Biochemistry
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Lecture - 10
Myoglobin and Hemoglobin

What we are going to do today is, we are going to start or rather study a special topic myoglobin and haemoglobin, since we studied about amino acids, their properties and proteins in general and enzymes. What we are going to do today is see how myoglobin and hemoglobin have an effect on the oxygen binding that is extremely important in our daily lives.

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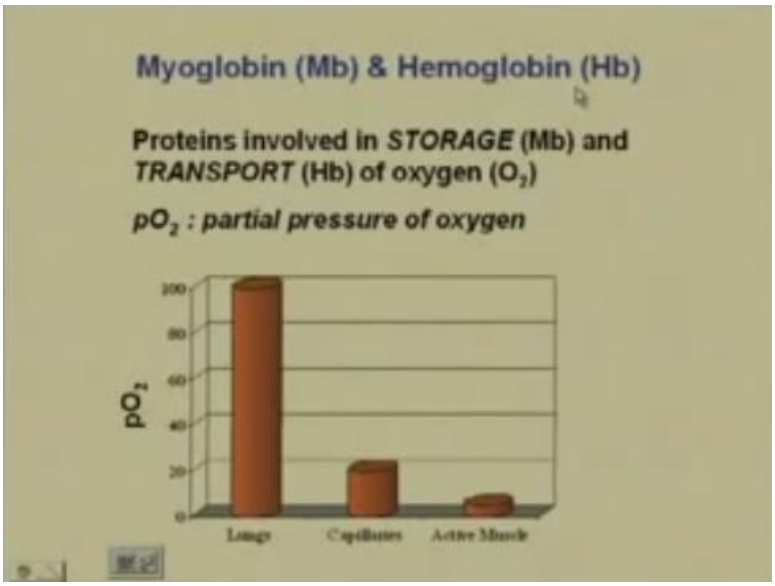

So if we go the first slide here, what we have is the two proteins, myoglobin and hemoglobin. Now these proteins are involved in storage that is primarily myoglobin and transport primarily hemoglobin of oxygen. Now we all know that we all breathing oxygen and we exhale carbon dioxide and so on and so for, but what we need to know is how this actually occurs okay. If we look at the partial pressure of oxygen, the partial pressure of oxygen in the lungs you see is the highest.

he highest why because we know that we breathing oxygen that goes to the lungs and it is passed through the capillaries through the active muscle where the oxygen is required for our activities okay. So in the lungs, we are going to have the largest partial pressure of oxygen followed by the capillaries followed by the active muscle.

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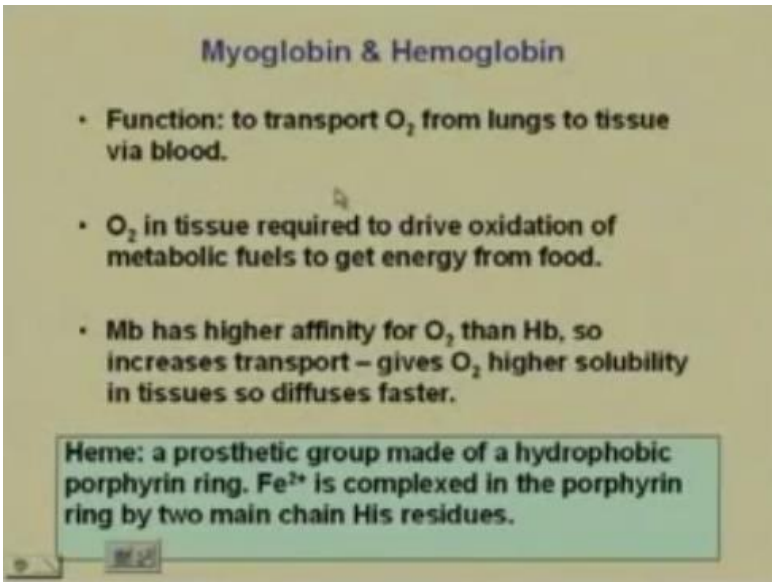

Now the function of myoglobin and hemoglobin is actually to consider the transport of oxygen. Hemoglobin, we will see how it transports oxygen, how it binds oxygen and so the case with myoglobin, but myoglobin acts small like a storage protein and hemoglobin more like a transport protein based on their specific activities or specific modes of binding of oxygen. Now the reason why we need the oxygen in the tissue obviously is for the oxidation of the fuels.

What are the fuels, the food that we intake right? When we study bioenergetics later on, we will see how actually we get the energy from the food. So, it is this breakdown of food that is going to provide us with energy and the oxygen in the tissue is required to drive this oxidation. We will also see that myoglobin has a higher affinity for oxygen than hemoglobin. So, it increases the transport and gives oxygen higher solubility in tissues.

Because that is where the oxygen is needed for the energy, for the oxidation of the fuels and so on and so for. So, this myoglobin, we will see has higher affinity for oxygen than hemoglobin, but the lower affinity of hemoglobin for oxygen is required in the fact that it is going to transport the oxygen. We will see how that works. Now each of these proteins have heme associated with it okay.

We will see what heme is, it is a prosthetic group that is made of a hydrophobic prophyrin ring and the ion 2+ that is part of what we call the iron in the blood okay that is where it is in

the heme, it is complexed in the prophyrin ring by two main chain, histidine residues of the polypeptide chain okay.

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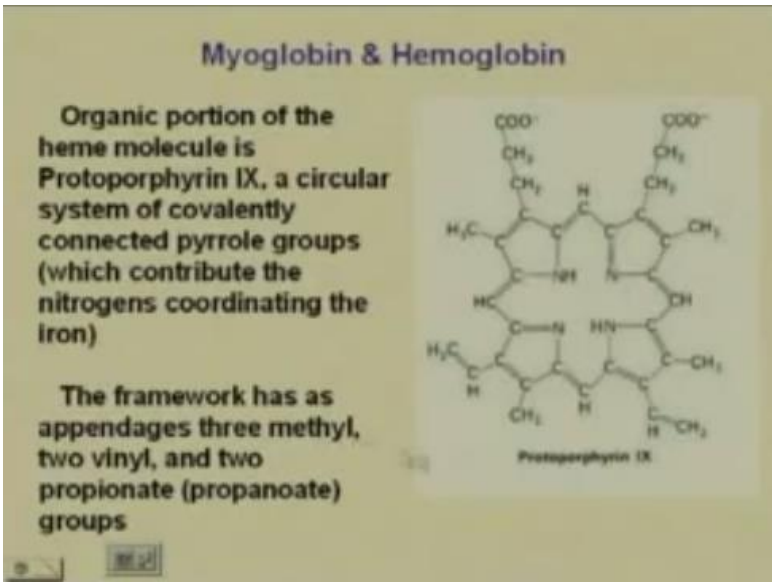

Now what is this Protoporphyrin IX, this is basically the structure of Protoporphyrin IX where what we have is we have a circular system. In this circular system, if you recognise these rings, these are actually pyrrole rings okay. The pyrrole rings are connected; you can see this network that is formed by the connection of the pyrrole rings, which actually contribute the nitrogens here that coordinate the iron in the heme. The organic portion of the heme molecule is therefore this.

So when we looking at this prosthetic group of myoglobin and hemoglobin, we have the organic portion of the heme molecule that is Protoporphyrin IX, a circular system as you can see of covalently linked, what are these, pyrrole groups okay. So we have this, this is one pyrrole, this is another pyrrole, this is another pyrrole and so on and so for. So when we link these pyrrole groups together, we have these nitrogen atoms that actually coordinate the iron for the heme group.

So what we have is if we look at this framework very carefully, you will see that there are three methyl groups, there is a CH3 here and there is a CH3 here okay. There are three methyl groups, there are two vinyl groups CH11CH2, CH11CH2 and there are two propionate groups CH2 CH2 CO-, CH2 CH2 CO-. So this is what is the organic portion of the heme molecule, this is Protoporphyrin IX to make this heme, what you have to do is coordinate and iron in the centre here okay.

