Course Name: Pulmonary Function Test -Interpretation and Application in clinical practice
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Hello everyone, welcome to this online lecture series, online course on Pulmonary Function Test, its interpretation and application in clinical practice. Myself Dr. Brinda Srinivasagopalane, Associate Professor Physiology, Chettinad Hospital and Research Institute. In today's topic in lecture number 3, we are going to see about Ventilation, Perfusion and Ventilation Perfusion Ratio. These are the objectives of today's session. We are going to see concepts on ventilation, dead space, concepts on perfusion, the relationship between the ventilation and perfusion and ventilation perfusion mismatching.

First to begin with on ventilation, in previous lecture series you would have read about the mechanics of ventilation, what are the muscles involved in the ventilations, what are the pressures that are altered during the ventilation process. So, basically what is ventilation? It is a process at which the air enters into the lungs and there is exchange of gas which takes place in the alveoli and the lungs. There are two types of ventilation, one is pulmonary ventilation and the other is alveolar ventilation. Pulmonary ventilation is just the amount of air that goes in and out of the lung in a given time during quiet breathing.

So, as we are normally breathing, the amount of air that travels in and out of the lung that is just the pulmonary ventilation. It is also called as minute ventilation or respiratory minute volume and it is calculated with the formula:

Pulmonary ventilation = Tidal volume X Respiratory Rate

So, the tidal volume is the amount of air that goes in and out of the lung per minute during quiet breathing and it is given to be 500 ml. The respiratory rate for a normal average person is calculated as 12 per minute. So, when you try to multiply both: the pulmonary ventilation is around 6000 ml per minute or 6 liters per minute.

Next is the alveolar ventilation, it is quite different from that of the pulmonary ventilation wherein the gas that is actually entering into the alveolus and that takes place in the gaseous exchange every minute. So, the gas that is only involved with the transfer of carbon dioxide and oxygen that is gas exchange inside the alveoli that ventilation alone is called as the alveolar ventilation. The normal value is around 4200 ml per minute and it is calculated with the formula:

Alveolar Ventilation = Tidal volume - Dead space volume X Respiratory rate.

We are going to see the details on the dead space in the coming up slides. So, the dead space is calculated to be 150 ml, we will see how to do that in the future slides.

Tidal volume we know it is around 500 ml, you subtract both and multiply by 12 you get the alveolar ventilation which is to be 4.2 liters per minute. You should note that the alveolar ventilation is lower than that of the pulmonary ventilation. Why because the all the gas that enters into the lung does not take part in the gaseous exchange. And the alveolar air can be collected as the last portion of the expired air during forceful expiration.

Next we are going to see about the dead space. So, dead space is the part of the respiratory tract where gaseous exchange does not take place. So, it is the three types of dead space, anatomical dead space, physiological dead space and the alveolar dead space. We are going to see the details of all the three dead space now. First anatomical dead space, we have already seen in lecture number 1 in the functional anatomy of lung regarding the Wiebel's model of lung, wherein the lung bronchioles are divided into several generations.

Here the anatomical dead space occupies from the nose till the terminal bronchial it is the 16th generation of the Wiebel model. So, this part is called as the conducting zone which is actually not involved in the gas exchange process. And that part forms the anatomical dead space and it is around 150 ml. How it is measured to be 150 ml is being done by the Fowler's method. So, Fowler's method it is also called as the single breath oxygen method which is used to calculate the dead space.

So, how this experiment is done? A patient is asked to inhale pure oxygen. So, you can see here pure oxygen is been inhaled by the patient and we know that in the lungs there is a mixture of gases which is nitrogen plus oxygen. So, when pure oxygen is getting inhaled part of that oxygen remains in the conducting zone and part enters into the alveoli. The patient is then now asked to expire. Once he expires the initial portion that he expires is only pure oxygen and does not have any nitrogen content in that.

