**Human Physiology**
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**Lecture – 38**
**Respiration - Part 2**

Now here is something I am going to tell you absolutely new focus on this. The blood that is flowing through the lungs. Let us look at only one RBC, forget about it - one RBC millions are there – but let us look at one RBC. Where is it coming from? It is coming from the heart ok from the right ventricle it is going towards. Now is it compulsory that that RBC will flow through an alveolus and will have an opportunity to get oxygenated? No, if it if that if that RBC happens to pass via a bronchi or a trachea ok or some smooth muscle tissue which is lining the trachea, is it getting an opportunity to pass through alveoli? No, does it get oxygenated? No it is passing through - like some other tissue. It is not going through it is not going through the that part of the lungs - where it will have an opportunity to oxygenate, are you getting the argument? After all there are major blood vessels in the lungs. They have their walls, they have their smooth muscles - they need oxygen and that RBC is not the RBC which flows through those organs is not going through alveoli. So, it is not getting oxygenated. So, what happens to that is a very interesting question we will try to answer.

The heart is somewhere here do not bother about it, but from the heart comes a very important blood vessel which you know already it is aorta what is it? Aorta. Aorta it is the same guy which shows compliance hello this is aorta ok. From the aorta and then of course you know these are the carotids which go to - carotids go through your neck to your brain but can you see author has drawn some two very small vessels and they are going to what they are going to the trachea and the bronchi. What about these vessels? Now let us see these vessels ok.

So, this here the dark blue indicates oxygenated blood and the light blue indicates deoxygenated blood. So, let us talk about the blood that is being pumped by the left ventricle. Where does it go? It goes in the aorta, but some of it goes via these vessels. It goes to the bronchial circulation - where does it go? Bronchial circulation - is it alveolar circulation? No, it is a part of the lung, but is it alveolar? No, it is part of what? It is a small component, but, it goes to the bronchial circulation. Are you ok so far? Now, the blood in the bronchial circulation, it goes into two channels some of goes into what you call as the deep bronchial veins and which go where? Follow the story it is very interesting - follow the story.

Let us go to the right ventricle - what kind of blood - deoxygenated blood are you ok? Some here blood will go into the pulmonary arteries - deoxygenated blood - it goes to the lungs. Gets fully deoxygenated - just follow the story. It comes out then before it goes to the heart - blood passing through the lungs - fully oxygenated - what is the target? Now go to the heart - left auricle and blood goes everywhere in the body - are you with me? There it receives some amount of deoxygenated blood - get the point - and what is this deoxygenated - that blood has already given is its oxygen? No, why because it has flown through the bronchi part where it was not go though the alveoli - where it did not get oxygenated ok. Therefore we have the blood from the bronchial circulation - so this connection shows that the blood is coming from the deeper part of the lungs - not the alveoli - the upper is coming from the alveoli and then they mix together and going to the left ventricle and then everywhere am I making sense there? So let me put it this way. You draw the sample from the pulmonary vein - oxygenated pulmonary vein - just as it is coming from the lungs, ok, and what do you find - partial pressure is 104mm Hg. how much is the partial pressure? 104 ok. Now you take another sample from the same vessel as it is ready to enter into the heart. Take the sample there and you find that the partial pressure is about 95, 96 mm Hg. There is a drop why is the drop? It is a mixture it is a mixture, so actually what goes to the heart is not fully - is not the blood that is fully saturated - there is a slight drop ok. And we call that blood as the shunt blood ok. So let us see so the blood comes from the aorta - now the blood that is going from the aorta - some of it goes bronchi - whereas some of it goes here some of it goes - just follow another what do you call it as - what is hilar bronchial vein? It goes to vena cava - so that is our traditional route. What are we doing just now? We are trying to find out how the body deals with the blood supply to that part of the lungs which do not have alveoli and which do not have the opportunity to get oxygenated, ok and that ok. Now this is very well seen - yes please. Sir there cannot be any - is there any rational behind this particular thing? The rationale is simple. The rational is that after all that part of the lungs which could have - no I think anatomically this might be a better way to let the blood go there - after all the quantity is very little, ok. I think the system evolved such that - it may be more circuitous route to take – if it is there, I do not know ok I am just guessing, ok.