So what we have is we have this circular system of the covalently connected pyrrole groups that contribute the nitrogens for the binding of the iron that is going to give the heme that is the prosthetic group for myoglobin and hemoglobin okay, so this is exactly what we have. So this is our Protoporphyrin structure that we saw in the previous slide and the heme differs from Protoporphyrin IX only in the coordination or the addition of the iron atom here.

The heme complex is inserted into the protein with the propionate groups that are these groups protruding into the solvent and the functioning portion of the heme is this tetracoordinated divalent Fe2+ iron okay and this is extremely important in the binding of oxygen that is required for the transport of oxygen and for the storage of oxygen and we will see how hemoglobin and myoglobin actually how the heme helps in doing this.

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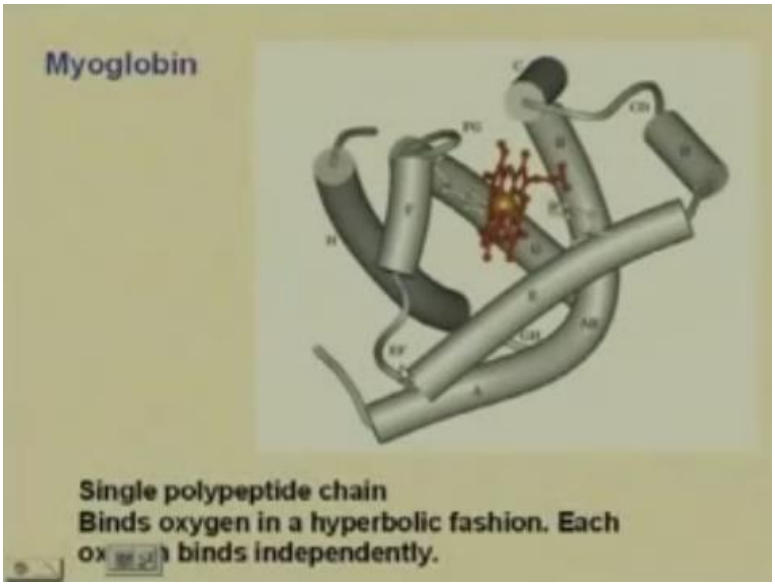

If we look at myoglobin, you can see this is myoglobin, it has a single polypeptide chain, so it is a monomeric protein, it binds oxygen in a hyperbolic fashion, we will see what that means and each oxygen binds independently okay. So what happens is you can see this one in red here is the heme okay. In the heme, you can see this yellow sphere that is the iron molecule that is attached to you can see actually linked to the histidine moieties again of the polypeptide chain okay.

So what we have in myoglobin is a single polypeptide chain, a single heme attached to it, so it will bind one oxygen molecule. Each heme binds an oxygen molecule and the fashion in which it binds is called a hyperbolic fashion, which we will see, what it means in a minute,

and how it is important in the functioning of myoglobin okay, because we have to remember that the structure of myoglobin obviously is going to dictate its function.

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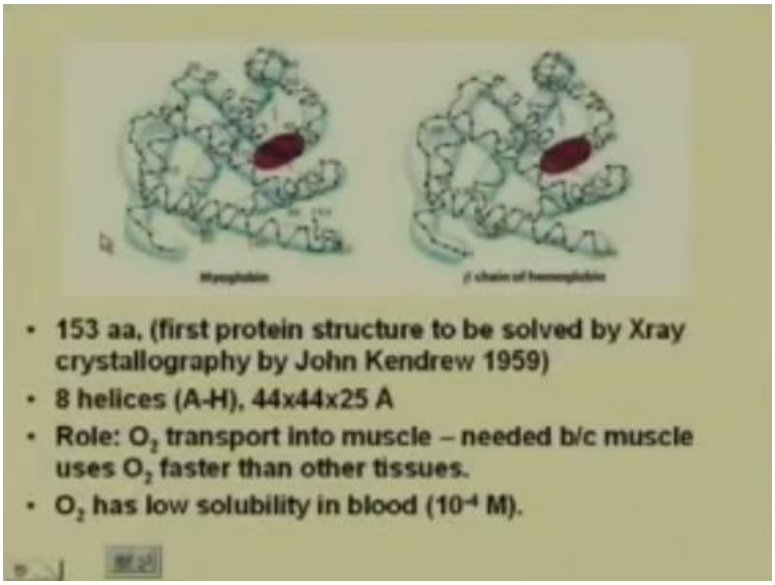

If we look at myoglobin, myoglobin is the first protein structure to be solved by X-ray crystallography by John Kendrew in 1959; this was followed by hemoglobin and then ribonuclease A. So, what we have in myoglobin, it is a single polypeptide chain and its role is oxygen transport into the muscle, it is needed because the muscle is going to use the oxygen much faster than the tissues of the lungs, because the lungs is always getting a supplier for oxygen.

But the tissue is using up the oxygen okay. So, the myoglobin is present more in the tissues why so that it can provide the oxygen that is required for the oxygen. Now what we have here is if we looked at what I have got on the right-hand side of this, this is the beta chain of hemoglobin, just the beta chain, you see how similar it is in structure to the myoglobin polypeptide chain okay.

But the difference between myoglobin and hemoglobin is that myoglobin is a monomeric protein where as hemoglobin is a tetrameric protein, it has two alpha chains and it has two beta chains okay. It is a tetrameric protein, but if you look at the beta chain, it has a very similar structure to the myoglobin and this is the heme portion of the molecule. If we look at the red portion here, it is the heme and so is this the heme in hemoglobin.

What is it mean; if this heme can bind one oxygen and hemoglobin has four such chains, what is it tell us about hemoglobin, that it can bind four oxygen molecules okay.

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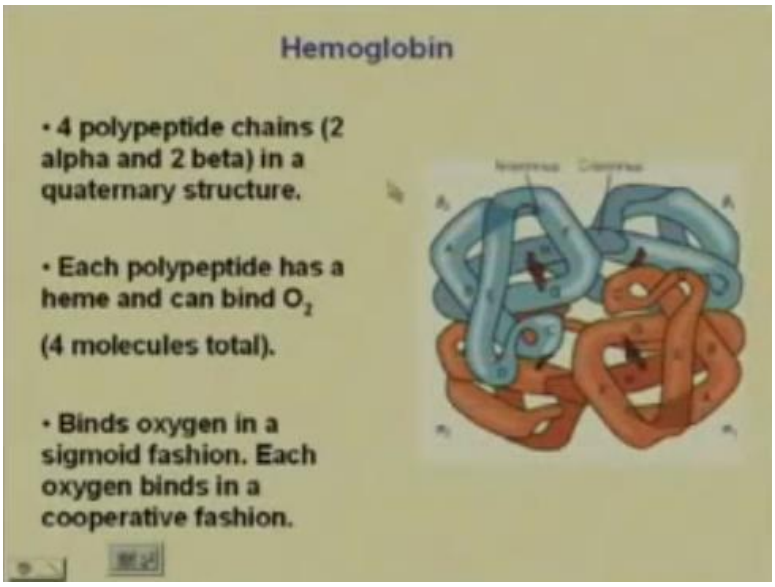

So what we have is we have the tetrameric protein hemoglobin, it has two alpha chains and two beta chains. Each of these have a heme associated with it, so there are four polypeptide chains, two alpha and two betas in the quaternary structure. Each polypeptide has a heme and it can bind oxygen and we will see that the oxygen binding is a sigmoid fashion, is in a sigmoid fashion and we will see what that means.

If you remember what we mentioned for myoglobin, it was in a hyperbolic fashion and this is in a sigmoidal fashion and each oxygen binds in a corporative manner. This is what I mentioned in one of the earlier classes that if one now you recognise that these hemes are going to bind an oxygen each. As soon as one heme binds an oxygen, it facilitates the binding of the oxygen to the other hemes, which is what is meant by cooperativity okay.