The patient is actually expiring into a nitrogen meter which is going to record the nitrogen concentration in the expired air. The initial breath will not have any nitrogen content because it is from the conducting zone of the lungs. So, once after a certain point then there is a nitrogen after a certain point, we have nitrogen that is been recorded in the nitrometer. And you can see the concentration of nitrogen rises up to a static level of around 60 percent. This rise in nitrogen is because the air is been expelled out from the alveolar space where there is a mixture of nitrogen concentration.

So, which means the initial part of the air which is pure oxygen and after that the air is a mixture of nitrogen and oxygen content which is been diagnosed in the nitrometer. Based on this we derive a formula:

$$\text{Dead space V D} = \frac{\text{Grey area (which is the area which has pure oxygen) X pulmonary ventilation}}{\text{grey area + pink area.}}$$

The grey area and the pink area is the total volume of expired air which is also calculated as the tidal volume.

So, the dead space can be written as:

$$\text{Volume of dead space} = \frac{\text{Grey area of dead space}}{\text{Tidal volume X Pulmonary ventilation}}$$

When we try to do the calculation based on the readings of the graph we get the anatomical dead space to be around 150 ml.

Next coming to the physiological dead space. Actually, the physiological dead space anatomical dead space is a part of the physiological dead space. In certain diseased lungs some alveoli are perfused, but actually not ventilated. What does that actually mean? If you take this as an alveolus of the lung and this as a blood vessel or a capillary which is close to the alveoli. So, there is always diffusion of gas across these alveoli.

So, air enter from the atmosphere into the lungs which is oxygen and carbon dioxide exits out from the capillaries out into the alveoli. So, from the atmosphere when air enters into the alveoli gas exchange takes place here. So, there will be certain parts of the lungs where in this gas exchange or this alveolus need not be ventilated that is it will not be ventilated with oxygen. So, in those cases that alveoli remain an unventilated alveolus. This unventilated alveoli plus the conducting zone that is the anatomical dead space together forms the physiological dead space.

So, that means, the total volume of gas in each breath that does not take part in gas exchange is called as the physiological dead space. And this is again measured experimentally by using Bohr's equation. So, what is Bohr's equation? Whatever alveoli air we are expiring out is mainly made up of carbon dioxide content. So, the alveolar carbon dioxide volume + the dead space carbon dioxide volume will be the total carbon dioxide in the expired air. So, based on this we are deriving a formula:

$$\text{Dead space} = \frac{\text{Tidal volume X (alveolar carbon dioxide concentration - the expired carbon dioxide concentration)}}{\text{Alveolar carbon dioxide concentration}}$$

And when we substitute the value: tidal volume as 500 ml or 0.5 and alveolar carbon dioxide concentrations as these we get the dead space to be 143 ml. So, an average dead space is around 140 to around 150 ml that is the physiological dead space. What is the relationship between a dead space ventilation and a tidal volume? It is very important dead space is always inversely related to the tidal volume. So, the larger the tidal volume the smaller will be the proportion of the dead space ventilation.

If the dead space volume is constant at 150 ml and the tidal volume alone changes one from 500 to 600 what will be the change in the dead space ventilation? What is the effect on dead space ventilation? So, if the tidal volume is 500 the dead space ventilation is 0.3 X pulmonary ventilation. If the tidal volume is 600 ml you can see that the dead space is decreased to 0.25 into pulmonary ventilation. So, we can see that is an inverse relationship between dead space volume and the tidal volume.

What is the physiological significance of alveolar ventilation? We know that the tidal volume is normally around 500, respiratory rate is 12 breaths per minute in a normal average person. Consider a subject A to be a normal person where in the pulmonary ventilation when you multiply both you get 6 liters per minute. Alveolar ventilation you have to minus the dead space volume you will get around 4.2 liters per minute this we have already seen in the previous slide this is for a normal person. Suppose we take a person who is rapidly breathing shallow breathing where in his respiratory rate will be very high it is increased to around 30 breaths per minute.