So here we have the blood that is coming into the lungs. What is the partial pressure? 40 now it has gone into the alveoli what is the partial pressure 104 ok. What is the oxygen partial pressure 104 ok so whatever oxygen has got into the blood I will call it partial pressure of oxygen 104 ok. Now 104 and then it is coming and then can you tell me why this drop is happening from 104 it is going to about say 96 95 96 why is the drop? The blood that has irrigated bronchi and then it goes to the heart and then from there to everywhere else and then it goes different issues it again falls back to 40. This point is very clear and we call this system - as this blood flow is called as what? Shunt flow. It is called as shunt flow, ok. So now let us see what happens to the blood going from there into left atria to left ventricle then to aorta - it has gone to different tissues. Let us take pancreas or liver or whatever and we now look at the blood pumped from the heart - it goes through major arteries, arteries – there is hardly any change in the blood partial pressure of oxygen so from the heart if it is coming 95 95 95 it is still 95 by the time it goes to arterioles it is still 95. It has not it has not dropped. Then it finally goes to meta arterioles and capillaries if we had capillaries it is still what? So the partial pressure here is almost same as the partial pressure of blood as if you retrieve it from the left ventricle 95 mmHg same. But the moment it comes into the capillary - now where are we? In a capillary and these are the target cells where the blood is going to supply its oxygen - and in the tissues what might be the partial pressure there? 23 no 23 - is an average value. It can be depending on the physiological state of the cell it can be 5 it can be 10 it can be 15, 20, 30 whatever. So given the averages of how much? 23 mmHg is the partial pressure extracellularly and as it comes extracellular maybe little more may be 40 mmHg. Now the blood arrives into the capillary, ok. Now the walls are suddenly very thin ok and there is an RBC going and in the RBC there is hemoglobin and that hemoglobin molecule is fully saturated - is having 95 mmHg pressure. Outside the capillary - there is fluid which has 40 mmHg and there is immediately there is a cell with 23 mmHg huge gradient. Are you getting the argument? As a result of huge gradient of hemoglobin it will lose its oxygen ok. And by the time the blood goes from here to here which is a distance of about 1 mm ok, and then the partial pressure is reduced to how much? What you have? Now it is in the veins and then that is what will be carried to the vena cava and back to the heart ok. Alright now because there is a gradient, so this blood is steadily flowing ok. So in the cell there are mitochondria and those mitochondria are continuously using oxygen. So there is a gradient it is maintained. You have to maintain the most important part - homeostasis - to maintain that gradient, ok. That is very well - your argument is fully answered in this question. What we are just understand is this very nice diagram. We will enjoy looking at this diagram. We are looking at partial pressure of oxygen at different levels right from outside ok outside is how much look at the first - in room - air around us. If it is dry what is the partial pressure there - you are ok. Then from there air goes into trachea - as it goes into the trachea it mixes with the air that is already there ok. Then it drops to where - 149 and then from there it goes where in the alveoli. In the alveoli it is about how much? 100 ok ok whatever it is 100, 100. Then it goes into the arterial blood - I mean now it is that mixture ok. Now it has reduced. The author tells us that it is about how much 92 ok. Then it will give away its oxygen to the tissues and then it will reduce to what 40 mm Hg. Now this is most important part - what is the partial pressure of oxygen in the mitochondria 2? Mitochondria actually they say that even 1 or 2 mm Hg of partial pressure - mitochondria is happy, ok. That is what it needs, ok. But it cannot do less than that - I mean it has to provided. So, actually we have this entire system ok geared over a process of evolution over millions of years. Given the fact that air around us is 160 mm Hg and your target is to take it to a mitochondria at partial pressure of oxygen that is low - the entire system is geared - that depends as to how much of hemoglobin? what is its affinity? At what rate heart is pumping? All that - ultimately our aim is - what is the aim? To make sure that mitochondria have a very steady partial pressure of about how much 1, 2 or 3 mm Hg. That is enough but for maintaining this you need that ok. Ok you can read about ok. We are talking about the other side other side. Means let us talk about that is only one function - the other function - ok please remember hemoglobin also has a very interesting role in transport of carbon dioxide - carbon dioxide we will talk about carbon dioxide I will come to those.