So the affinity for oxygen increases for the other hemes as soon as one of the hemes binds the oxygen, which is why it is said that it binds in a cooperative fashion okay.

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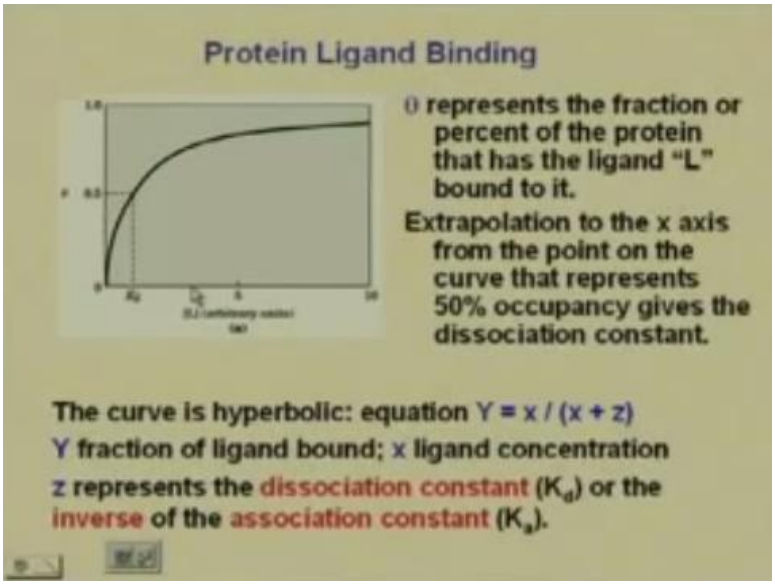

In general, now if we look at protein ligand binding, we will see how we can extrapolate this or how we can see what it means in terms of myoglobin and hemoglobin. Now usually what we mention here all the way it is represented is you represent it in the fraction or the percent of the protein that has the ligand bound to it okay. So 100% would mean that if you had a larger amount of ligand concentration, all the protein sites would be bound with the ligand.

Now what we have is this is what is meant by a hyperbolic curve right. The general of this is Y=x/(x+z). What is this Y, the Y is the fraction of the ligand bound okay, it represented as theta also. The fraction of the ligand bound x is the ligand concentration and z represents the dissociation constant. What is the dissociation constant, when we are considering a protein and ligand bound together when it associates, we have an association constant and when it dissociates we have a corresponding dissociation constant, which is what, what is the dissociation constant? it is just the inverse of the association constant.

Now when we are looking at this hyperbolic curve, you recognise that when I have 50% saturation as it is called, because if I have enough ligand concentration and all my protein sites are bound, I have a saturated situation right. Now when I reach 50% saturation here, it means that my Y or the fraction of ligand bound is half 50%, now that 50% corresponds on the x axis to the dissociation constant because of the ligand concentration associated with it.

Why because we have a hyperbolic equation corresponding to Y=x/(x+z), where x is our ligand concentration and z is the dissociation constant. So what are we saying, we have extrapolation to the x axis from the point on this hyperbolic curve that corresponds to a

fractional occupancy of 0.5 or 50% saturation means that corresponding, whatever we have corresponding on the x axis is the dissociation constant fine.

Now we are going to see how we can utilise this for the binding of oxygen, not only to myoglobin, but also to hemoglobin, which actually behaves a bit differently.

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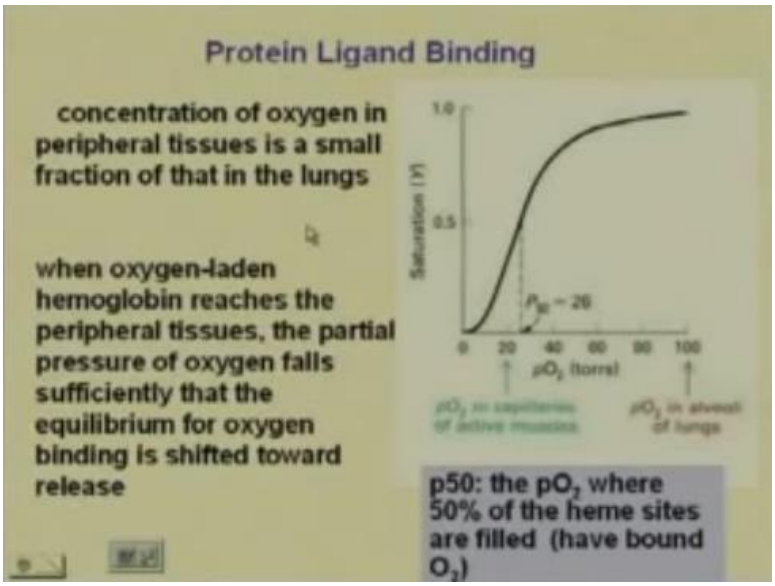

So, if we go to protein ligand binding in general, we will study this in more detail later on, what we were talking about is we are talking about a fraction that is occupied. What is occupied, the protein sites are bound with oxygen. So, we have a concentration of oxygen in the peripheral tissues, what do you expect the oxygen concentration to be in the tissues less than that is there in the lungs right.

When we are looking at the oxygen concentration in the tissues, it is less than that is there in the lungs. What is that mean, it means that the ligand concentration in the lungs is higher right, if the ligand concentration is higher in the lungs, what do you expect in the lungs, you expect 100% saturation right, but when the ligand concentration is low, where is the oxygen concentration low, in the tissues okay.

So we will not even have 50% saturation then, but as we increase the amount of oxygen, this is why measured in terms of the partial pressure of oxygen. As you increase the partial pressure of oxygen, when you reach the lungs you will have 100% saturation. Now the way this is measured is we measure something called p50. The p50 is the partial pressure of

oxygen where 50% of the heme sites are filled. What is that mean? that means in myoglobin, you have just one heme site right?

So that basically, it is filled or it is unfilled, but for hemoglobin what can you have, you can have one, you can have two, you can have three or you can have four, but usually what happens it sees that at all are non-situation. Because as soon as one of the oxygen molecules binds to one heme what does it do, it behaves in a cooperative fashion and it helps the binding of the other oxygen atoms also, so the oxygen atoms bind very quickly.

So what do we have the concentration of oxygen in the tissues is a small fraction of that in the lungs that we understand. Now when oxygen-laden hemoglobin reaches the peripheral tissues, the partial pressure of oxygen falls, so what happens is the saturation is less, so hemoglobin will release the oxygen right. So what is happening is when in the situation where the partial pressure of oxygen is high in the lungs, hemoglobin will take up the oxygen.

Since it is circulating in the blood, what is happening, when it is coming to a point near the tissues, the partial pressure of oxygen is low, so what is happening to it, it is releasing it. There is a dissociation, you have to remember that there is an equilibrium. The Hb+O2 giving you as we call HbO2 is an equilibrium situation, so at one time you are shifting it to the left of the equilibrium, at one time you are shifting it to the right of the equilibrium.

When is it going to go to the right, it is going to go the right when the ligand concentration or the oxygen concentration is high like it is in the lungs okay.

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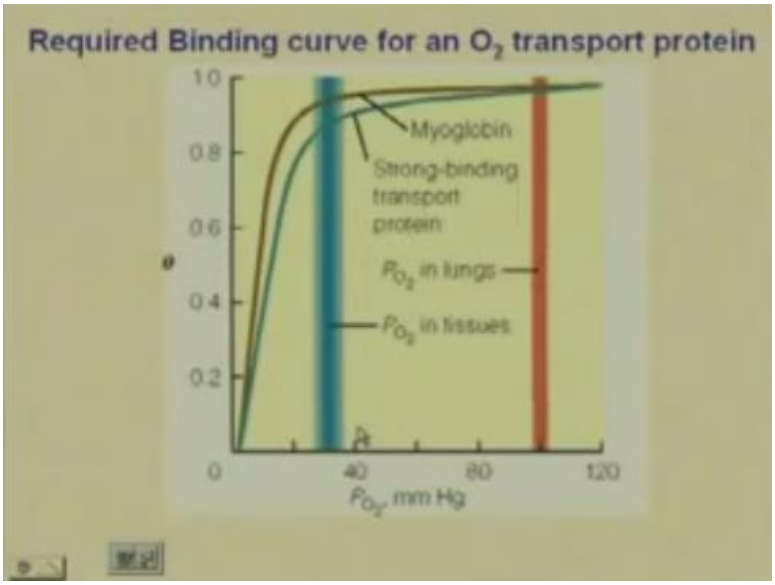

Now I want you to understand this very clearly. Suppose we have a situation where I have an oxygen transport protein okay, now if you look at the curve on top that is in purple here or the darker curve, this is the curve for myoglobin that binds oxygen in a hyperbolic fashion. What we have on the y axis is the fraction and we have on the x axis is the partial pressure of oxygen.

