Biochemistry - I

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Lecture-12
Special Topic: Myoglobin & Hemoglobin

What we are going to do today is we are going to start or rather study a special topic myoglobin and hemoglobin. 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. If you go to the first slide here what we have is the two proteins myoglobin and hemoglobin.

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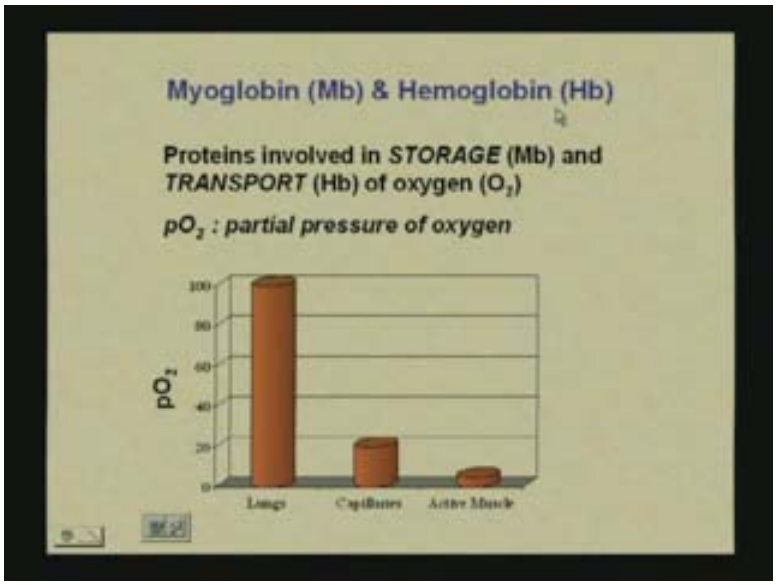

These proteins are involved in storage, that is primarily myoglobin and transport primarily hemoglobin, of oxygen. We all know that we breathe in oxygen and exhale carbon dioxide. What we need to know is how this actually occurs. If we look at the partial pressure of oxygen, the partial pressure of oxygen in the lungs is the highest. Why? Because we breath in 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. In the lungs we are going to have the largest partial pressure of oxygen, followed by the capillaries, followed by the active muscles. Now the function of myoglobin and hemoglobin is actually to consider the transport of oxygen. We will see how hemoglobin transports oxygen, how it binds oxygen and so the case with myoglobin. But myoglobin

acts like a storage protein and hemoglobin more like a transport protein based on their specific activities or specific modes of binding of oxygen.

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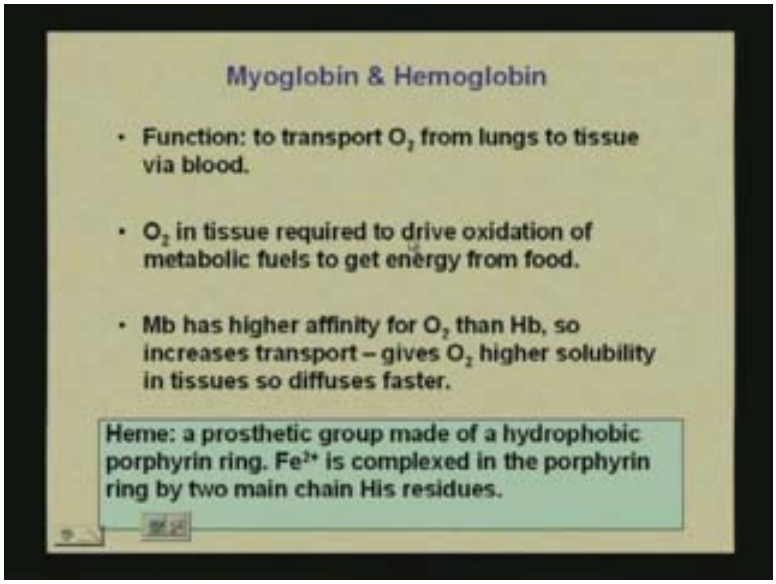

The reason why we need the oxygen in the tissue is for the oxidation of the fuels. What are the fuels? The food that we intake; when we study bioenergetics later on we will see how actually we get the energy from the food. It is this breakdown of food that is going to provide us energy and the oxygen in tissue is required to drive this oxidation. We will also see that myoglobin has a higher affinity for oxygen than hemoglobin. It increases the transport and gives oxygen higher solubility in the tissues because that is where the oxygen is needed for the energy, for the oxidation of the fuels. Myoglobin 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. Each of these proteins has heme associated with it. We will see what heme is. It is a prosthetic group that is made of a hydrophobic porphyrin ring and the iron 2+ that is part of what we call the iron in the blood. That is where it is in the heme. It is complexed in the porphyrin ring by two main chain histidine residues of the polypeptide chain.

What is this protoporphyrin IX? This is basically the structure of protoporphyrin IX, where we have a circular system. In this circular system these rings are actually pyrrole rings. 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 this. When we are looking at this prosthectic group of myoglobin and hemoglobin we have the organic portion of the heme molecule that is protoporphyrin IX a circular system of covalently linked pyrrole groups. This is one pyrrole. This is another pyrrole and this is another pyrrole. When we link these pyrrole groups together we have these nitrogen atoms that actually coordinate the iron for the heme group. If we look at this frame work very carefully you will see that there are three methyl groups; there is a $–CH_3$ here, there

is $-CH_3$ here and there is $-CH_3$ here. So there are three methyl groups, there are two vinyl groups $-CH=CH_2$, $-CH=CH_2$ and there are two propionate groups $CH_2-CH_2-COO^-$, $CH_2-CH_2-COO^-$.
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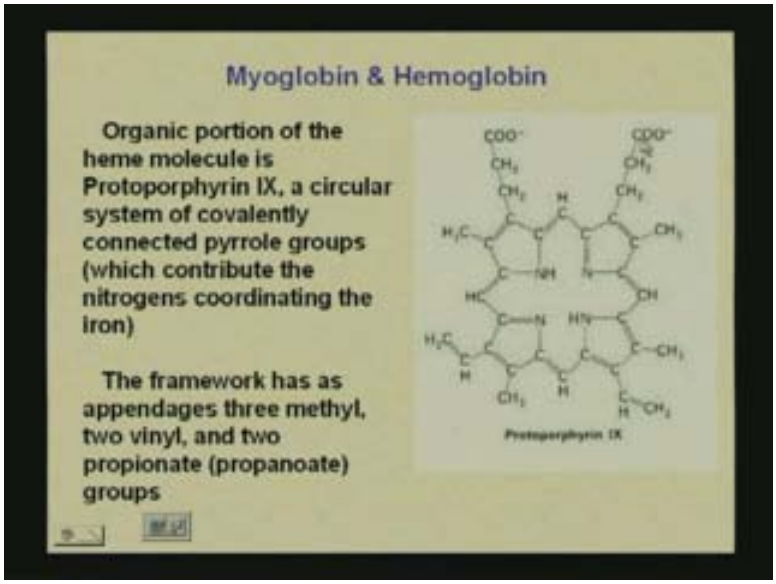

This is the organic portion of the heme molecule. This is protoporphyrin IX. To make this heme what you have to do is coordinate an iron in the centre here. We have the circular system of covalently connected pyrrole groups that contribute the nitrogens for the binding of the iron that is going to give the heme that is the prosthetic group for myoglobin and hemoglobin. This is exactly what we have.