So, we are looking - I am sure you are familiar with the earlier part. In this particular part the author tells us something different. In the alveolus, what is the partial pressure of carbon dioxide please - 40 mm Hg? How much it is? This carbon dioxide and the blood that is deoxygenated blood that is coming from the heart - what is the partial pressure of carbon dioxide there? 45, 45. So it is 45 here ok and it is 40 there ok. So there is gradient. As a result of that you keep on tracking it and you find that by the time you are done almost one third the distance of the capillary – CO2 is gone - means it has come down from 45 to 40, ok. And as the blood goes it will remain 40. So the partial pressure of carbon dioxide goes on oscillating between 40 and 45. By the time you go to the tissues you go to 45 - then you again go back to the lungs get rid of that 5 extra come back to 40. And this is how it keeps on operating. So, how does it work in the tissues again blood is coming - oxygenated blood - it has what partial pressure of carbon dioxide is there? 40 mm Hg in the tissues it is how much? 46. 46 outside is 45 this gradient is good enough. It will pick up the carbon dioxide and then as a result of 40 CO2 40 will become how much? 45. 45 and that is what will be carried to the heart and then to the lungs for getting rid of that carbon dioxide.

Let us look at this very amazing molecule. Again back to the structure of hemoglobin. It is in quick steps. Guyton tells us about the two molecules of succinyl CoA + glycine they come together and this molecule we will call as what please? Pyrrole. Good, good - four pyrroles come together to give rise to what? Protoporphyrin. Protoporphyrin 9 - then if proto- porphyrin ring gets an iron molecule it becomes what? Heme. Heme - What do you call it as protoporphyrin ring. It is like a coin you know it is flat that molecule is flat and these are not amino acids, ok. No, no this is not amino acid, this is not a protein, ok. This heme group then goes and sits at the center of a large protein molecule, ok. And then it becomes hemoglobin - the protein molecule itself is globin, ok. It combines with the heme - heme consists of what - protoporphyrin at the center of which there is an iron atom are you ok so far ok.

And if you look at the structure of this molecule - author tells us that the there are 1, 2, 3, 4 ends - and there is nitrogen. Parts of that molecule - they hold the iron molecule in its position, ok. And then this protein molecule, ok. How many protein molecules are there? There are 4 protein molecules - ok it is a tetramer. Two of them are called alpha 1 alpha 2, beta 1 beta 2. Total 4 of them ok. Now each one them has 4 heme groups. Each heme group is capable of binding to one molecule of oxygen - O2. So, one molecule of hemoglobin can carry how many molecules of oxygen? 4. And when it binds to 4, we will say that the molecule is saturated, ok. And what should happen when the RBC with its hemoglobin as it is travelling through the lungs. There is an opportunity for the molecule to pick up the oxygen.