Now the partial pressure of oxygen in the lungs is high, the partial pressure of oxygen in the tissues is low. If this is the hyperbolic curve for myoglobin okay, what we have in the blue curve here is a strong binding, why do I say a strong binding, if you have a hyperbolic curve it means that even at a low pressure of oxygen, you have reached 80% saturation, is that clear, when you have a low pressure of oxygen. Let me draw it here.

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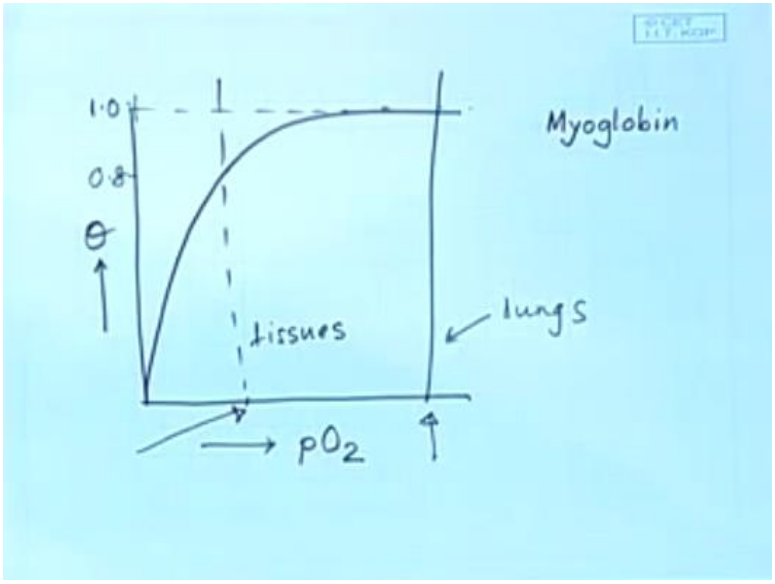

When we have a low pressure of oxygen, what are we looking at we are looking at a fraction or a saturation; here what are we looking at, what is the x axis the partial pressure of oxygen. What we are saying is we are looking at the curve for myoglobin now.

Myoglobin behaves in a hyperbolic fashion. So, this is the situation in lungs, this is the situation in tissues. So, what can we say, we can say that even when the partial pressure is low, myoglobin will not easily dissociate the oxygen from the heme, is that clear? So what are we saying, we are saying that the partial pressure of oxygen in the lungs is high, the partial pressure of oxygen in the tissues is low.

And if we have the binding in a hyperbolic fashion, this is 100% saturation, so we have a fraction here of one, this is a 0.8, what am I saying, I am still 80% saturated with the oxygen even at the tissues okay and that is what I want. But if we go back to the slides here, then if we look at now the myoglobin curve, what is there in the myoglobin curve, even at the concentration or the partial pressure of oxygen in the tissues, myoglobin still is more than 80% saturation right, but if you want a transport protein.

What is a transportation supposed to do, it is supposed to take in the oxygen and release it, is that clear? The hemoglobin has to release the oxygen, if it does not release the oxygen; it is no point in binding it. So, if we have a strong binding transport protein, what is going to happen, it is going to be efficient in binding, but inefficient in unloading, is that clear. Because Hemoglobin has to release the oxygen, if it does not release the oxygen, it makes no sense for it to bind it okay.

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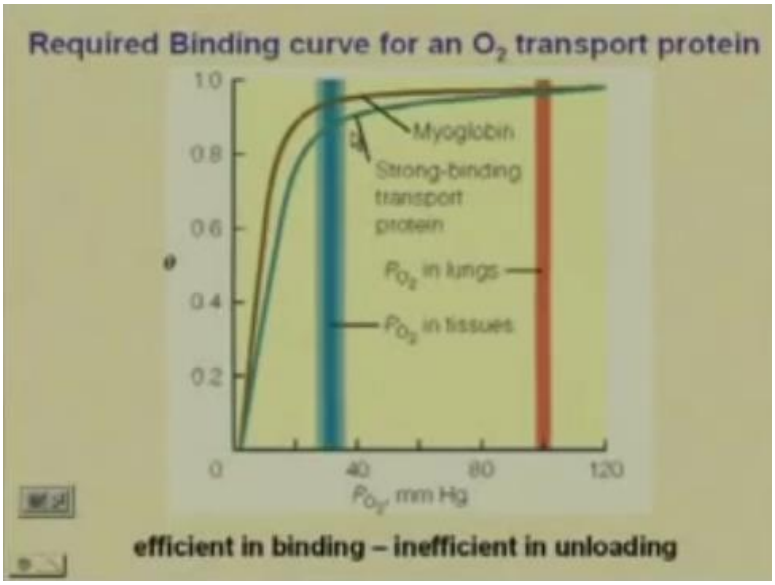

So what we have here is we have a strong binding transport protein, it is very efficient in its binding. It is still 80% saturated at the lower concentration in the tissues, but the tissues need the oxygen and if the oxygen is still bound, then it is no point, it has to be released okay. So what happens if let see we have something like this.

If we have a weak binding transport protein, myoglobin remains as it is in a hyperbolic fashion so it has, it is more than 80% saturated in the lungs as well as in the tissues, but if we have a week binding transport protein, what is going to happen to this, it is going to be efficient in releasing the oxygen right, because at the pressure of partial pressure of oxygen in the tissues, the saturation is low, so it will release the oxygen, but it is not very efficient in the binding right.

It is pretty inefficient because even when I am close to 100 mmHg, I still do not have even 70% oxygen bound right. So, in this case, I have something that is efficient in the unloading, but inefficient in the binding right. So, in this case, I have a weak binding transport protein. In the previous case, we had a strong binding transport protein, but none of this is helping me, why because in the lungs I have to have what, I have to have strong binding and in the tissues, I have to have it released okay.

So, I (()) (27:44) have to have a combination of methods, where it will be what; it will be efficient in binding and also efficient in the unloading right. So, we have to have a transport protein that is going to behave like this. How is going to behave, it is going to be highly

saturated in the lungs and it is going to the efficient in the unloading of the protein and unloading oxygen in the tissues.

So, what do we have, what is this then curve depicting, what is this curve depicting, it is telling you that you have something that is efficient in binding and also efficient in unloading. This is the sigmoidal curve of hemoglobin. So, what does Hemoglobin do, it is very efficient in taking up the oxygen in the lungs and it is also efficient in unloading the oxygen in the tissues, which is what you want okay.

So this is what would be the required binding curve for a protein that would transport oxygen, but for myoglobin, it is a storage protein. If myoglobin were also like this then what would have happened in the tissues, all the oxygen will be lost okay, but myoglobin is highly saturated even at the low partial pressure at the tissue level okay, which is essential because it is a storage protein.

