Human Physiology Prof. Nishikant Subedar IISER-Pune

Lecture – 35 Physiology and Introduction of Respiration - Part 1

So, we will now take a look at the physiology of respiration. You know this very well - you know something about it something like what? Well every cell needs oxygen and not only that we also need to get rid of carbon dioxide. And oxygen must flow. Oxygen has to flow and oxygen always flows from higher partial pressure to lower partial pressure. Now before I go ahead any further I would ask you to do something today. Please read once again about surface tension, water surface tension hello. You know about it I know about it but just make sure. Second thing what I want you to do today is read about partial pressure. And read about how the gases diffuse in one medium or across from one medium to another medium or what drives. So read about it in today. If you read about it that will make my life a little easy and it will work out good for you also. So please, please remember these points. What did I tell you - read about what? How does the oxygen diffuse - in what direction? What is it that permits the drive, okay. So we have an elaborate respiratory system the aim of the respiratory system is of course to make sure that we get the oxygen and then we increase the surface area in the form of what you have alveoli and the huge surface area we provide for the gaseous exchange to happen. We have an elaborate respiratory system. We take in air - oxygen in our system which is transferred into the blood and then once it gets into the blood then to the issues. The cardiovascular system comes into play. It takes the oxygen everywhere to the different tissues okay. And then we see as to how the oxygen is transferred from the blood to the different cells – look - the ultimate target is mitochondria. Every cell has mitochondria okay. That is the ultimate target okay. That tiny organelle in your cell which is always crying for oxygen is mitochondria, okay. So you need to provide oxygen to the mitochondria and then what we do try to do is we will try to look at how do we control ventilation. We take in air take out air - that is ventilation okay. How do you ventilate and how the ventilation is controlled by the brain - plays a key role in controlling ventilation. We will talk about ventilation and of course we will talk about the hemoglobin and its role in the transport of oxygen. And of course we will talk about - taking oxygen to the remote cells, okay. It is equally important to get rid of the carbon dioxide in the opposite direction. And so let's see this. I am sure this is a very familiar diagram. We are looking at the passage - we start at the level of the glottis and through the sound box then you have the trachea and from the trachea - the trachea branch into two bronchi, the, branch and branch and branch, okay. You need ultimately reach your alveoli something like you have 300 million alveoli. Surface area almost as big as a tennis field. Then you have the trachea, the bronchi and you ultimately go to this and then you find that you are - where are the lungs - they are in our thoracic cavity, very good. Thoracic cavity it's an airtight cavity, okay. That's very important and on the lower side of course you can identify the diaphragm, there. Okay which separates the thoracic cavity from the abdomen. And then we'll find that - this is a very interesting picture. You take a section right across the chest okay - the sternum okay - which is this part - sternum is right at the bottom. At the top can you see the single vertebra there hello - in the vertebra can you see that opening where the spinal cord will pass through, okay. And then you will have the right lung and the left lung and then of course you will have the pulmonary trunk, the blue one here which will carry the artery which is carrying the deoxygenated blood to the lungs. And the oxygenated blood is coming by the vein by these red vessels and then these are the two bronchi and which will branch and branch and this gives to an idea as to how actually they are very close to the heart. The lungs are very close and the vessels are very large and they are very elastic. We'll talk about it a little later. So you have trachea okay and then the trachea branch first you have bronchi going to the left and right okay and then each bronchus divides and then divides and then divides every time it divides we'll call it as a generation. So first generation, second generation, third generation - it has been found that the human respiratory system - it divides how many times? How many generations there can be read on that column. How many times does it divide - 23 times so 23 generations. By then you can imagine what is huge number of the tiny tiny tiny bronchioles, okay, which will go and finally terminate in an alveolus, okay. Single alveolus and the diameter of alveolus about hundred and hundred and fifty microns very small okay. And one of the major problems of the respiratory system of ours is that it should not collapse. You understand what I mean okay. If you draw here, if there is negative pressure, it will just it just collapse. You know just you don't want to collapse. You want to make sure it doesn't collapse. Then you have to fortify it okay but if you fortify too much okay then that fortification will come in the way of the gaseous exchange okay. So you have to strike a balance so on one hand - you go from the trachea to bronchi and then bronchi first generation second generation third generation and then as the tubes become narrower and narrower okay. Then you need to cover them with the cartilages - cartilages supporting system. But finally when you go to the alveolus there you don't have any cartilages system and the only