Now let us appreciate this image. These are the protoporphyrin rings - there can you see the iron at the centre, ok. Now there is a huge protein molecule and that has those ribbons you understand the protein molecules have ribbons and cords. There are several alpha helices and they are they are labeled as A B C D whatever and one of them is one of the helix is called as F and that helix has an amino acid - histidine. Histidine is an amino acid and that histidine binds to iron - means what am I talking about? I am talking about how the porphyrin ring is coming in contact with the protein molecule - there is a histidine there are there is a huge quaternary structure of that hemoglobin molecule. It has at a particular place a histidine molecule - for that you will have to go into the chemistry of hemoglobin - which we are not doing. And that histidine molecule is directly bound to iron ok. This is of great relevance and I will come to that shortly and look at the two states in which the molecule can shift when there is no oxygen it can take oxygen and then when it takes oxygen it looks like. This is called as oxygenation - what is it called as? Oxygenation ok. Guyton makes a point very clear - it is not oxidation - it is oxygenation. It is a very loose bond ok. It can readily form and it is reversible - so if oxygen is there it will loosely bind - and if the oxygen is not available it will just go away so it can readily shift between two different states. The reaction is very rapid requiring less than 0.01 seconds. Read the bottom line - it is interesting. Approximately 25 trillion RBCs are there and that each RBC is packed with how much of hemoglobin molecules can you read for me? Huge amount talking about it packed within RBCs, ok. Now you cannot really understand hemoglobin molecule unless you go through the process of how the hemoglobin molecule keeps on changing depending on the amount of partial pressure. Or in simple language depending on how much of oxygen it is carrying and what are the different stages that influence the affinity of oxygen for the hemoglobin. Let me clarify. First of all there is a very small percentage - 2-3 percent of oxygen can go through the blood in dissolved form. Hemoglobin has no role - no hemoglobin has no role to play in that - but that is only low 2-3 percent, ok. About 98-97 percent of the oxygen that is being carried through the blood is bound to hemoglobin - because hemoglobin greatly increases the capability - I mean 30 times 40 times 50 times is huge. We really cannot do without hemoglobin. Go to the top curve and let me go to the next one to really explain to you what the story is. Let us see. You have to understand this graph. Do not miss the point. I try to make it as simple as possible. Very simple on the x-axis here what do we have - partial pressure of oxygen, ok. Partial pressure of oxygen. Let us take a look at the blood that is just coming out of the lungs. So if you are there then I would say that you are here, am I right. Ok - we are here ok and when you are here and supposing you are having 100 ml of blood - I think I did not miss this slide - let us do it because without this you cannot go further. There some basic properties of hemoglobin. 100 ml of blood contains how much? 15 grams hemoglobin. 1 gram of hemoglobin binds with about 1.34 ml of oxygen.How much you can carry? How much oxygen? You have to remember -100 ml of blood with 15 grams of hemoglobin can carry about 20 ml of oxygen. You have to remember these numbers, ok. So under healthy conditions - 100 gram of blood contains 15 grams of hemoglobin and can carry 20 ml of oxygen. Done. This is expressed as 20 volumes percent - that is the way the physiology people use the language - what is 20 - 20 volumes percent. It means that 100 ml of blood, equipped with 15 grams of hemoglobin, will carry how much of oxygen - 20 ml. And then - let us move here - so if we are here - collect 100 ml of blood that has just been through lungs, are you with me? 100 ml that is just come from lungs. We presume that it is oxygenated and its partial pressure is about here, ok. Then it should carry what volume of oxygen? 20 ml ok. And given that all those molecules are in 100 ml of blood - that I am having in front of me - presuming that all its RBCs - all the hemoglobin molecules each hemoglobin molecule has four sites for oxygen - they are all occupied - therefore I will go there and I will say that the saturation is 100 percent. Have you been able to coordinate three very important things in oxygen in terms of volume ok. When it is fully saturated means make sure that all the sites are occupied and then the partial pressure is 100 mmHg. Now I will ask a very interesting question. what happens if the partial pressure of oxygen - I am not taking it from lungs - I am taking it from somewhere else and it is not 100, but it is 80. Are you with me? That is question I am asking if it is not 100 and if it is 80, then what is the status of other parameters? Means now I am not here ok - I am here - in that particular case what is the amount of oxygen I am still having maybe 19 hello - it is little less is it 20. Now it is not 20. It is a little less than that. Then you can go from this point - you can go to saturation or if I go now to 40 - why will I go to 40? I will go to 40 because - tell me why? I am going to 40 because this is in the tissues ok. When I am going to the tissue, I am collecting the blood that is – ok - let me put it this way - I am collecting the blood from vena cava ok. You are ok so far. Vena cava - that blood should have partial pressure of 40 mm Hg. So if I take that blood - that blood still has how much volume of oxygen? 