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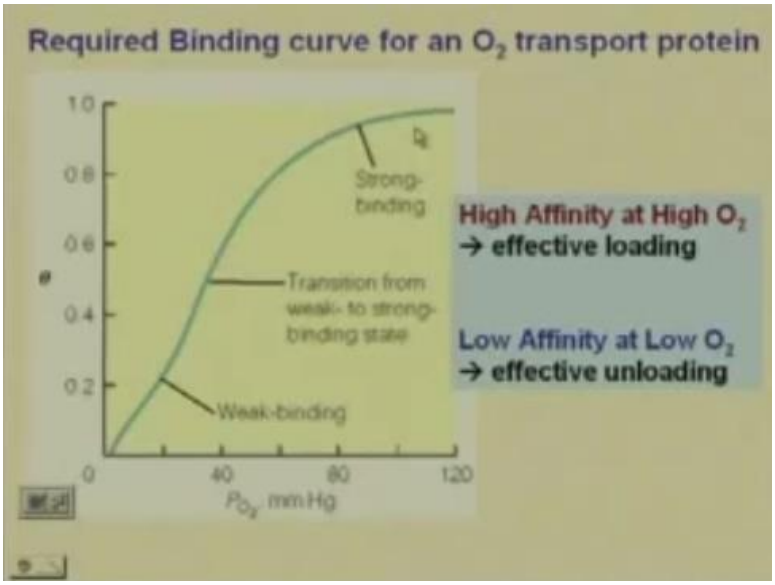

Now so what do we have here, we have a transition from a week binding state to a strong binding state. So this is the curve for hemoglobin, which is, what is called in a sigmoid fashion. The rise is in a sigmoid fashion where we have high affinity at high oxygen partial pressure, which means we have affected binding. When we are at this stage, we have low affinity at low oxygen levels, which means it is effective in unloading the oxygen okay.

So that is the optimum that the hemoglobin can do okay, it will bind it strongly; it will release it also strongly depending on what, depending on the partial pressure of the oxygen. So, you

would have it bind in a sigmoid fashion, it would have high affinity at high oxygen why because you want efficient binding, effective loading, it would have low affinity at low oxygen, so you would have effective unloading of the oxygen okay.

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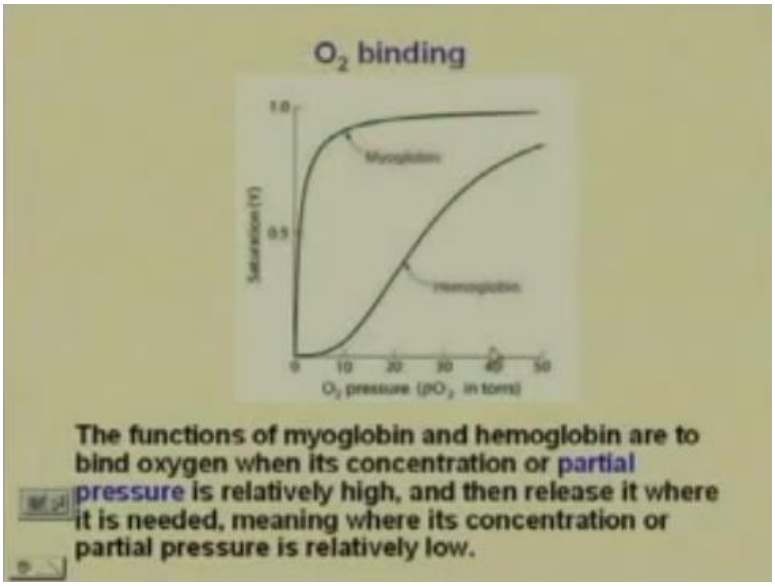

So, this is what we have saturation, the partial pressure of oxygen, this is the myoglobin curve for oxygen binding that is a hyperbolic curve. This is a sigmoidal curve for hemoglobin and you understand why it has to be a sigmoidal curve and why this has to be a hyperbolic curve okay.

So, the functions of myoglobin and hemoglobin are to bind oxygen when its concentration or partial pressure is relatively high and release it where it is required okay. It cannot just keep on binding tightly to it, because otherwise you would not get oxygen where you need it okay. So, when the partial pressure is low, it is going to release it. So, when you are in dire need of oxygen, you come to this, then myoglobin which is the storage protein, will release the oxygen at that point only.

So, you are panting for breath, you have run up the stairs because you are late for class okay. Then your myoglobin, your tissues lack the oxygen, the myoglobin will come to the rescue and because your pressure has gone down, it will give the oxygen that is required okay. So this is why the curves are shape like this and you have understood why hemoglobin has to be bind in a sigmoidal fashion and myoglobin in a hyperbolic fashion okay.

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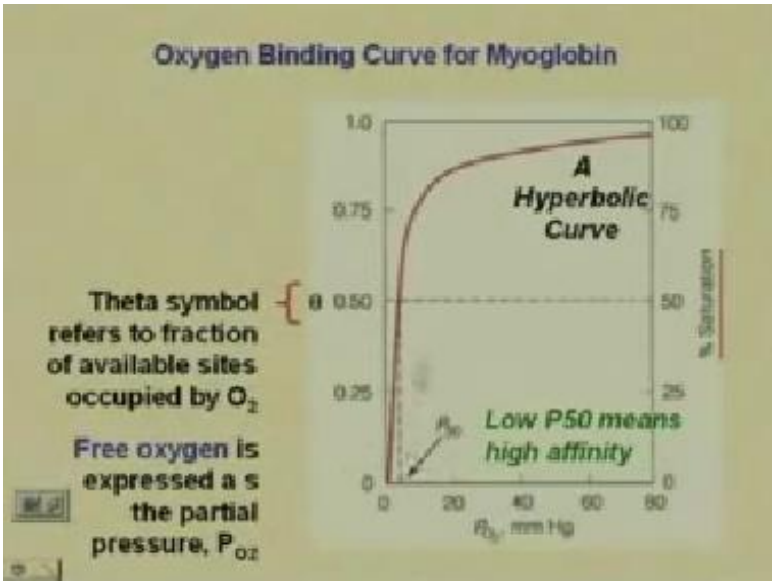

So, what do we have, we have the fraction of sites, a hyperbolic curve and we have a low P50. What is this P50, The P50 is a partial pressure at which is 50% saturated. If you have a low P50 it means, you are half saturated at a low pressure, so you have a low concentration of the ligand and you are already highly saturated. What does it mean? means you have a high affinity. You have a high affinity if at a low concentration, you are 50% saturated right. So, we have this oxygen binding curve for myoglobin.

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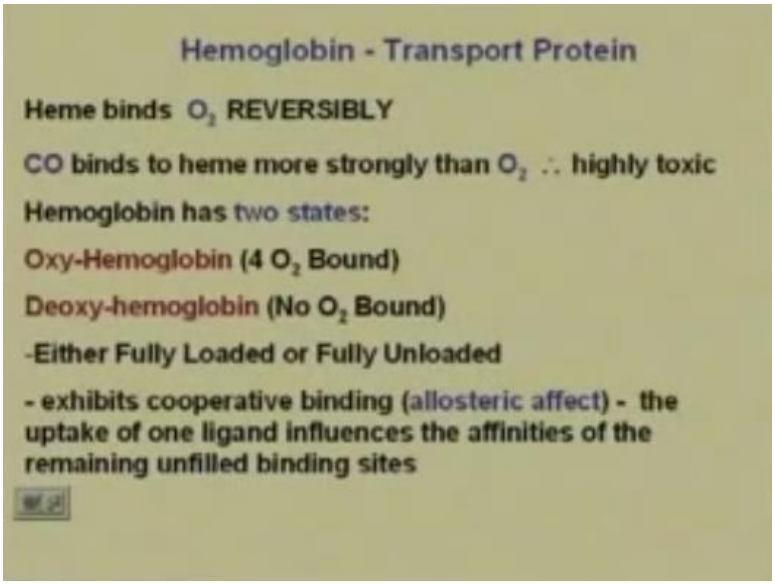

If you look at hemoglobin, we have hemoglobin bind oxygen reversibly okay. These are the features of the transport protein hemoglobin. What are they, it binds oxygen reversibly, you know carbon monoxide is a poison, why is that, carbon monoxide binds more strongly to heme than does oxygen which is why it is highly toxic. It will not release the carbon monoxide okay, very easily so it is highly toxic.