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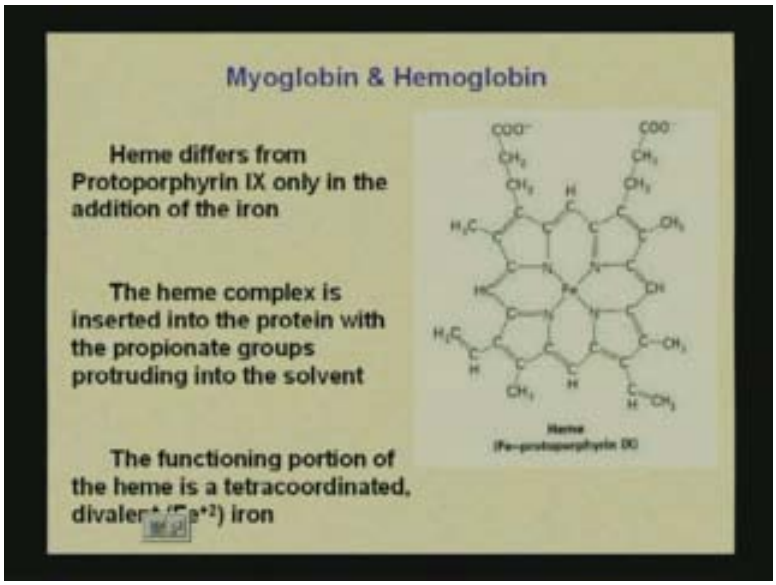

This is our protoporphyrin structure that we saw in the previous slide and the heme differs from protoporphyrin IX only in the coordination or the addition of the iron atom here. The heme complex is inserted into the protein with the propionate groups protruding into the solvent and the functioning portion of the heme is the tetra coordinated divalent Fe^{2+}, iron 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 heme, hemoglobin and myoglobin actually helps in doing this. If we look at myoglobin it has a single polypeptide chain. So it is a monomeric protein.

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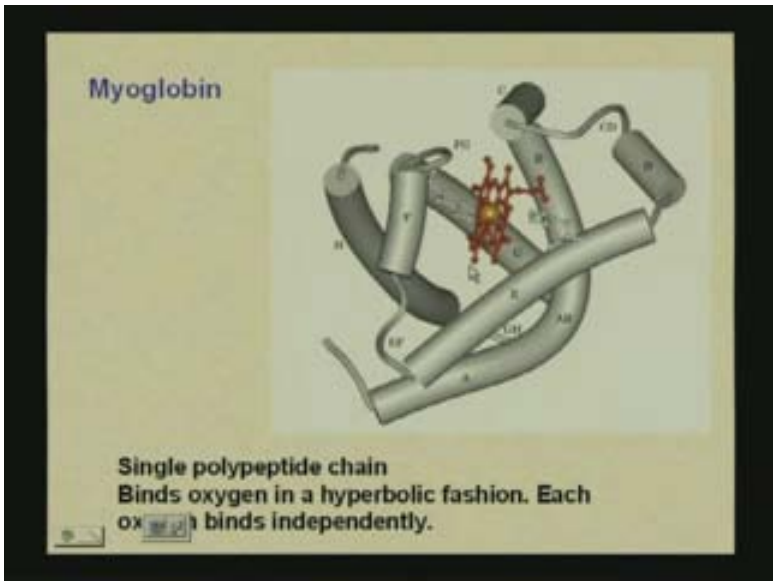

It binds oxygen in a hyperbolic fashion and each oxygen binds independently. This one in red here is the heme. In the heme you can see this yellow sphere that is the iron molecule that is linked to the histidine moieties of the polypeptide chain. So what we have in myoglobin is a single polypeptide chain, 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 called a hyperbolic fashion and we will see what it means and how it is important in the functioning of myoglobin because we have to remember that the structure of myoglobin is going to dictate its function.

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. Myoglobin 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 or the lungs because the lungs is always getting a supply of oxygen but the tissue is using up the oxygen. The myoglobin is present more in the tissues so that it can provide the oxygen that is required for the transport. If we look 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. But the difference between myoglobin and hemoglobin is that myoglobin is a monomeric protein whereas

hemoglobin is a tetrameric protein. It has two alpha chains and it has two beta chains. 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.
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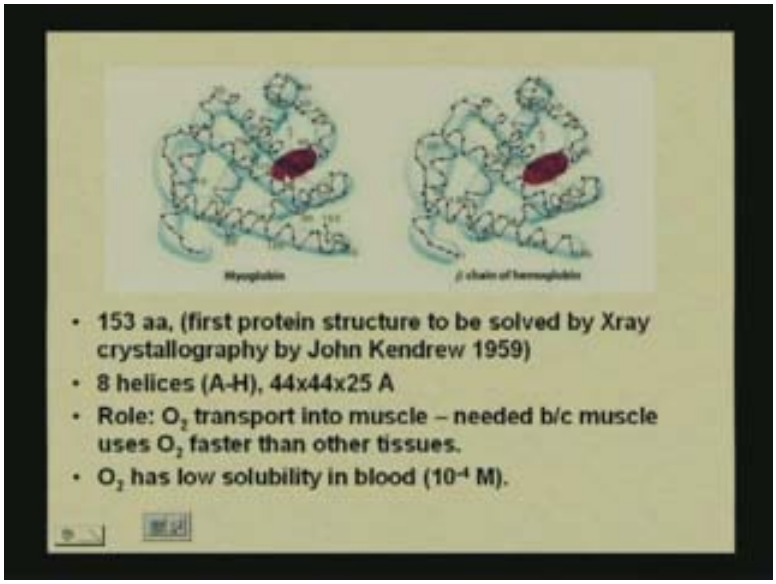

If we look at the red portion here it's the heme and so this is the heme in hemoglobin. If this heme can bind one oxygen and hemoglobin has four such chains what it does tell us about the hemoglobin? It can bind four oxygen molecules. So we have the tetrameric protein hemoglobin.

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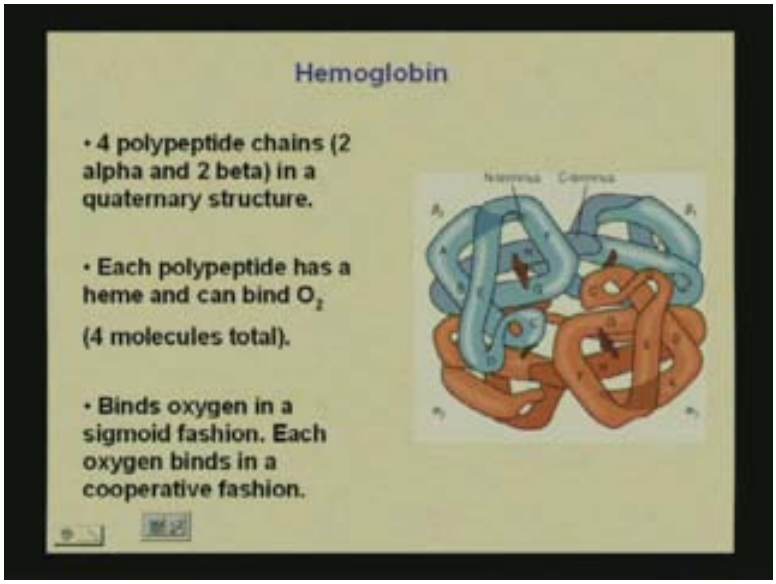

It has two alpha chains and two beta chains. Each of these have a heme associated with it. So there are four polypeptide chains; two alpha and two beta in the quaternary structure. Each polypeptide has a heme and it can bind oxygen and we will see that the oxygen binding is in a sigmoid fashion. If you remember what we mentioned for myoglobin it was in a hyperbolic fashion and this is a sigmoidal fashion and each oxygen binds in a cooperative manner. This is what I mention in one of the earlier classes. 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 heme which is what is meant by cooperativity. So the affinity for oxygen increases for the other hemes as soon as one of the heme binds the oxygen. Which is why it said that it binds in a cooperative fashion.