As he breathes rapidly the amount of air filling in and out of the lungs is going to be very less it is around only around 200 ml. So, and when for this patient when we try to calculate the pulmonary ventilation, it will be around 6 liters per minute, but the difference is the alveolar ventilation where in the alveolar ventilation when you minus the dead space volume and multiply with the respiratory rate the alveolar ventilation is markedly decreased to around 1.5 liters per minute. This is very important why because whenever the air inside the alveolar is going to get reduced the oxygen content in the blood also be reduced because there is decrease in the diffusion of gases across the alveoli. So, such patients will tend to have hypoxia and hypercapnia.

So, hypoxia when there is decrease in the arterial oxygen content and hypercapnia there is increase in the arterial carbon dioxide concentration. So, in patients with rapid shallow breathing there is high possibility of hypoxia and hypercapnia. What is alveolar dead space? As I said there is a third dead space called as an alveolar dead space it is slightly different from the physiological dead space where in we do not include the anatomical dead space here. So, it is just the volume of the air in the alveoli that does not take part in the gaseous exchange that is the alveolar dead space. In a normal person the anatomic and physiological dead space are usually normal and equal and all alveoli are functioning normally in the lung.

But in person with partially functional or non-functional alveoli in some parts of the lung the physiological dead space is 10 times more than the volume of the anatomical dead space. So, it could be as high as 1 to 2 liters, from 150 ml to 1 to 2 liters. So, the physiological dead space is of more clinical importance compared to that of an anatomical dead space. Coming next to the distribution of ventilation, the air volume that enters into the lungs does not get evenly distributed into the lungs. In a normal erect individual, the air that enters into the lungs or gets ventilated in the lungs depends upon the gravity.

So, when there is gravity acting upon on the lung it pulls the lung downwards it pulls the lung downwards away from the chest wall. So, what happens the pleural pressure here increases as well as the intra alveolar pressure increases. When the intra alveolar pressure increases there is pulling away or it goes up in a bigger size and there is entry of more air into the alveoli. Whereas, when you see in the base of the lung, the alveoli are smaller in size because the alveolar pressure is comparatively low in the base of the lung compared to that of the apex of the lung. So, you can see in this graph that this the ventilation is higher in the apex of the lung and comparatively it is lower at the base of the lung because of the changes in the trans pulmonary pressure or the intra alveolar pressure.

The gravity alone is not the reason for this distribution of ventilation in the lungs. There are other reasons such as airway resistance and compliance which is already dealt in the previous lecture. For example, in restrictive lung diseases compliance is affected. So, there will be decrease in the air entry into the lung in obstructive lung diseases there is increase in resistance which is also going to alter the ventilation of the lungs. Next, we are going to see about the perfusion of the lungs.

The lung is actually has a blood supply from three routes one from the pulmonary blood vessels, second from the bronchial circulation, third from the lymphatic capillaries. First is the pulmonary circulation. So, pulmonary circulation includes the pulmonary artery and the veins. So, from the right side of the heart the pulmonary artery takes the deoxygenated blood into the lungs where oxygenation takes place and the veins carry the oxygenated lung blood again to the left side of the heart and that goes in for the systemic circulation.

So, this is the pulmonary circulation. The second is the bronchial circulation wherein it the bronchial arteries supply the smaller and larger bronchioles of the lungs and third is the lymphatic circulation which carries the waste products or the particulate matters from the alveoli outside into the lymphatic channels. The distribution of pulmonary blood flow again it varies similar to that of ventilation, but there are small changes or differences in that. Well, ventilation is more on the apex and less on the base it is completely opposite with that of the perfusion. The pulmonary circulation is generally a low pressure and a low resistance, but a high capacitance vessel and this pulmonary blood flow through the lungs will depend upon three important factors. One is the pulmonary arterial pressure, pulmonary venous pressure PV and pulmonary alveolar pressure P capital A.

