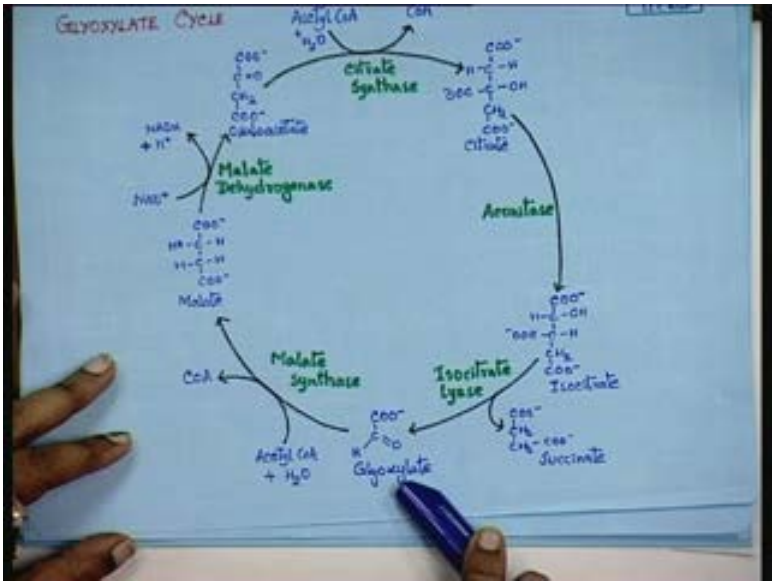

This gltoxylate cycle in plant is taking place in the glyoxyzone of the cell.

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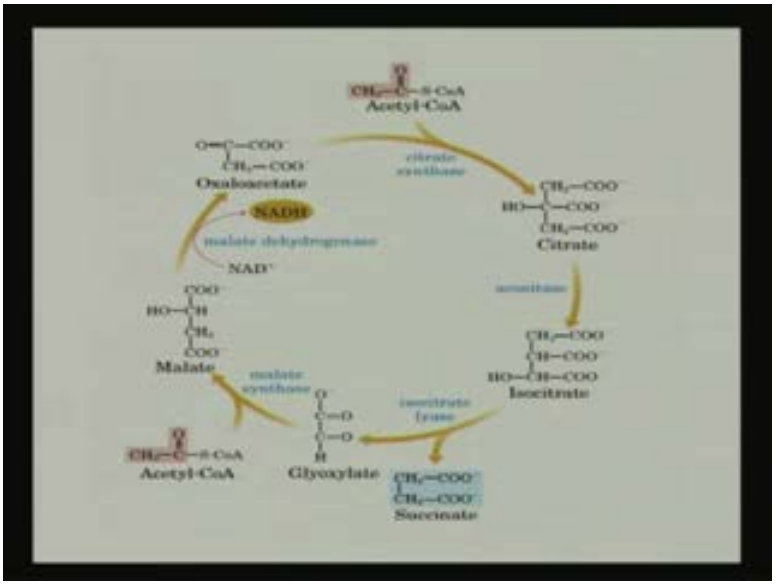

Now see, acetyl coA in the presence of this particular acetyl coA in presence of oxaloacetate is converted to citrate. This citrate is getting converted to isocitrate. You see this, after this reaction it is similar to that of this TCA cycle. As soon as isocitrate is produced it is producing succinate and these six carbon is broken to four and to this glyoxylate. And here another molecule of acetyl coA is needed to produce this malate and once again oxaloacetate is formed. And in this way when we see this particular path way we can find that this TCA cycle, this glycolytic process, TCA cycle, urea cycle, glyoxylate pathway, this gluconeogenesis and all this pathways which are simultaneously going on inside the cell are playing a significant role. And how we have seen the one intermediate products are been utilized for one pathway to another through the shuttle system. And this way in a very complex reaction, N number of reaction reactions are simultaneously going on inside the cell inside the living system. Thank you very much.