In general now if we look at the protein ligand binding we will see how we can extrapolate this or what it means in terms of myoglobin and hemoglobin. Now usually what we mention here or the way it is represented is you represent it in the fraction of the percent of the protein that has the ligand bound to it.

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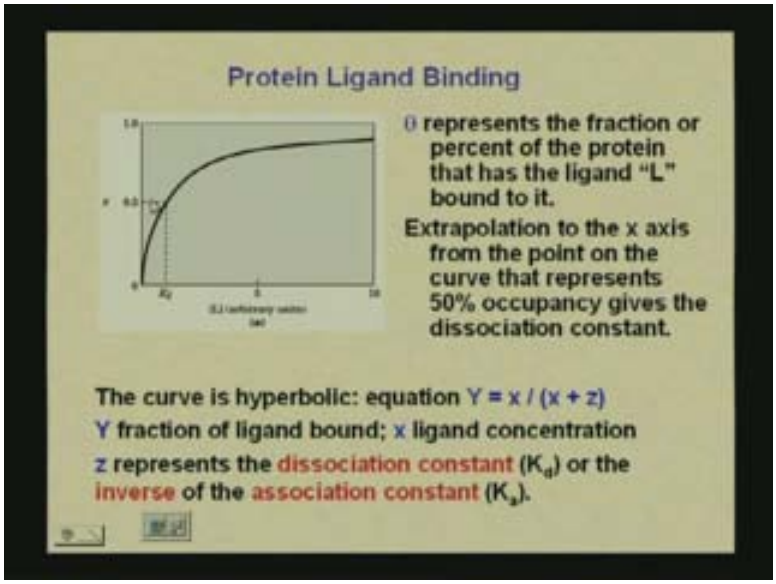

So 100% would mean that if you had a larger amount of ligand concentration all the protein sites would be bound with the ligand. This is a hyperbolic curve. The general equation of this is Y = x / (x + z). What is this Y? The Y is the fraction of the ligand bound. It is represented as theta also, the 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 a ligand bound together, when it associates we have an association constant and when it disassociate we have a corresponding disassociation constant. What is the disassociation constant? It is just the inverse of the association constant.

Looking at this hyperbolic curve when I have 50% percent saturation as it is called because if I have enough ligand concentration and all my protein sites are bound I have a

saturated situation. When I reach 50% saturation here it means that my Y or the fraction of the ligand bound is half, 50%. 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 a ligand concentration and z is the dissociation constant. We have extrapolation to the x axis from the point on this hyperbolic curve that corresponds to a fractional occupancy of point 5 or 50% percent saturation means that whatever we have corresponding on the x axis is the dissociation constant. Now we are going to see how we can utilize this for the binding of oxygen not only to myoglobin but also to hemoglobin which actually behaves a bit differently. If we go to a protein ligand binding in general we are talking about the fraction that is occupied. What is occupied? The protein sites are bound with oxygen. 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 is in the lungs? When we are looking at the oxygen concentration in the tissues it is less than that is there is in the lungs. What does that mean? It means that the ligand concentration in the lungs is higher.

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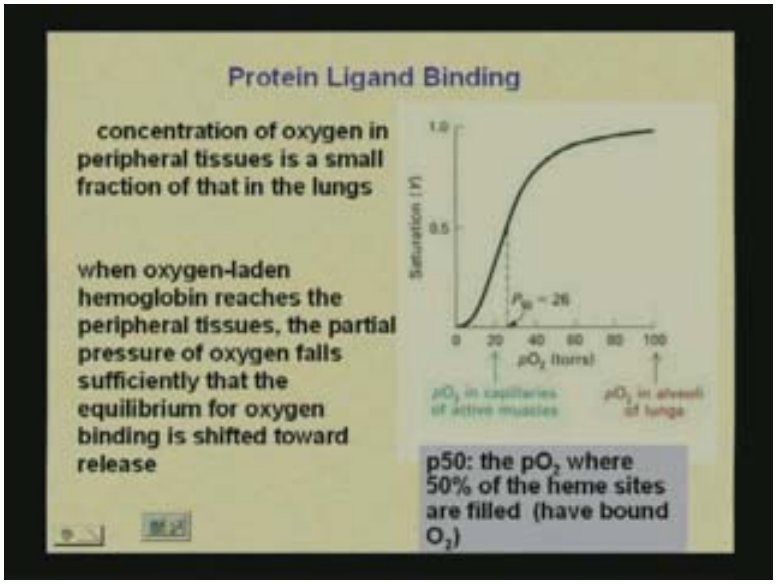

If the ligand concentration is higher in the lungs what do you expect in the lungs? You expect 100% saturation. But when the ligand concentration is low where is the oxygen concentration low? In the tissues; we will not even have 50% saturation there. But as we increase the amount of oxygen that is measured in terms of the partial pressure of oxygen, as we increase the partial pressure of oxygen when you reach the lungs you will have 100% saturation. The way this is measured is we measure some thing called p50. p50 is the partial pressure of oxygen where 50% of the heme sites are filled. That means in myoglobin you have just one heme site. That is either filled or unfilled; but for hemoglobin you can have 1, you can have 2, you can have 3 or you can have 4. But usually what happens is these are all …… situations because as soon as one of the oxygen molecule binds to one heme it behaves in a cooperative fashion and it helps the binding of the other oxygen atoms also. So the other oxygen atoms bind very quickly.

The concentration of oxygen in the tissue is a small fraction of that in the lungs. When the oxygen laden hemoglobin reaches the peripheral tissues, the partial pressure of oxygen falls. So what happens? If the saturation is less the hemoglobin will release the oxygen. 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 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 disassociation. You have to remember that there is an equilibrium. The Hb + O_2 giving you as we call HbO_2 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.

Suppose we have a situation where I have an oxygen transport protein. If you look at the curve on top - the darker curve this is the curve for myoglobin that binds oxygen in a hyperbolic fashion.