So, these pressures varies in different part of the lungs from the apex to the high lung to the base. So, based on this the blood flow also varies on all these zones of the lungs because of the action of gravity, but when the patient is in a supine position blood flow is almost equal in all parts of the lung greater in the posterior regions and lesser in the anterior regions, but the gravitational effect will have an uneven distribution of blood flow in the lungs. So, that will divide the lungs into three functional zones. First is zone 1, in zone 1 you can see that the alveolar pressure is much greater that is this is the alveoli the pressure in the alveoli is much greater than the arterial pressure which carries the deoxidated blood and then the venous pressure. So, when the alveolar pressure is greater than the arterial pressure the capillaries will tend to collapse and there will be no blood flow across the capillaries and actually in normal lung this does not exist this zone does not exist that is considered to be zone 1.

Next considered coming to the zone 2, here the arterial pressure is rightly greater than that of the alveolar pressure, but the fact is it does not happen at all times. The arterial pressure here will be highest only during the systole of the heart that is when the heart contracts blood at that time the arterial pressure will be greater than the alveolar pressure which will result in the flow of blood across the pulmonary arteries ok. So, this effect is called as the damming effect where there is partial collapse of the capillaries during the diastole period and opening up of the capillaries during the systole period also referred to as waterfall effect or intermittent blood flow and that forms the zone 2. Zone 3 portion of the lung here you can see the arterial pressure is greater than the venous pressure greater than the alveolar pressure. So, which means the capillaries remain open at all times and there is continued flow of blood at all times and the blood flow is maximum at the base of the lung.

The blood flow is greater at the base of the lung as the capillaries are remained open at all times. So, the distribution of pulmonary blood flow is across the 3 zones zone 1, zone 2 and zone 3 with the maximum blood flow in the zone 3 or the base of the lung. There is there are certain factors that regulate the pulmonary blood flow. One major factor is the oxygen level that has a major effect on the blood flow. So, whenever there is decrease in the oxygen concentration that is like hypoxia there is intense vasoconstriction diverting the blood flow to well-ventilated alveolus.

So, that there is a definite diffusion of gases that takes place. What are the other factors that cause pulmonary vasodilation and pulmonary vasoconstriction? Pulmonary vasodilation when there is high PaO_2 concentration nitric oxide, acetylcholine, dopamine and bradykinin all these causes vasodilation of pulmonary blood vessels and more blood flow to the lungs. Pulmonary vasoconstriction is when the oxygen content is very low when there is high carbon dioxide or acidosis these causes constriction of the pulmonary blood vessels. So, that it diverts the blood to well-ventilated alveoli. So, that the diffusion process takes place and the other vasoconstrictors also include angiotensin, leukotriene, serotonin and endothelial.

Coming to the ventilation perfusion ratio, we have seen concepts on ventilation, we have seen concept on perfusion, how both are related and how it is clinically important. So, what does ventilation perfusion ratio signify? It signifies the gaseous exchange. The major function of the lung or the alveoli is to undergo gaseous exchange. So, considering this as an alveoli again oxygen enters into the alveoli which enters into the capillary blood vessels and there is exchange of carbon dioxide from the capillary blood vessel outside into the alveoli.

This is a gaseous exchange process. For this process to be maintained at optimum level we need a normal ventilation and normal perfusion. So, for that it is been expressed as Va/Q the ratio is represented as Va/Q and a normal Va/Q ratio is said to be 0.84. So, how it is calculated? We already know the alveolar ventilation is 4.2 and the perfusion is 5 which is equaling equal to the cardiac output of 5 liters.

So, the normal Va/Q ratio is 0.84. So, when ventilation exceeds perfusion, the perfusion ventilation perfusion is usually greater than 1 that is when V is more Va is more than Q the ratio is more than 1. When perfusion Q is more than Va definitely the ratio is less than 1. This maintenance of Va/Q ratio to 0.84 is very important for maintaining normal concentration of oxygen and carbon dioxide in the blood. If there is mismatch in this Va/Q ratio due to abnormality in the pulmonary blood flow or ventilation that could result in an impairment of oxygen and carbon dioxide diffusion or transfer across the alveoli.