Now hemoglobin has two states, oxyhemoglobin, as a name implies where we have four of the oxygen bound, why do we have four because we have four subunits, each subunit has a heme, each heme is going to bind an oxygen. We also have deoxyhemoglobin, where no oxygen is bound and usually as I said it is either fully loaded for fully unloaded.

So, we either have an oxyhemoglobin or deoxyhemoglobin and the binding is a cooperative fashion, it is something that I mentioned last time what is called an allosteric effect, where the uptake of one ligand that is one oxygen molecule is going to influence the affinity for the binding of the other oxygen molecules, so it is going to help or facilitate the binding of the other oxygen molecules.

So, what we have is a reversible binding of oxygen to give four oxygen bound in what is called oxyhemoglobin, no oxygen bound is deoxyhemoglobin. So, we would have deoxyhemoglobin at low pressure of oxygen, we would have oxyhemoglobin at a high partial pressure of oxygen and we have all (()) (35:10) situation where it is either oxy or deoxy and it exhibits cooperative binding.

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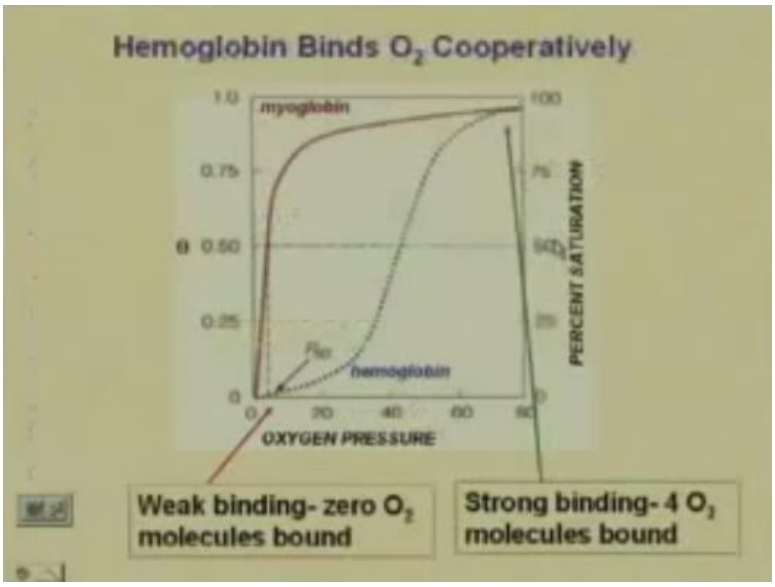

So this is (()) (35:20), the P50 for hemoglobin is low. Low affinity at low pressure, it has low affinity. At high pressure, it has high affinity, which is why it is this sigmoidal curve. Myoglobin has a higher P50, why because it reaches 50% saturation faster at a lower concentration of oxygen.

So, what do we have, we have strong binding here for the hemoglobin where four oxygen molecules are bound and we have a weak binding here where nothing is actually bound yet and we gradually reach this saturation okay. So, we have the cooperative binding, which is why actually this is sigmoidal because you have cooperative binding, this is sigmoidal and this is a hyperbolic fashion of myoglobin okay.

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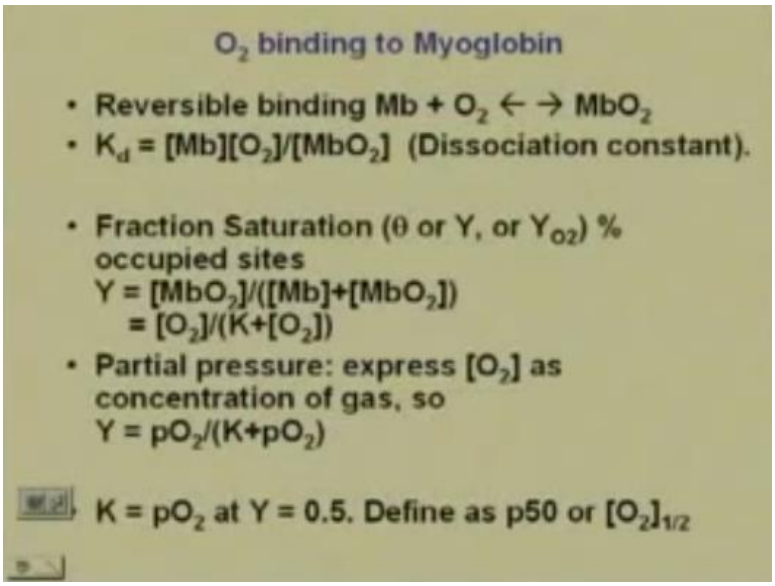

Now we have to come to some expressions. If we have reversible binding okay, that means we have Mb myoglobin plus oxygen in a reversible because we know we have to release the oxygen when we will need it, giving you Mb O2. What is this K d, it is a dissociation constant, so if I wrote it this way, I would have an association constant because I am associating the oxygen with the myoglobin and the inverse of this is the dissociation constant.

What do I have, I have Mb O2, the concentration of myoglobin, concentration of oxygen and the concentration of the Mb O2 and where is the oxygen binding, it is binding to the heme of the myoglobin. Why do not you work out a fractional saturation okay, suppose you want to know the fractional saturation, say Y, what is Y, Y is going to be equal to Mb O2 divided by Mb plus Mb O2 right.

Because Mb O2 is what, what is bound and the total amount is the free Mb that has not bound plus the Mb O2. So if we rearrange this, we can express it in terms of the oxygen concentration (()) (38:26) some algebra okay. So what do we have, we can get the partial pressure pO2 in terms of Y when you know what the K is and you know what the pO2 is. At

50% saturation, what do you have, this is just like the hyperbolic fashion curve that I showed you for protein ligand binding in the beginning where you have what Y=x/x+z okay.

So when you have this pO2, now we know what the partial pressure of oxygen is, if we have this equal to K, then obviously we have 50% saturation. So, the 50% saturation that is p50, is defined when we have Y=0.5 and that is possible when K=pO2 okay, in the expression here. So what do we have, we have a specific dissociation constant that we have defined and we have a fractional saturation that has been defined and we know that this fractional saturation would be 50% when the K value is equal to the pO2.

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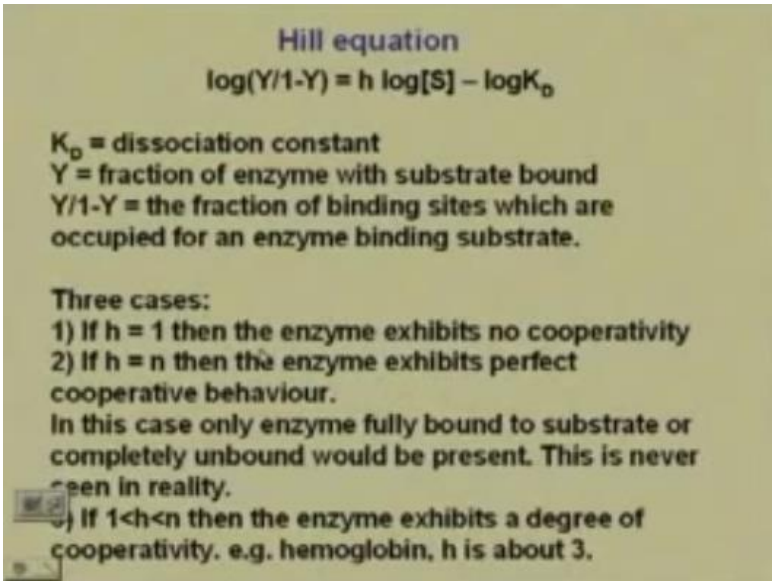

Now this is what is called a Hill equation okay. What we have here is if we look at the expression, we have a log Y, what is Y, Y is the fraction of the enzyme with substrate bound to it divided by 1 minus Y, it is log Y divided by 1 minus Y is equal to h, we will see what this h means, log S, what is S, S is the substrate concentration, which in this case is going to be oxygen minus log K d.