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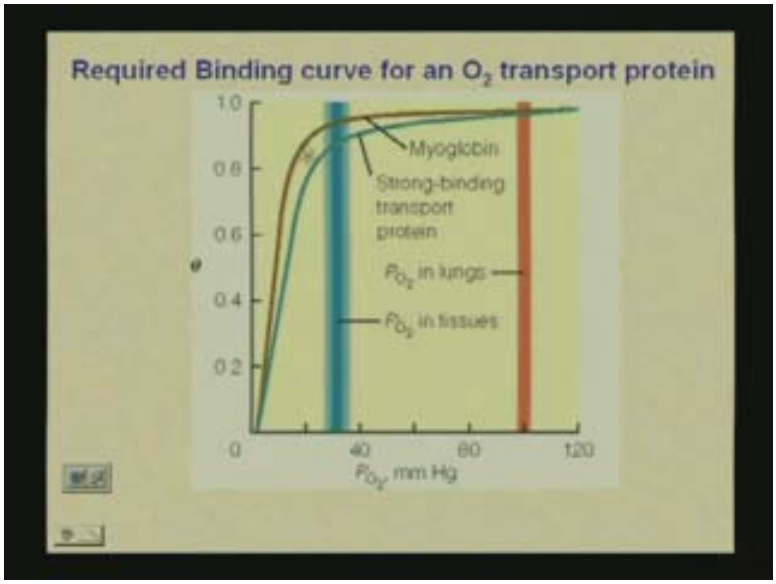

What we have on the y-axis is the fraction and what we have on the x-axis is the partial pressure of oxygen. The partial pressure of oxygen in the lungs is high. The partial pressure of oxygen in the tissues is low. This is the hyperbolic curve for myoglobin. What we have in the blue curve here is a 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. When we have a low pressure of oxygen we are looking at a fraction or saturation. What is the x axis? The partial pressure of oxygen. We are looking at the curve for myoglobin now. Myoglobin behaves in a hyperbolic fashion. This is the situation in lungs. This is the situation in tissues. We can say that even when the partial pressure is low myoglobin will not easily dissociate the oxygen from the heme. 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. We have a fraction here of 1, this is say 0.8.

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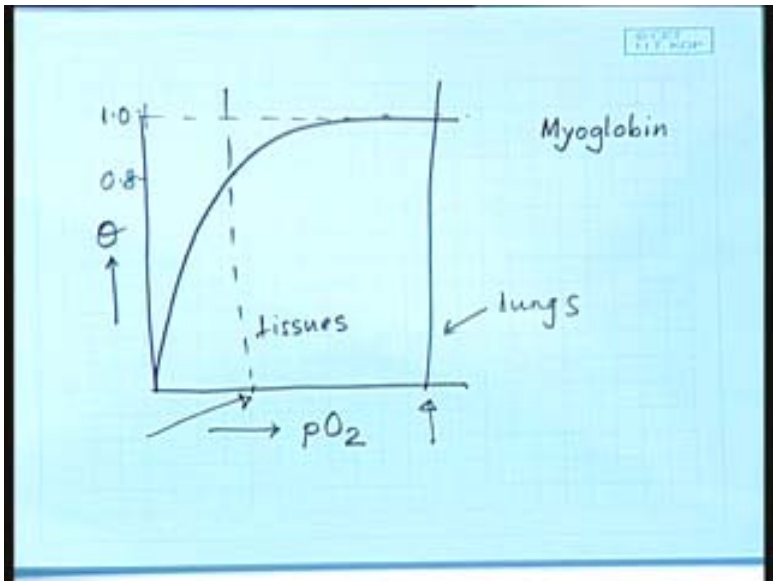

I am still 80% saturated with the oxygen even at the tissues and that is what I want. But if we go back to the slide here, now if we look at the myoglobin curve what is there in the myoglobin curve? Even at the concentration of the partial pressure of oxygen in the tissues myoglobin still is more than 80% saturated. But if you want a transport protein what is the transportation supposed to do? It is supposed to take in the oxygen and release it. The hemoglobin has to release the oxygen. If it does not release the oxygen there 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 because hemoglobin has to release the oxygen. If it does not release the oxygen it makes no sense for it bind it. If 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.

What happens if we have something like this? If we have a weak binding transport protein myoglobin remains as it is in a hyperbolic fashion. So it is more than 80% saturated in the lungs as well as in the tissues. But if we have a weak binding transport protein what is going to happen to this? It is going to be efficient in releasing the oxygen. Because at the partial pressure of oxygen in the tissues the saturation is low it will release the oxygen. But it is not very efficient in the binding. It is pretty inefficient because even when I am close to hundred million meter mercury I still do not have even 70% oxygen bound. In this case I have something that is efficient in the unloading but inefficient in the binding.

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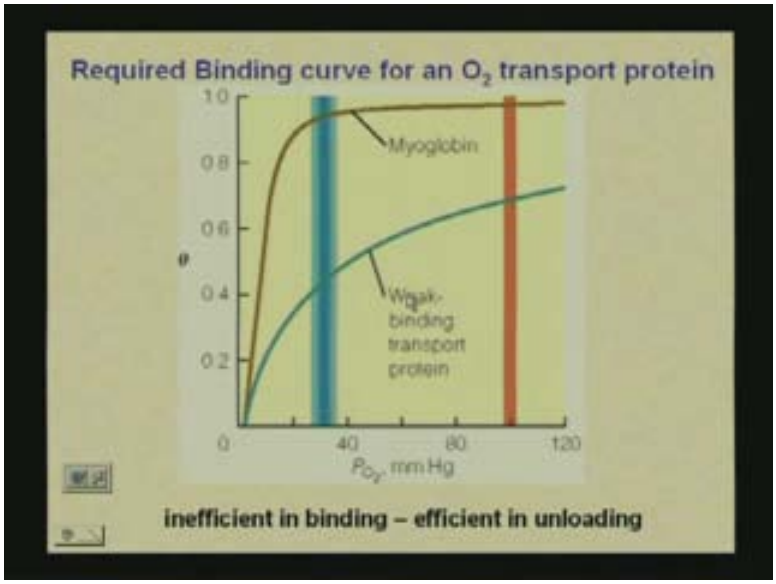

In this case I have a weak binding transport protein. In the previous case we had a strong binding transport protein but none of this is helping. Why? Because in the lungs I have to have strong binding and in the tissues I have to have it released. So I sort of have to have combination of methods where it will be efficient in binding and also efficient in the unloading. We have to have a transport protein that is going to behave like this. It is going to be highly saturated in the lungs and it is going to be efficient in the unloading of the oxygen in the tissues. What is this curve depicting?

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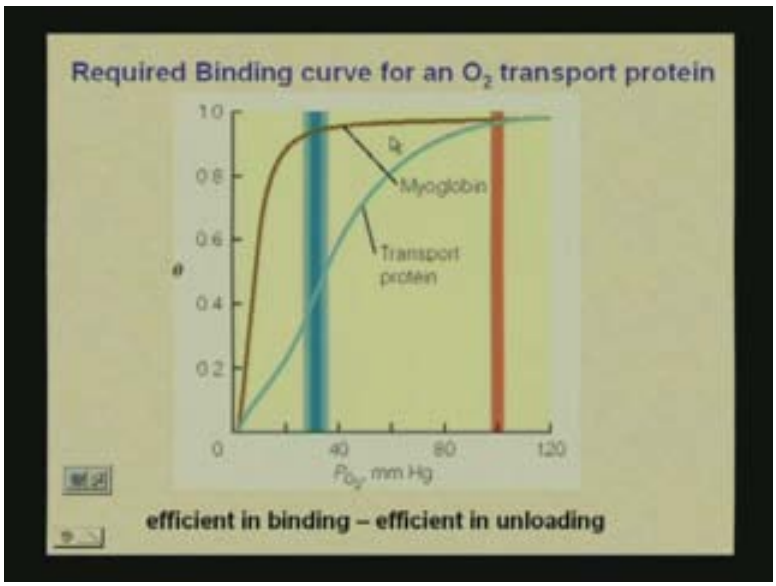

It is telling you that you have something that is efficient in binding and also efficient in unloading. This is the sigmoidal curve of hemoglobin. Hemoglobin is very efficient in taking up the oxygen in the lungs and it is also efficient in unloading the oxygen in the tissues which is what you want. This is the required binding curve for a protein that would transport oxygen. But myoglobin is a storage protein. If myoglobin were also like this then what would happen in the tissues? All the oxygen will be lost. But myoglobin is highly saturated even at the low partial pressure at the tissue level which is essential because it is a storage protein. Here we have transition from a weak binding state to a strong binding state.