Now, coming to the regional difference in the Va/Q ratio like there is a difference in ventilation and perfusion across the different zones of the lung. So, is the ventilation perfusion ratio. We know that the ventilation is maximum at the apex of the lung and perfusion is maximum at the base of the lungs. So, based on this the Va/Q ratio is also noted.

We can see that the Va/Q ratio is maximum 3.3 at the apex of the lung and it is low 0.63 at the base of the lung and it is equal to 1 at the hilary region of the lung. The normal Va/Q ratio at the apex of the lung is greater than 1 why because ventilation is more than perfusion and it is low at the base of the lung because perfusion exceeds that of ventilation. What are the effects of alterations in the Va/Q ratio? When the Va/Q ratio is normal that is when it is 0.84 everything is normal gas exchange is also going to be normal and the concentration of oxygen and carbon dioxide are at normal levels, P O 2 is 104, P C O 2 is 40.

The problem occurs when there is alteration in the Va/Q ratio due to alteration in the ventilation or perfusion in the lungs. So, when there is more alveolar ventilation than that of perfusion the extra alveolar air that is present in the alveoli gets wasted. And when it keeps on going like that and the Va/Q is infinity when the ventilation alone happens and there is no perfusion at all that is the perfusion is 0 which means there is no exchange of gases that is going to takes place in that alveolus. So, there is going to be change in the alveolar air compensation compared to that of normal. Here the alveolar air compensation the P O 2 will be 149 and the P C O 2 will be 0 mm Hg because there is no diffusion of gases as there is no

perfusion.

On the contrary when we take when the blood flow is present, but there is no alveolar ventilation. Again, there is not going to be any diffusion of gases there is no oxygenation of the blood and the blood that is going to go to that alveolus is just a wasted blood. We do not call it as a wasted blood we call it as a shunted blood which means it does not get oxygenated. And when this ratio goes to 0 when there is absolutely no alveolar ventilation and only perfusion present there is again change in the alveolar gas composition wherein the alveolar air is a P O 2 is around 40 and the P C O 2 is around 45 millimeters of mercury. This can be further understood by this graph where you have P O 2 concentration in the x axis P C O 2 concentration in the y axis and we try to plot in with the Va/Q ratio.

When the Va/Q is normal you have normal P O 2 concentration of 104 and normal P C O 2 of about 40. When the Va/Q ratio is infinity, you can see that the P C O 2 concentration is around 0 here and the P O 2 concentration is maximum to around 149. Again when Va/Q is 0 the P C O 2 concentration is high to about 45 and the P O 2 concentration is around 40 same to what we have explained in the previous slide this is a graphical representation of the same. Coming to the clinical significance of altered Va/Q. When does the alveolar ventilation gets altered in lot of clinical conditions such as bronchial emphysema, bronchial asthma, emphysema, pulmonary fibrosis, pneumothorax, congestive heart failure and there is uneven pulmonary perfusion in case of shunts anatomical shunts like tetralogy of phthalate, pulmonary embolism and increased pulmonary resistance.

So, this uneven ventilation of perfusion is not very good because it does not cause diffusion of gases. So, no proper oxygen content into the blood that could result in a tissue hypoxia. There is a clinical importance here with the ventilation wherein the apex of the lungs is most affected in case of pulmonary tuberculosis. Why? Because it is more ventilation which means there is more amount of air flow to that part of the lungs. So, more bacteria can get lodged in at the same time there is decreased perfusion in the apex of the lung.

We know that the blood usually carries the W B C's which are defense against any bacteria. So, less blood flow to that part of the lung less washing away of the bacteria from that area. So, that is why we tell the apex of the lung is most of commonly affected in case of pulmonary tuberculosis. Coming to the ventilation perfusion mismatch and shunts there are two types of shunts one is the anatomical shunt and a physiological shunt. Anatomical shunt occurs when the mixed venous blood bypasses the gas exchange unit.