thing that will keep it expanded is the air in it. Is the air in it - we'll talk about it okay. So what we'll do is, we'll start from the level of nose and we'll go all the way all the way just take a look at the different types of cells that you will encounter. Different epithelial cells the air is coming in contact with the cells. Does it really? No it doesn't. Why because you don't want the cells to dry. Okay. So the entire lining of your system is covered with a mucus. It has to be covered okay. Please remember every cell has to have an environment and that's that environment has to be a watery fluid - which is secretion from some of the cells okay. You can't allow the cell to dry okay. Because you don't want to allow the cell to dry therefore in the entire system you have - can you see the brown cell there - and then - there are series of brown cells. What do you call them as? Call them as goblet cells. Goblet cells are in your alimentary canal - there are millions of goblet cells in one nasal passage - there million goblet cells and they essentially secrete a mucopolysaccharide like substance. It is a combination of several substances which are continuously keep the entire system wet. And then there you see those tiny tiny yellow cells these are the basal cells. These are the stem cells okay. Because you know why because the cells are covered by mucus - continuously flowing which often will bring a lot of material from outside okay. We inhale not only air, but we often inhale polluted air or whatever dust particles, pollens and number of things and they could damage the cells. So there is a continuous turnover of cells and therefore the nature has provided us with stem cells. What do you call the stem cells as - basal cells. Are you with me? So we have basal cells - will be on keep on replacing the old cells - new cells will come okay. Then there are ciliated cells they are very interesting. You can see their cilia. Now the cilia are very interesting because they keep on beating that's a function of cilia okay. And when they beat what they really doing is - they drive the mucus - we have a cilia okay and so let's say you go into your nose deep inside no nose okay and then - you are breathing and along with the waft of air that you take in there's a dust particle - that dust particle is caught somewhere in your nasal passage and it is caught fortunately on the mucus system. But you want to get rid of it how do you get rid of it. Because then there are the cilia come into play. They keep on beating okay that's a normal function in what direction do they keep on beating. This interesting they keep on beating in the direction of the pharynx what direction – pharynx - why in the direction of pharynx - because the mucus in which the dust particle is trapped it will go towards the pharynx and once in the pharynx it will get swallowed into the esophagus. Now you see the our respiratory system can't tolerate even the tiny foreign particle but our alimentary canal can. It can handle lot of it because we are probably so much food okay. So it can handle but our respiratory system cannot. But now imagine a system in which you are breathing and there's an dust particle that got through all your nose and then it got in the trachea. And then it got stuck in the bronchi. Do you appreciate the problem? Then how do you deal with it. No - you are also right but I'll come to that - the answer to that question is again cilia, again cilia. But these cilia are beating in opposite direction, hello. Look at the direction I mean you have to appreciate the beauty of the nature. A single cilia itself which is located anywhere in the passage of your respiratory system right from your lungs to the pharynx is beating upwards so that so that the mucus will go along with the dust particle in your esophagus. But the ciliary cell - there in the bronchi which will now will beat in opposite direction. So that will again go to the pharynx and then into your esophagus then always ask a question how do the cilia sitting in the nose beats the cilia in downward direction and that in the trachea beat in the opposite direction, Hello. I don't know the answer okay. I just want you to appreciate how amazing that there are certain cells which are called as a Clara cells. They detoxify the substances. There are certain neuroendocrine cells which are sensory - which are sensitive to carbon dioxide, air pressure, and H ions etc. So we have a sensory system and we'll talk about it a little later okay. So this is just to show you - this is the section through right through your neck you can see the trachea and that's the esophagus and as you go deeper and deeper you can see as you go into the bronchi - of course there is a initially there is a thick layer of smooth muscles in your trachea, okay. So there is cartilage and thick and smooth muscles as you go this smooth muscle are there. Can you see the smooth muscles there okay. They are there and in the case of asthma okay or in the case of allergic reactions those smooth muscles - they contract and then the nasal passage is obstructed. Are you with me okay. In the nasal passage if the mucus is sitting there then really to obstruct your passage of air and then you have a typical wheezing sound. Have we all experienced it sometime? The wheezing sound that happens okay. It is very uncomfortable okay. Here is an example of a healthy system and here is the system where - as a result of the inflation information - I am sorry the passage is occluded. And then another interesting thing that happens is as a result of allergic reaction