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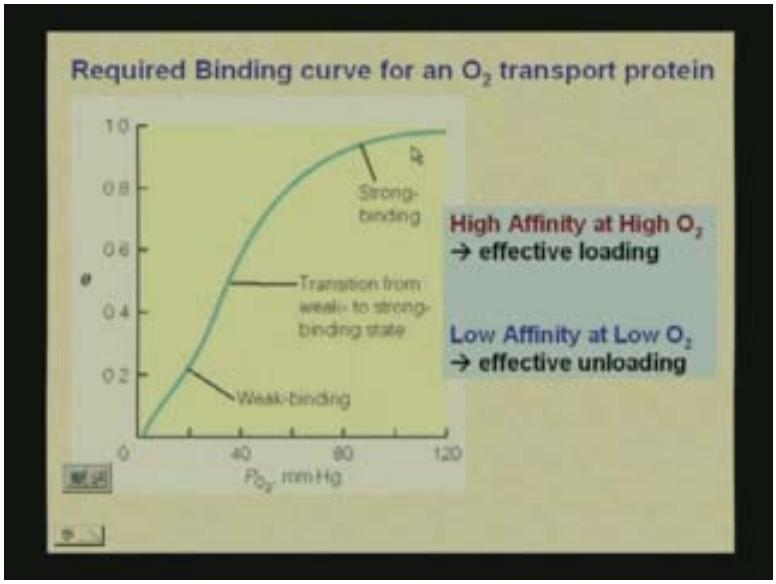

This is the curve for hemoglobin which is what is called in a sigmoid fashion. The rise is in a sigmoid fashion where we have high affinity at high oxygen partial pressure which means we have effective binding. At this stage we have low affinity at low oxygen levels which means it is effective in unloading the oxygen. So that is the optimum that the hemoglobin can do. It will bind it strongly; it will release it also strongly depending on the partial pressure of the oxygen. So you would have it bind in a sigmoid fashion. Then it would have high affinity at high oxygen because you want efficient binding and effective loading. It would have low affinity at low oxygen so you would have effective unloading of the oxygen. So this is what we have; saturation at 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.

The functions of myoglobin and hemoglobin are to bind oxygen when its concentration or partial pressure is relatively high and release it when it is required. It cannot just keep on binding tightly to it otherwise you will not get the oxygen when you need it. When the partial pressure is low it is going to release it. When you are in dire need of oxygen, when

you come to this, the myoglobin which is the storage protein will release the oxygen at that point only.

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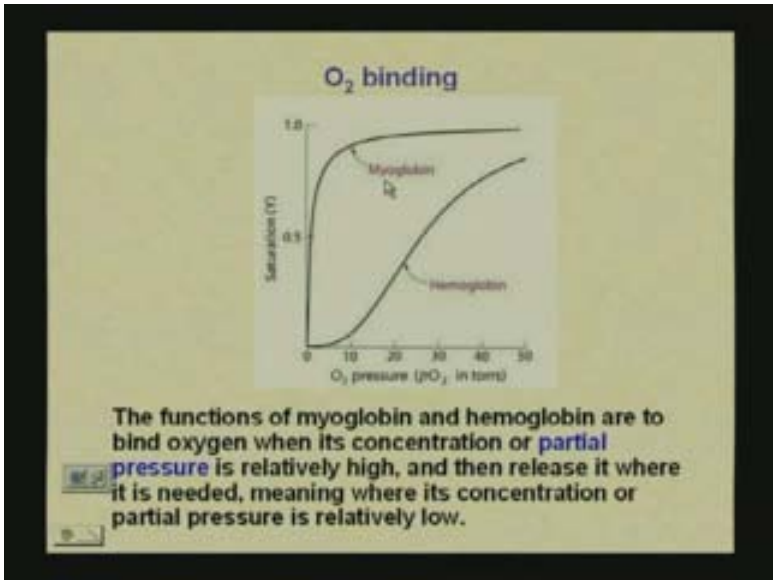

You are panting for breath. You run up the stairs because you are late for class. Your tissues lack the oxygen; myoglobin will come to the rescue and because the pressure has gone down it will give the oxygen that is required. This is why the curves are shaped like this and you have to understand why hemoglobin has to bind in a sigmoidal fashion and myoglobin in a hyperbolic fashion. So what do we have we have? The fraction of sites a hyperbolic curve and we have low p50.

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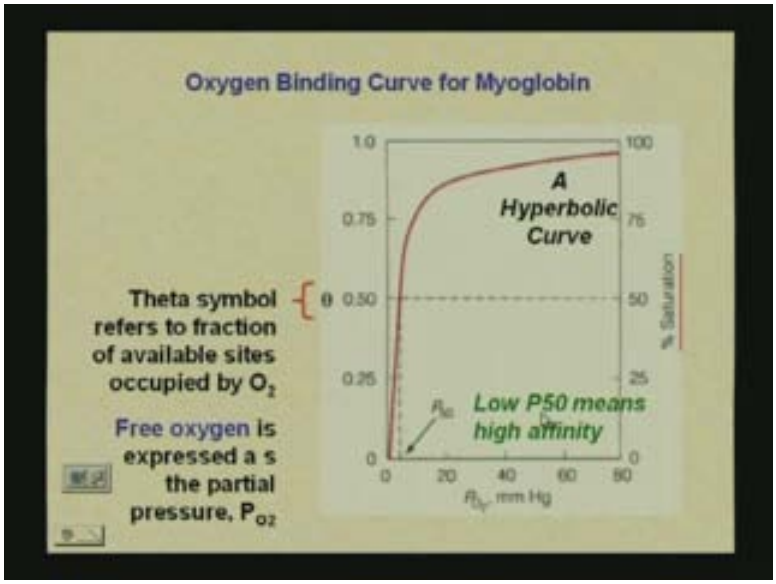

What is this p50? The p50 is the partial pressure which is 50% saturated. If you have low p50 it means you are half saturated at a low pressure. So you have a low concentration of the ligand and you are already highly saturated. What does it mean? It means you have a high affinity. You have high affinity if at a low concentration you are 50% saturated. We have this oxygen binding curve for myoglobin. If we look at hemoglobin we have hemoglobin bind oxygen reversibly.