So, you can see that this capillary does not have in contact with the alveoli. It this anatomical shunt occurs when the mixed venous blood bypasses the gas exchange unit and goes directly into the arterial circulation. So, it does not involve an oxygenation process and there is no oxygen content in this shunted blood that is called as an anatomical shunt. Whereas, in the physiological shunt the there is pulmonary blood flow to the alveoli, but there is no alveolar

ventilation could be due to an obstruction in the flow of air into the alveoli could be tumor or a foreign body etcetera. So, the lung is having perfusion, but no ventilation that is the Va/Q ratio is of 0.

So, here the perfused blood perfusing this unit is mixed with the venous blood and there because there is no ventilation no gas exchange and the blood leaving this unit remains deoxygenated like mixed venous blood. So, these are the two types of shunts anatomical shunt and physiological shunt. This is a diagram which again shows the Va/Q ratio alteration where there is a normal Va/Q 0.8 where there is adequate oxygenation across the alveoli or Va/Q infinity that is there is ventilation, but without perfusion that is actually called as a dead space. When the Va/Q is 0 it is actually called as a shunt because perfusion is present, but there is no ventilation.

What are the clinical approaches to the diagnosis of Va/Q mismatch? There are simple diagnostic methods which can either assess the severity of Va/Q mismatch or if there is any shunt present and it is very important to know that. First method is diagnosis of exclusion. So, whenever we have a patient with hypoxia there are lot of differential diagnosis that we can include like reduced inspired PO 2 due to high altitude or due to reduce alveolar ventilation or decreased diffusing capacity or Va/Q mismatch. In case if the altitude is appropriate, you can rule out this diagnosis, if the spirometry values are normal to that of ventilation you can rule out this diagnosis. The diffusion capacity is decreased, but that is actually very rare condition so you can rule out that.

So, you can come to a diagnosis of Va/Q mismatch by diagnosis of exclusion. Another way is alveolar atrial gradient of oxygen. This is very commonly routinely used in case of ICU where we will take the blood glass analysis of the patient and we will try to find out the arterial and alveolar oxygen concentration and find the difference between the both. For that first we are obtained the arterial blood glass analysis and we which and find out the PaO2 and the PaCO2 concentrations.

We assume that the mean PaCO2 is same as that of the measured PaCO2. So, to use the alveolar gas equation and we compute the mean of PaO2 from the mean PaCO2 and then we find to we compute the difference of PaO2 alveolar oxygen concentration to the arterial oxygen concentration. We get the difference and we can find the Va/Q mismatch. Once we have diagnosed to have a Va/Q mismatch it is important to distinguish whether it is a shunt or which can be surgically corrected or it is due to other conditions and that can be done by effect of breathing of 100 percent oxygen. So, when there is a substantial shunt that is present whatever oxygen, you give with 100 percent oxygen still they will have a low arterial PaO2 values. Because breathing 100 percent oxygen, oxygen will increase the mean alveolar PaO2 without increasing this is very important without increasing the arterial PaO2 concentration.

Therefore, there will be a substantial difference in the arterial oxygen difference that is the arterial alveolar oxygen gradient of PaO2. So, this is another way of distinguishing between a shunt which can be surgically corrected or other conditions due to Va which is resulting in Va/Q mismatch. This is a summary slide showing the perfusion in the first where there is a difference in the perfusion in different zones of the lungs. You can see the zone 3 with the maximum perfusion this is a graph showing the ventilation perfusion Va/Q and this is a picture that shows the mismatch of Va/Q normal which is close to 1. When there is no perfusion, it is infinity when it is not ventilated the Va/Q is 0.

These are my references and you can further read on these books if you have any questions. And this is the topic on ventilation perfusion ratio. Thank you for your patient listening. If you have any questions, please put forward in the discussion group, I will be happy to answer and wish you all a happy learning experience. Thank you.