Actually, you can work it out from the previous expression that we had for the Y okay. You can try and work that out, it is just the previous expression worked out and returned in this fashion that has a specific name to it called the Hill equation. In the expression, what we have Y/1-Y which is the fraction of binding sites, which are occupied. The K d is the dissociation constant and h is the factor that actually gives us some information about the type of binding okay.

If this h is equal to 1, it means that there is no cooperativity, what is cooperativity mean; it means that the binding of one ligand molecule, one substrate molecule is going to activate the binding of the other ligand molecules. If there is no such cooperativity, say hemoglobin was non-cooperative, what it would mean that if one heme bound the oxygen, it did not matter to the other subunits. We have three cases here, h can be 1, h can be n, what is n, n is the number of sites that you have okay. So, what is n for myoglobin 1, what is n for hemoglobin 4 okay.

Now when h is equal to 1, then the enzyme exhibits no cooperativity. If h is equal to n, then you have perfect cooperative behaviour. Usually, this does not occur and if you have something a number between 1 and n, then you have a certain degree of cooperativity. What is that mean, it means that you can have a value in between the total number of sites that are available and 1.

What does this cooperativity mean, it means that you can have the ligand bound to one of the heme, of one of the subunits that will effect, facilitate the binding to the others and then you can plot what is called a hill plot where can you tell me what you are going to plot, you are going to plot log (Y/1-Y) on the y axis versus log S, and the slope is going to tell you this is also called the hill coefficient, it is going to tell you what the hill coefficient is okay.

So what do we expect the hill coefficient for myoglobin to be 1, because it is equal to n, there is only one site, but for hemoglobin we expected to be less than four why because there is cooperativity okay.

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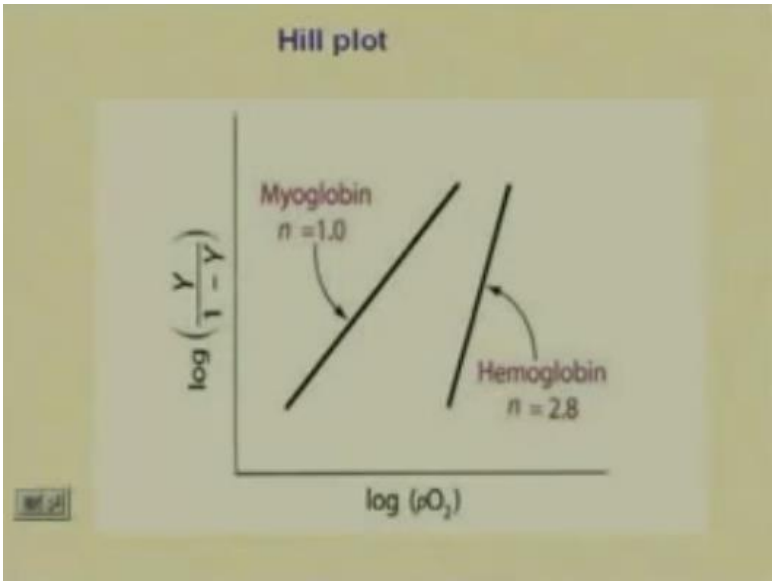

So that is exactly what happens, this is what we have. What is our measure for s, substrate concentration is measured by the partial pressure of oxygen in this case, so when we have log (Y/1-Y) what do we get, for myoglobin we get n=1 and for hemoglobin we get n=2.8 okay? This is what is the hill plot and these values are called the hill coefficient okay.

So actually, what is happening to hemoglobin, what is happening to hemoglobin at low partial pressure of oxygen, at low partial pressure of oxygen, it is bound weakly right, and at high partial pressure of oxygen it is bound strongly. So actually, this is the mixture of two curves, a weak binding curve and a strong binding curve okay. That is what we have on the next slide okay.

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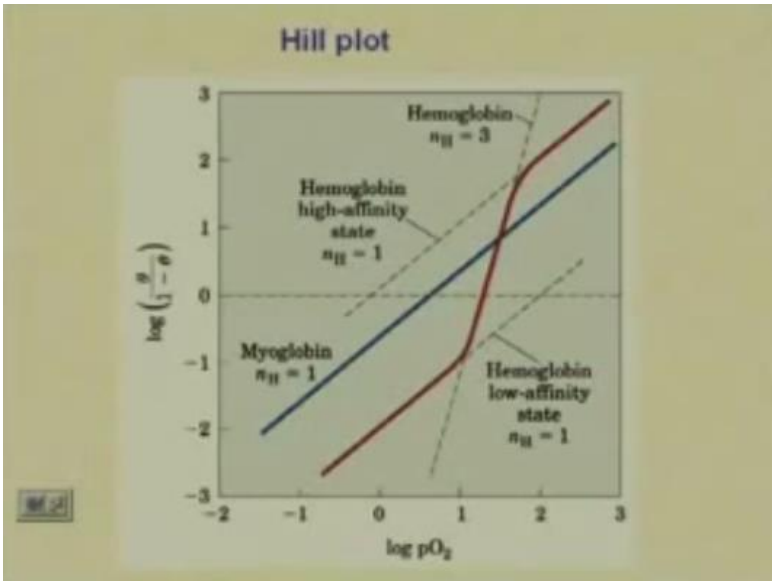

Try and understand this, what we are looking at is, we are looking at a hill plot, what do we have on the y axis log Y/1-Y versus log pO2, which is basically log x fine. Now when the pressure of oxygen is low, then there is no cooperativity yet why because a ligand molecule has not attached to it, the heme yet. You get the cooperativity after the ligand has attached to the heme right.

As soon as, one ligand attaches to the heme, when is that going to happen, that is going to happen at the specific pressure. So when you reach that pressure, then what is going to happen, if we reach this pressure then say that at this point here, what do we have at this point, at this point we have the n H, that is the hill coefficient equal to 1 because the ligand molecular has not yet bound to the heme as soon as one of them gets bound to the heme.

So one we have one of the oxygen molecules bound to one of the hemes, in one of the subunits, it is going to start or facilitate the binding of the other oxygens. So what you are going to have is your going to have a short increase what, where in the saturation because of the sigmoidal fashion of the curve, you are going to get a sharp increase in the saturation as you increase the pressure beyond the definite level why because you have the cooperativity because as soon as one of them binds.

It is going to help bind the other ones right and then you come to this level where again when you have reached the high affinity state, there is nothing more that can be bound to it okay, it is reach the higher saturation level okay. So it is this point when these slope that we will consider for the hill equation, that is going to give us a value close to 3 and for the myoglobin we are going to get a value of 1 okay.

So this explains the hill plot for hemoglobin and myoglobin okay. What are we going to get, we get a hill coefficient of myoglobin that corresponds to 1, a hill coefficient of hemoglobin that corresponds to 3 okay.

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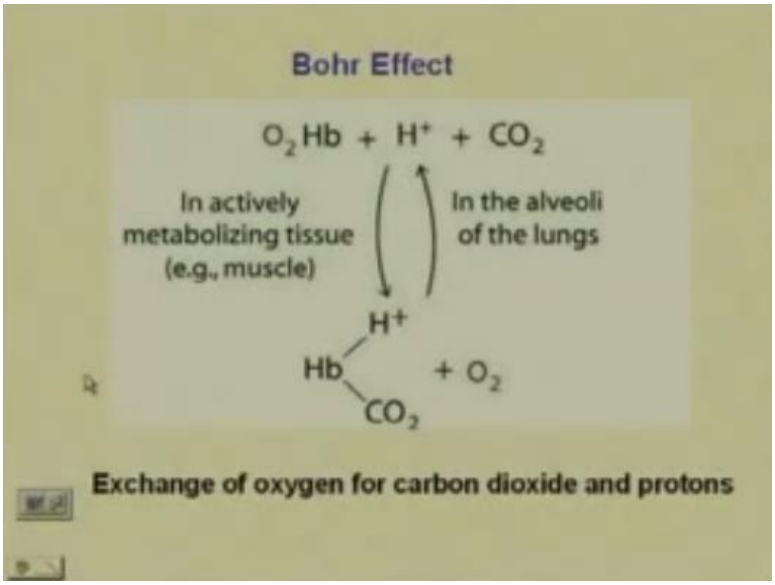

Now there is another thing that we just need to understand, something called the Bohr Effect. What is this Bohr Effect, we are not going into the details of all this, but what is happening is the hemoglobin has bound the oxygen to it right, where in is it binding the oxygen to it in the lungs right?