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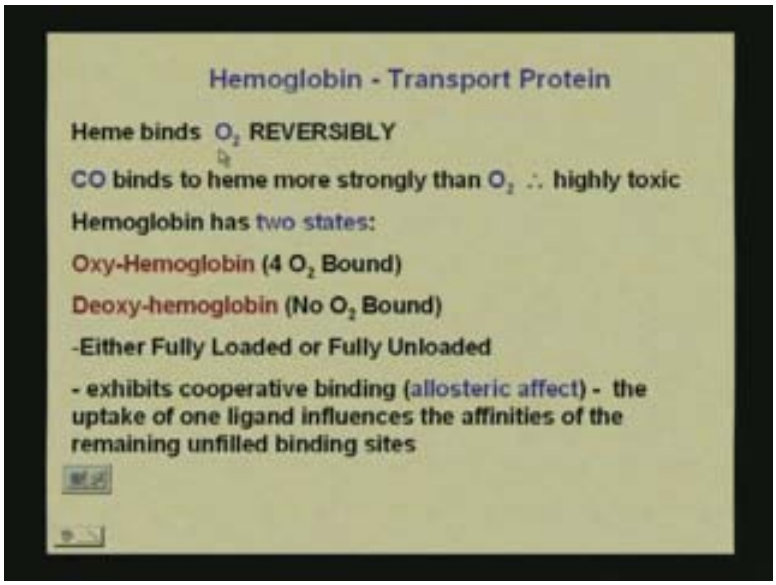

These are the features of the transport protein hemoglobin. What are they? It binds oxygen reversibly. You know carbon monoxide is a poison. Why is that? Carbon monoxide binds more strongly to heme than does oxygen which is why it is highly toxic. It will not release the carbon monoxide very easily so it is highly toxic. Hemoglobin has two states. Oxy-Hemogobin as the 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 deoxy-hemoglobin when no oxygen is bound and usually it is either fully loaded or fully unloaded. We will have either oxy-hemoglobin or deoxy-hemoglobin and the binding is in a cooperative fashion. It is something that I have 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. It is going to help or facilitate the binding of the other oxygen molecule. What we have is a reversible binding of oxygen to give four oxygen bound in what is called oxy-hemoglobin and no oxygen bound in deoxy-hemoglobin. We would have deoxy-hemoglobin at the low pressure of oxygen, we would have oxy-hemoglobin at a high partial pressure of oxygen and we have all or none situation where it's either oxy or deoxy and it exhibits cooperative binding.

This is our p50 for hemoglobin. At low pressure it has low affinity and at high pressure it has high affinity which is why it is a sigmoidal curve.

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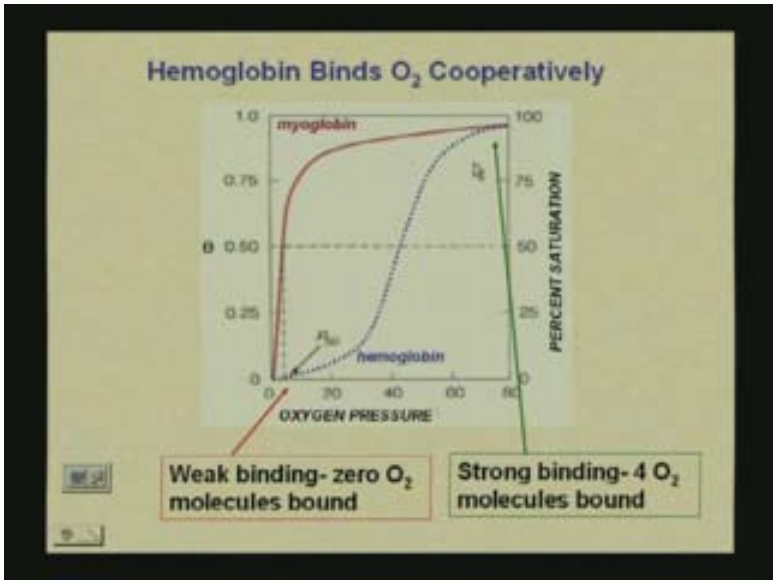

Myoglobin has a higher p50 because it reaches 50% saturation faster at a lower concentration of oxygen. We have strong binding here for the hemoglobin where 4 oxygen molecules are bound and we have weak binding here where nothing is actually bound yet and we gradually reach this saturation. We have the cooperative binding which is why actually this is sigmoidal. Because you have cooperative binding this is sigmoidal and this is hyperbolic fashion for myoglobin. We have to come to some expressions.

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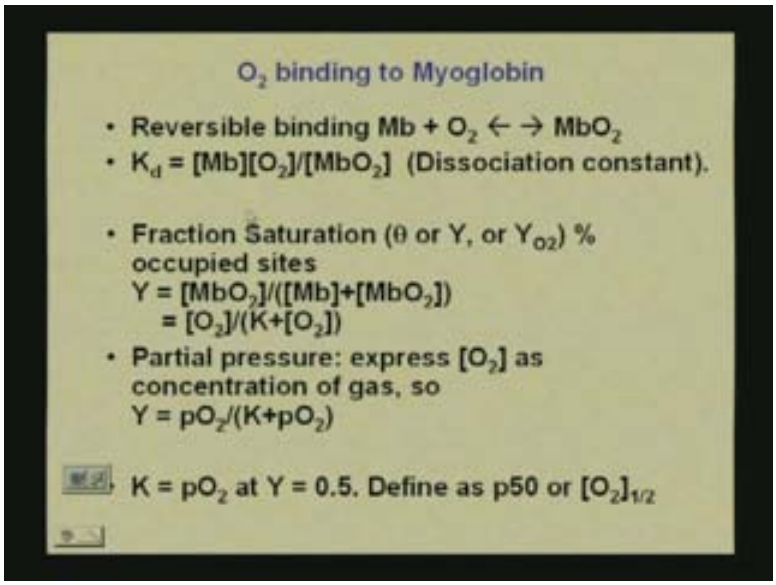

If we have reversible binding that means we have Mb, myoglobin plus oxygen in reversible because we know we have to release the oxygen when we need it giving you

MbO_2. What is this K_d? It is the dissociation constant. If had written 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. I have Mb, O_2, the concentration of myoglobin, the concentration of oxygen and the concentration of MbO_2 and where is the oxygen binding? It is binding to the heme of the myoglobin. Why don't you work out a fractional saturation? Suppose you want to know the fractional saturation say Y. What is Y? $Y = [MbO_2]/ ([Mb] + [MbO_2])$. MbO_2 is what is bound and the total amount is the free Mb that has not bound plus free MbO_2. So if we rearrange this we can express it in terms of the oxygen concentration just by some algebra.

We can get the partial pressure pO_2 in terms of Y when you know what the K is and what the pO_2 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 $Y = x /(x+z)$. When you have this pO_2, we know what the partial pressure of oxygen is. If we have this equal to K then we have 50% saturation. So the 50% saturation that is p50 is defined when we have Y equal to 0.5 and that is possible when K is equal to pO_2 in the expression here. 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 pO_2.

This is what is called a Hill equation.