- we talked about those mucus cells - you know goblet cells okay. The goblet cells are stimulated and they hyper-secrete okay. So you have a lot of secretion which you can't deal with. If you want to get rid of it okay expectoration but that doesn't really happen and then it settles and these smooth muscles get this point and don't forget this smooth muscles have adrenergic receptors of beta 2 type. Smooth muscles in your respiratory system is under the control of these autonomous nervous system. So they can be controlled they can be controlled by the post ganglionic fibers of the sympathetic nervous system which will release norepinephrine. Norepinephrine will act on the plasma membrane of the smooth muscles and these smooth muscles plasma membrane are equipped with a receptor - what kind of receptor - beta 2 beta 2 and under the influence of norepinephrine. They relax they do exactly opposite to what happens in heart. They relax okay. And if you give parasympathetic stimulation - the parasympathetic nervous system will constrict them and the action of parasympathetic nervous system is via muscarinic receptors. Are you with me? So is there innervation of the sympathetic action via beta 2 receptors. What is the response of the smooth muscles? Dilation, relaxation so if a patient with a severe asthmatic attack is brought to you, what would be your prescription? Give a beta blocker if he is not a heart patient okay. Say that loudly beta agonist. Simply give an injection of epinephrine okay. It is a fire brigade like response not a great idea but it gives you instant relief, okay. So, you can give a sympathetic agent so, the patient is on beta-2 receptors agonist - beta 2 receptors are sensitive to epinephrine they are more sensitive to actually less to norepinephrine more to epinephrine. What is the source for epinephrine very good. Adrenal that is the source and that is the end response. Of course it will be generated via the beta 2 receptors. After 23 generations you finally have the final branch. This is a simple histological picture can you see those tiny holes. What is an alveolus? Each alveolus is like a pocket and the terminal branch will go and terminate there, okay. I told you just now. What is the diameter of this alveolus? What is the diameter across 150 microns 150 to 200 microns. Say that loudly - how much 100 to 200 microns. And if you take the whole view, You can see the bronchi and then you can see the bunch of alveoli. Now what is really interesting about it this is, you see the single alveolus there's another alveolus and you know something there is a duct between the two. So if if air gets into one alveolus but it doesn't get into alveolus via the branch, then the air from one alveolus can go to the adjoining alveolus in the neighborhood, okay. So let us see what we have here. We have the branch going along with that I am sure you can see the branch of the artery which brings the deoxygenated blood and the deoxygenated blood will flow right on the periphery of each alveolus and then it will get oxygenated and the oxygenated blood will be taken back to the heart. So each alveolus will have several capillaries, okay. Blood will come deoxygenated will flow through the capillary. We already know that the length of a capillary maybe half mm or at the most 1 mm. Flow through it, the blood gets oxygenated, okay - it will join together and finally it will go. The second thing is what is so conspicuous about here - can you see those yellow lines which author has drawn for our convenience those yellow lines. These actually form of connective tissue which is providing elastic fibers. Is it intracellular? Is it extracellular? It is extracellular matrix which is very unique to lungs that forms what do you call as you can - see them here around each here so in this image there you see the author is focused on the elastic fibers of capillaries. Are the capillaries, the red ones there are the capillaries, hello. Can you follow that the red ones are there but the yellow

ones are what? Elastic and this shows the elastic fibers. You know why we talking so much about the elastic fibers. This is because - I'll talk about it when we do the mechanism of respiration. I think I'll talk about it in a couple of slides we'll go there. Now we are looking in a single alveolus, okay. You want the cells which are lining the a single alveolus - squamous epithelium - it is flat okay. so can you see tile like cells - hexagonal or pentagonal, Whatever, okay. They are extremely flat cells - the distance across maybe 6 or 7 microns, but the thickness maybe 1 micron or 1.5 microns. They're extremely thin cells, extremely thin cells for obvious reason. So they facilitate the gaseous exchange. Therefore they are extreme thin we'll call this the cells - these flat cells - we'll call as cell type 1. What do you call them as cell type 1. About 90% of the cells are cell type 1 and they form the squamous epithelium and they are flat cells. About 10% of the cells which author has color coded are called as the type 2 cells. What do you call them as? Type 2 cells, okay. And these type 2 cells are interesting because they keep they secrete a range of phospholipids. What did I say - they secrete a range of phospholipids. You see the moment I talk of phospholipids you must talk of a molecule hello that has a head and there is a charge and there are tails and there is no charge - are you with me, okay. Such compounds are being secreted, okay - phospholipids a range of different phospholipids are secreted by the type 2 cells and those substances serve as surfactant. What did what word - I use surfactants are - they are like detergents - we use for washing clothes. The surfactants - they will reduce the surface tension of water are you with me. They form a layer you see if the water directly comes in contact with air hello then the attraction for one molecule of water with another molecule