Now when it comes to a lower partial pressure of oxygen, what it is going to do, it is going to release the oxygen right. Now as it where is it going to do this in the tissues right, so there is basically an exchange of oxygen for carbon dioxide and protons okay. So essentially what is going to happen now is you are going to release the oxygen and it is going to become deoxyhemoglobin, but it is going to be associated with the carbon dioxide and the H+.

Eventually, actually what is going to happen, is what is going to happen to the pH, what is going to happen to the pH then, if I have an increased amount of H+, it is going to decrease okay. So the binding curve is going to change in the pH right, and how should it change, it should change in such a fashion that the oxygen is released at the tissue level.

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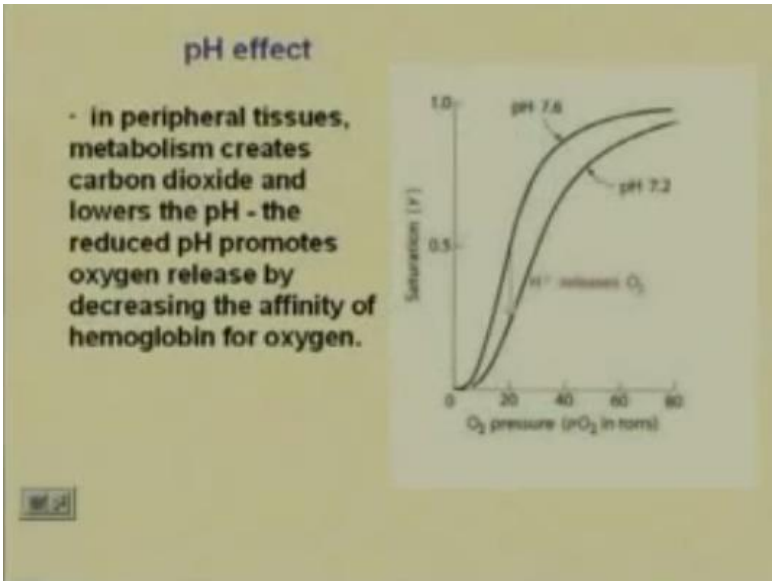

So what do we have, this is what we have. At a higher pH, we have the peripheral tissues here. The pH is 7.6 as we have the carbon dioxide release the H+. What is happening, this lowers the pH as it lowers the pH, suppose you are at a specific partial pressure of oxygen here, the pO2 says 20. What is going to happen when the pH is lower, the oxygen is going to release, why because the saturation is going to be less.

If there is a decrease in the saturation because of the decrease in the pH, what is that mean, oxygen is going to be released and where is this going to occur in the tissues okay. So in the tissues, you are going to have the metabolism that is going to create carbon dioxide lower the pH, reduced pH is going to promote oxygen release because the affinity for the oxygen of hemoglobin is less, the saturation is less at a lower pH.

If the saturation is less at a lower pH, it means oxygen is going to be lost and that this exactly what you wanted to do. You wanted to supply the oxygen at the tissue level, so that you can have the oxygen released okay. So this is exactly what happens.

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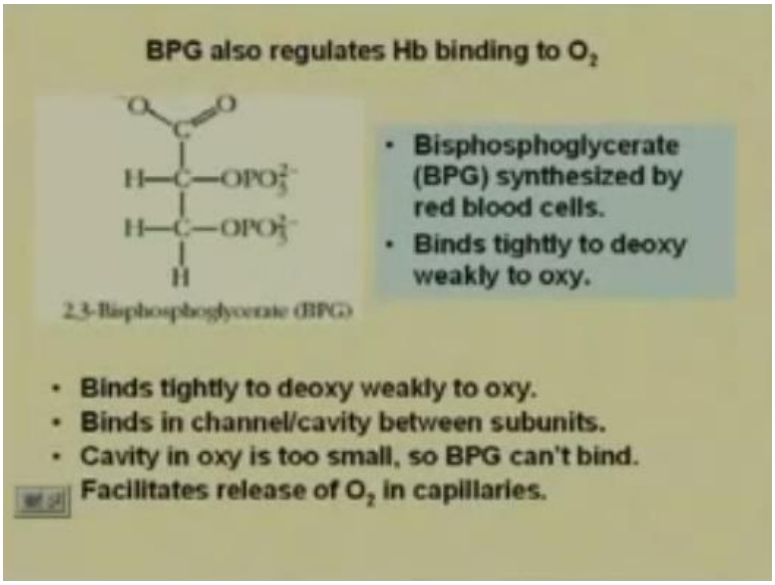

This is a one interesting thing that we might consider. This is called BPG okay, this is just for an interesting application of what the body actually can do. This is BPG is Bisphosphoglycerate. It is synthesised by the red blood cells and it binds not to oxyhemoglobin, but binds very tightly to deoxyhemoglobin, what is deoxyhemoglobin, when the hemoglobin does not have oxygen bound to it, it is called deoxyhemoglobin.

This BPG binds two deoxyhemoglobin and what happens is the cavity that is present in deoxyhemoglobin is large enough to hold the BPG molecule in there okay. Now once it holds the BPG molecule, then can you tell me what is going to happen to the oxygen, then if the deoxy is binding the BPG, then the oxygen will not be bound to it, it will be released okay.

Where can this be useful, where, where can it be useful; where there is less oxygen, no, where there is less oxygen available. Suppose you are climbing a mountain, there is less oxygen available; BPG is produced in the red blood cells more. So that it binds to the deoxy and you do not need as much oxygen as you would require okay.

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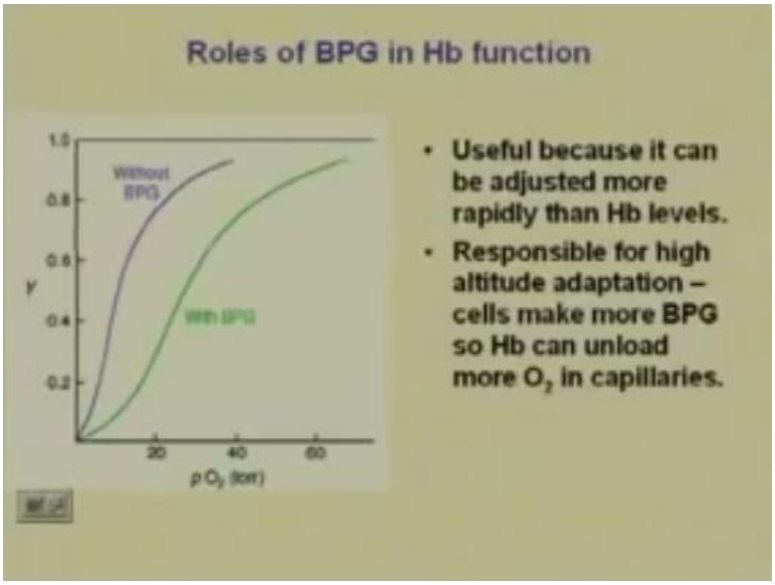

So that is exactly what happens. It is useful because it can be adjusted more rapidly than Hb level, so instead of adjusting the hemoglobin level, what you adjust is the BPG level that is what the body does for you okay. So, when you have high-altitude, it adapts so that it can unload more oxygen to the capillaries where you need, but it will not require the hemoglobin to bind the oxygen, because the deoxy has already bound the BPG okay. So, we will stop here today. Thank you.