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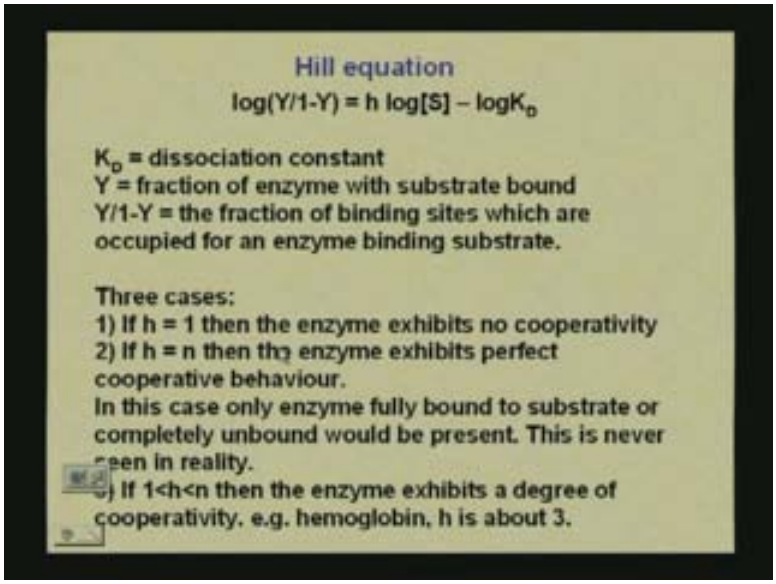

If we look at the expression we have log Y. What is Y? Y is the fraction of the enzyme with substrate bound to it divided by 1-Y. It is log Y divided by 1-Y and is equal to h, we will see what this h means, log S. What is S? S is the substrate concentration which in this case is going to be oxygen minus log K_D. Actually you can work it out from the previous expression that we had for the Y. You can try and work that out. It's just the previous expression worked out and written in this fashion that has a specific name to it

called the Hill equation. In the expression Y/1-Y, Y 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. If this h is equal to 1 it means that there is no cooperativity. What is cooperativity? It means that the binding of one ligand molecule to 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? If one heme bound the oxygen then it did not matter to the other subunits. We have three case here h can be 1, h can be n. What is n? n is the number of sites that you have. So what is n for myoglobin? One. What is n for hemoglobin? Four. When h = 1 then the enzyme exhibits no cooperativity. If h = n then you have perfect cooperative behavior. Usually this does not occur and if you have something a number between 1 and n then you have a certain degree of cooperativity. 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 subunits that will facilitate the binding to the others and then you can plot what is called Hill plot where we are going to plot log Y/1-Y on the Y axis versus log(S) and the slope is going to tell you what is called the Hill coefficient. What do we expect the Hill coefficient for myoglobin to be? One because it is equal to n there is only 1 site. But for hemoglobin we expect it to be less than four. Why? Because there is cooperativity. That is exactly what happens. This is what we have. What is our measure for S?

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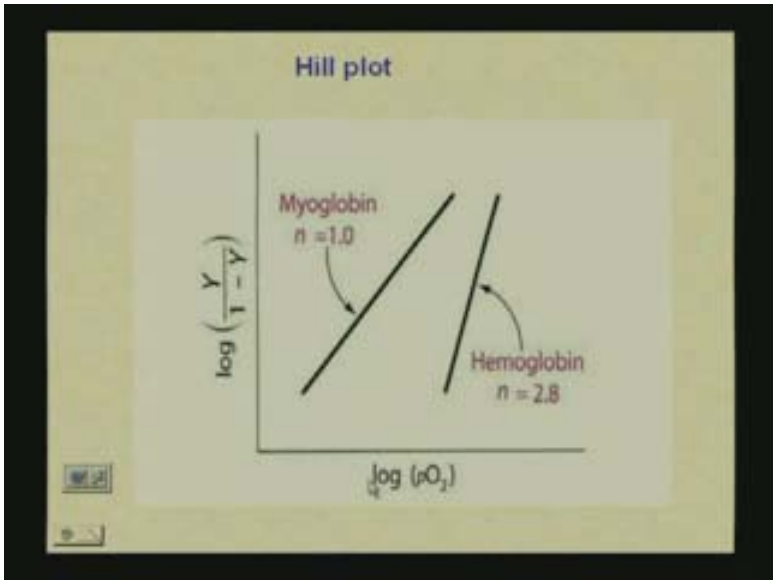

Substrate concentration is measured by the partial pressure of oxygen in this case. So when we have log Y by one minus Y what do we get? For myoglobin we get n equal to 1 and for hemoglobin we get n equal to 2.8. This is the Hill plot and these values are called hill coefficients. Actually what is happening to hemoglobin at low partial pressure of oxygen? At low partial pressure of oxygen it is bound weakly and at high partial pressure of oxygen it is bound strongly. So actually this is a mixture of two curves a weak binding

curve and strong binding curve. That is what we have in the next slide. Try and understand this. We are looking at a Hill plot.

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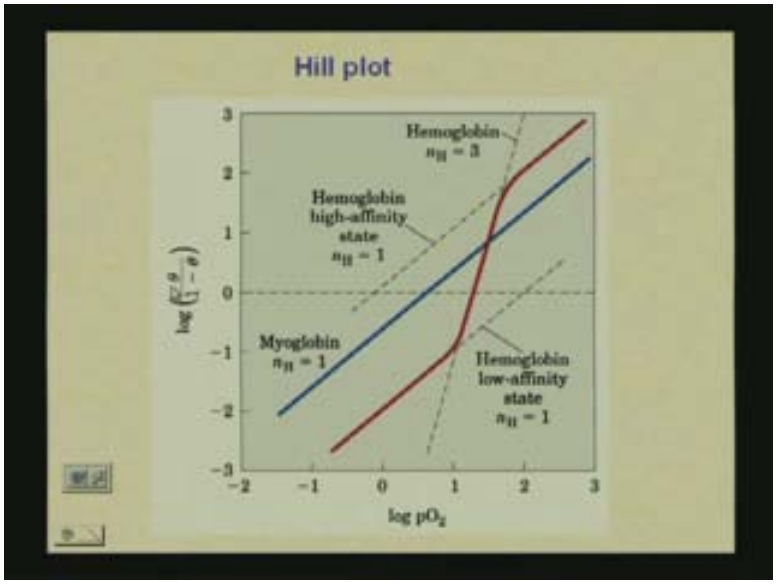

What do we have on the y axis? log Y/1-Y versus log pO_2 which is log (S). When the pressure of oxygen is low then there is no cooperativity yet because a ligand molecule has not attached to the heme. You get the cooperativity after the ligand has attached to the heme, as soon as one ligand attaches to the heme. When is that is going to happen? That is going to happen at the specific pressure. When you reach that pressure then what is going to happen? If we reach this pressure then at this point we have n_H that is the Hill coefficient equal to 1 because the ligand molecule has not yet bound to the heme. As soon as one of them gets bound to the heme we have one of the oxygen molecules bound to one of the subunits. It is going to start or facilitate the binding of the other oxygen. So you are going to have a sharp increase 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 a definite level. Why? Because you have the cooperativity as soon as one of them binds it is going to help bind the other ones. 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. It has reached the high saturation level. It is this point when this slope that we will consider for the Hill equation is going to give us a value close to 3 and for the myoglobin we are going to get a value of 1. This explains the Hill plots for hemoglobin and myoglobin. We get a Hill coefficient of myoglobin that corresponds to 1, a Hill coefficient of hemoglobin that corresponds to 3.

There is another thing that we need to understand something called the Bohr effect. What is this Bohr effect? We are not going to go in detail of all this but what is happening is the hemoglobin has bound the oxygen to it. Where is it binding the oxygen to it? In the lungs.