15. Isn't it extremely revealing that the blood that is going to the tissue has 20 ml - the blood is coming is still 15. This is lot. Why do you think nature has this margin? Absolutely correct – the answer – margin - margin means if you suddenly start working that 15 may go down to 14, 13, 12, 10 ok but - you still have a lot of oxygen, ok. So we call this as the oxygen dissociation curve. What do you call it as? Oxygen dissociation curve. And the thing that you readily note and that defies our common sense is that - the line is not a straight. The line is a sigmoid line, ok. Now why is that line a sigmoid line is another interesting question and let us try see. So it still has about 15 ml of oxygen. As we are going to take you to my favorite place. My favorite place is Ladakh. I have never been there but still - ok now no no - try to appreciate the beauty of the molecule. We are looking at the molecule and what a great molecule it is. So the pressure of oxygen in the blood ok - this is on the x-axis. I mean when I am at sea level we are somewhere here as far as alveoli are concerned. Where are somewhere here at sea level. When you go to Ladakh - you are not here but you are here - you agree with me because - oxygen is less there and I am not able to get what? Oxygen. It is rarefied so I do not get it. So I am somewhere here even when I am here - I mean this is a massive drop ok from 100 to 80 ok 20 percent drop in terms of what? Availability of oxygen - from here to here - to live at Ladakh - but if I were to do that how much of oxygen is still there per 100 ml of my blood 18, 18 so from 20 to 18 is not a great drop. Are you getting the point as to why the nature has come up with this particular dissociation curve where such a huge difference with reference to from here to there, but we are see 18 is still good ok. It is not 15 it is not 12 it is just 18. So again that is the advantage of - had it been a straight curve - you would not have had that advantage ok. So the nature has come up with this property. We are now looking at the normal pressure - a normal arterial - we are somewhere around 100 and normal venous is 40. When you are doing exercise you actually go here somewhere venous blood you are not 40 you are less ok. But there is enough buffer or enough margin so as to give you - the affinity - follow the point - the affinity of hemoglobin to oxygen is dependent on the pH of the blood. On what? pH and this is extremely important. I'll tell you yet another secret of hemoglobin. It is very meaningful. I'll tell you - you are doing exercise - rigorous exercise - as a result of that your skeletal muscles are generating huge amount of carbon dioxide - as a result of that the carbon dioxide can combine with water and give rise to carbonic acid that carbonic acid can ionize and give rise to $H^+$ ions those $H^+$ ions - where is this happening? In your muscles. Those $H^+$ ions can lower the pH of your blood slightly. When the pH of the blood is lower - the affinity for hemoglobin - the curve is moved to the right. Which means the affinity of hemoglobin for oxygen is reduced. Hello are you getting it? And let us see. You are here somewhere or go straight ok. Now there the middle one is the normal what is the pH there in the middle – 7.4 normal. You are doing great amount of exercise as a result of $H^+$ ions - the pH of the blood has fallen to 7.2 - it never really happens but let's consider for understanding it has fallen – where 7.2. Now at this pH as the blood is flowing through the skeletal muscle what is happening to the affinity what is happening to the affinity which was here what is happening to the affinity of the blood for oxygen is reduced. It is what reduced. Means what - it will liberate more oxygen more readily. It makes sense. Why does it make sense? Because the muscles need more oxygen. Are you with me? It is very interesting ok. So depending on the need at a given place the hemoglobin decides whether I am going to increase my affinity for oxygen or decrease my oxygen and exactly opposite happens when the same blood flows through the lungs ok. The pH again goes up when the pH goes up its affinity for oxygen goes up - but in the lungs abundance of oxygen - so it can combine with the oxygen more rapidly. So look at this again and just keep on looking at the hemoglobin molecule. When it is going through the lungs ok because now there are so many H+ ions now no those H+ ions - they have gone. I will tell you what happens to the carbonic acid – it is again converted into water and carbon dioxide and carbon dioxide is released. Once carbon dioxide is released ok the number of H+ ions goes down so the pH moves upward - once the pH moves upward then this curve moves in this direction and hemoglobin has more affinity for oxygen. Now I am going to show you a very interesting picture. I don't want you to read anything - but just look at the pictures. Do you identify this guy on the on the right who is he? Still nobody half of you don't know who is he? who is he? I am talking of his dad ok Christian Bohr what is his name? Christian Bohr what is his name? Christian Bohr. This response of hemoglobin to reduce the affinity of the hemoglobin to oxygen depending on the pH is called as Bohr's effect. What is it called as? Bohr effect. Read the bottom line. At the bottom what does it say this is called the Bohr effect. You are not going to confuse what Bohr is I have told you the entire relationship ok. So you know Bohr ok he was a medical person Christian Bohr was a medical person and Neil Bohr - we all know ok. So got it very clear don't forget it. ok that's why the history of science is interesting.