of water is very high I'll call it a surface tension. We call it as surface tension are you with me - and it happens when the layer of water is coming in contact with air, okay. Therefore I asked you to read please. You know about surface tension. Then there are certain macrophages, okay. Some of those dust particles which could not be dealt with by the cilia in the upper part by draining them downwards or they could not be handled by the lower part of the trachea by draining them upwards those will finally be taken by phagocytosis and then the macrophages themselves will travel okay into the pharynx and then will be in then will be swallowed into the alimentary canal, okay. What are we talking about? We are talking about the system that tries to keep our respiratory system clean, okay. And of course as we move along – of course can you see a capillary here a capillary here - so this this particular the author has shown about six. There are far more capillaries which invest almost every single alveolus. This is just to emphasize that the macrophage there which will devour or phagocytose the dust particles this is to give you an idea. We have a scanning electron photomicrograph of an alveolus. Can you see these alveoli and this is the duct through which the air will pass. This is a section through the bronchi, okay, for pulmonary ventilation. So let us try to understand the mechanism as to how air comes in and goes out. And now here I will talk about the elastic fibers which I showed you in one of the previous slides. So we have a box here or a cage, here, okay, which is lined by the ribs and the skeletal muscles and on the lower side there is a diaphragm. You can control the movement of your diaphragm willfully it's a skeletal muscle and so you see both the lungs okay and the trachea, okay. And the trachea then branches into bronchi - this is the only way by which the lungs are actually communicating with the rest of the body. The lungs are actually floating in the thoracic cavity. They are not attached anywhere - as if you are having lungs by the neck very funny language okay. But you have

the message. I am holding what trachea, bronchi - one lung here one lung here - this is also floating. It is only here that the lungs really come in contact with the rest of the body. What you call as the root of the lungs. So when the lungs will either compress when you try to expire there or they will expand when we inhale the air. In either cases outer wall of the lungs will slide on our chest cavity. So this is the chest cavity inner surface and if this is the lungs the lungs keep on continuously sliding on one another and to facilitate that sliding there is a thin layer of lymph. Are you with me? This thin layer of lymph now let's see what would make the lungs - essentially inspire - we are able to take in the air in the lungs because of the negative pressure on the outside. What did I say? Just how the negative pressure on the outside will generate the negative pressure. On the outside - most important - is the diaphragm and of course the ribs and then the sternum. So for really that to happen, what we need to do is this. Is the diaphragm dome shaped? It is dome-shaped okay. When you inspire or you inspire because this dome shaped diaphragm flattens and when it flattens, okay, it increases the volume of the thoracic cavity, point number one. Two additional things happen number one, your clavicle or the collarbone - it goes up and number three your sternum goes forward and your ribs go a little downwards. All that adds to the increase in the volume of your thoracic cavity. As a result of that - the lungs expand but for the lungs to expand there is absolutely no other way but to take in the air there in only one passage - that passage is through your nose - of course - through the mouth but let's forget it so through your through your nose. You can take in the air so as the volume of the thoracic cavity expands, you can see the sternum goes forward, the clavicle goes upward and the the diaphragm which is like a dome it becomes flat. You take the air in your lungs and who tells the diaphragm to contract and relaxed the diaphragm. When it contracts it becomes flat, as a result of increase in the volume of the thoracic cavity right. Why does it happen because diaphragm has to be told it's not like heart, it has to be told by whom? The brain. How does the brain tell the diaphragm that you keep on doing the respiratory movement. It is told by I will take you to the neck hello, in the neck you have cervical vertebrae. I will draw your attention to – how many cervical vertebrae are there in your neck? Seven. How many are there – seven. Very good. I'll draw your attention to the spinal nerves which come at the level of C3, C4, and C5. Are you with me. The spinal nerves which will come out of your neck vertebra at what level C3, C4, and C5 -these nerves - they get together and they will go down through your neck and they will supply or they will innervate the diaphragm. These nerves which are on the right hand on the left will called as phrenic nerve. What do you call them as very good what do you call them as phrenic nerve, okay. And these phrenic nerves keep on discharging rhythmically. It is only when the phrenic nerve discharges okay that our diaphragm - which is like this - becomes like this - and increases the volume and then we take in air - so inspiration is happening. Why, because if you take a knife okay if take a knife and cut the phrenic nerves, you got the message why am I doing it? Just to impress on you the importance of what it's so important. It is just that the phrenic nerves are so important, okay, they have to - every day they have to send action potential if they don't that is the end.