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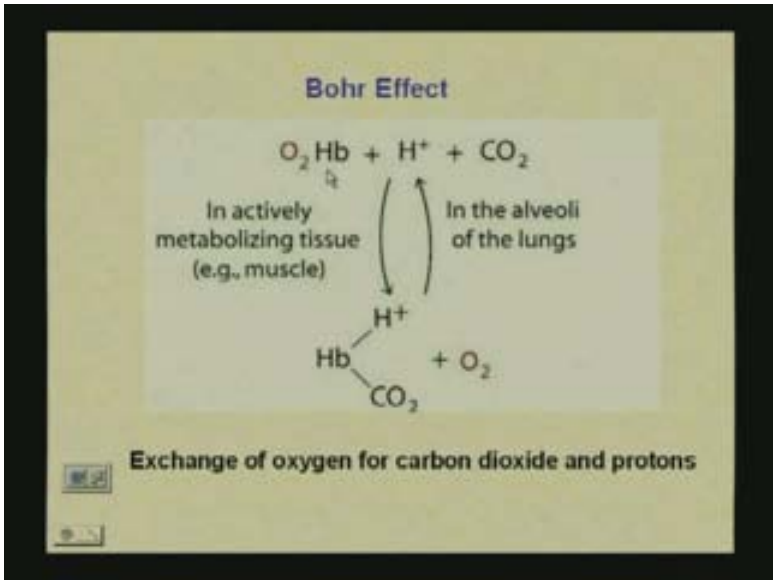

When it comes to a lower partial pressure of oxygen what it is going to do? It is going to release the oxygen. It is going to release it in tissues. There is basically an exchange of oxygen for carbon dioxide and protons. What is going to happen now is you are going to release the oxygen and it is going to become deoxy-hemoglobin. But it is going to be associated with the carbon dioxide and H^+. What is going to happen to pH? If I have an increased amount of H^+ it is going to decrease. So the binding curve is going to change with change in the pH and how should it change? It should change in such a fashion that the oxygen is released at the tissue level. This is what we have. At a higher pH we have the peripheral tissues here. The pH is 7.6.

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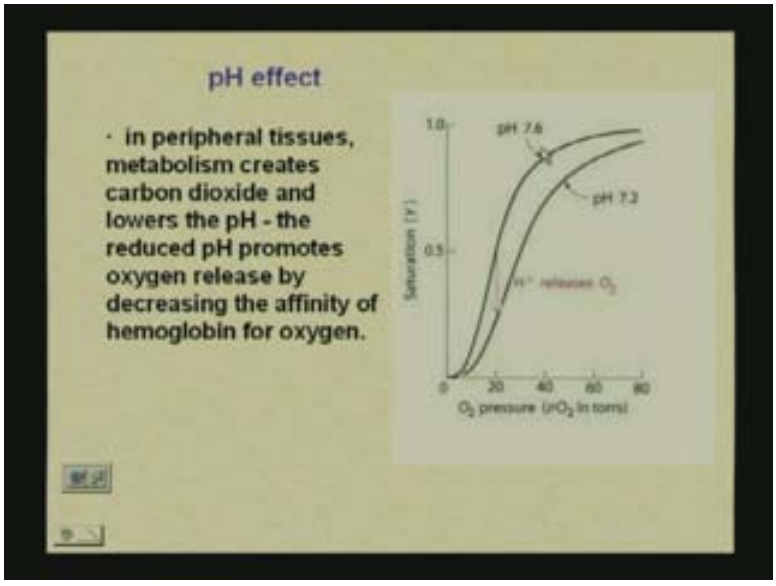

As we have the carbon dioxide release the H^+ what is happening? This lowers the pH. As it lowers the pH what is going to happen? Suppose you are at specific partial pressure of oxygen here at pO_2 say 20. What is going to happen when the pH is lowered? The oxygen is going to release. Why? The saturation is going to be less. There is a decrease in the saturation because of the decrease in the pH. What does that mean? Oxygen is going to be released and where is this going to occur? In the tissues. 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 lower pH it means oxygen is going to be lost and that is exactly what you wanted to do. You wanted to supply the oxygen at the tissue level so that you can have the oxygen released. So this is exactly what happens. This is one interesting thing that we might consider. This is called BPG. This is just for an interesting application of what the body actually can do. This BPG is Bisphosphoglycerate.

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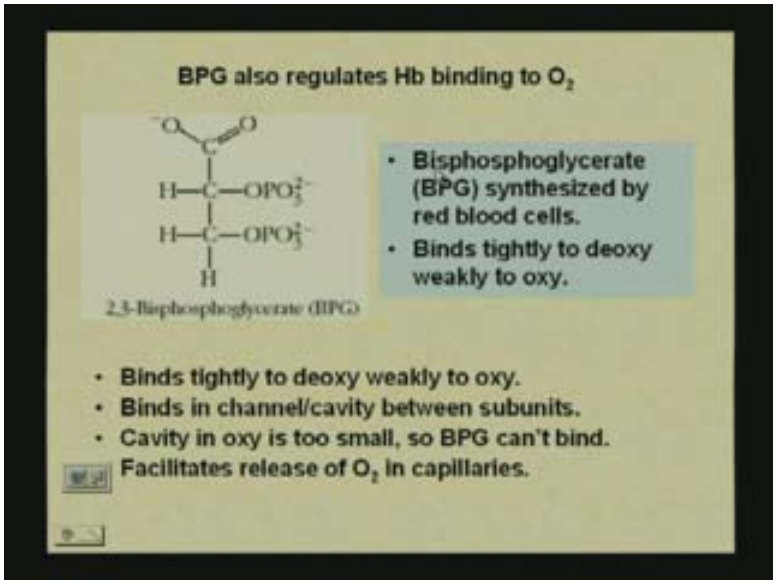

It is synthesized by the red blood cells and it binds not to oxy-hemoglobin but binds very tightly to deoxy-hemoglobin. What is deoxy-hemoglobin? When the hemoglobin does not have oxygen bound to it, it is called a deoxy-hemoglobin. This BPG binds two deoxy-hemoglobin and what happens is the cavity that is present in deoxy-hemoglobin is large enough to hold the BPG molecule in that. 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. Where can this be useful? 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. So that's exactly what happens.

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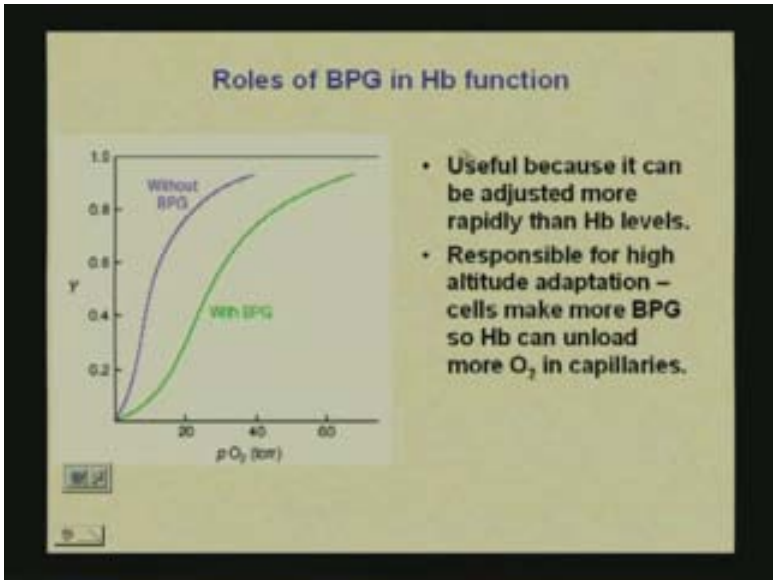

It is useful because it can be adjusted more rapidly than Hb levels. So instead of adjusting the hemoglobin level what you adjust is the BPG level. That's what the body does for you. When you have high altitude it adapts so that it can unload more oxygen to the capillaries where you need but it will not require the hemoglobin to bind the oxygen because the deoxy has already bound the BPG. We will stop here today. Thank you!