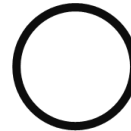# RESPIRATORY SYSTEM
Physiology

◉ Sheet ◯ Slide

Number: - 7

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Doctor: -

When we talked about obstructive lung diseases, we said that there are some tests done to diagnose these diseases, these tests are:

1- The most important test is the ratio between FEV1 and FVC, if it was less than 80% then the patient has an obstructive lung disease.
2- The middle FVC (between 25% and 75%), and we said that this test is sensitive.
3- The maximum expiratory flow rate.
4- There is another sensitive test which is not frequently done, used to diagnose early obstruction in the airways, before the symptoms appear, it is called **CLOSING VOLUME or Nitrogen washout technique.**

NOTE: its important to diagnose lung diseases in early stages as chronic bronchitis and emphysematous changes are irreversible.

Read the following figure to understand the mechanism of the test:

In the apex the intrapleural pressure is equal to -8 mmHg, so the alveoli are already inflated and according to what we learned about the compliance the ventilation here will be low as we can't inflate already inflated lung*

In the base the intrapleural pressure is equal to -2 mmHg, so the alveoli are partially inflated and according to what we learned about the compliance the alveoli here are in high compliance state (phase 2), so they can be inflated easier and the ventilation here will be higher
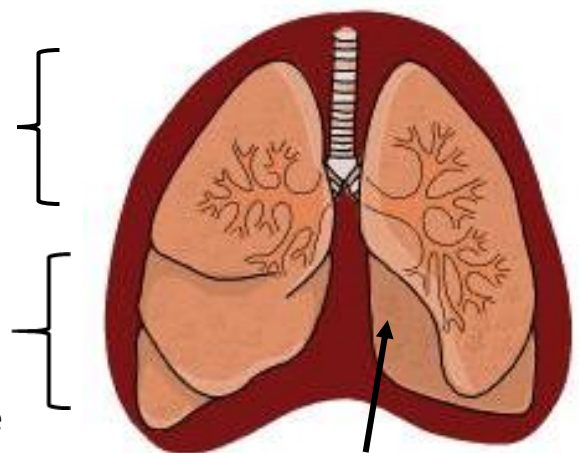
The heart is sitting here, and the lung extend 15cm above it and 8cm below it, so we end up that the total height of the lung is 30cm nearly.

So, the end result that the ventilation in the base is higher than the ventilation in the apex and most of the inspired air goes to the base.

Now we are going to discuss how to detect early obstruction using the third test:

*Refer to sheet 5, page 7 to know more about the compliance and the inflation relationship

In the single-breath nitrogen washout technique, the person makes a full exhalation (all the way to RV). The air present in the lungs at this point will be mostly in the upper part and the nitrogen concentration will be higher. The lower part of the lungs will be closed and contain little nitrogen. The patient then inhales 100% oxygen (PO2= 760 mmHg) to TLC. Now the lungs are maximally filled with gas. This breath will fill the entire dead space with pure O2. Some oxygen also mixes with the alveolar air but does not completely replace this air.

Note:

- Remember that we took previously that the last part of the inhaled air remains in the anatomical dead space, so it will be filled with pure O2.
- The upper alveoli will be filled first but they will be closed soon as they are already inflated so the nitrogen in them won't be diluted too much and its concentration will remain high.
- The base alveoli will be filled more as they get higher ventilation, so the nitrogen in them will be diluted by the high concentration of inhaled pure O2, and its concentration will be lower than it in the apex.

Then the person expires through a rapidly recording nitrogen meter, which makes the record shown in the figure.
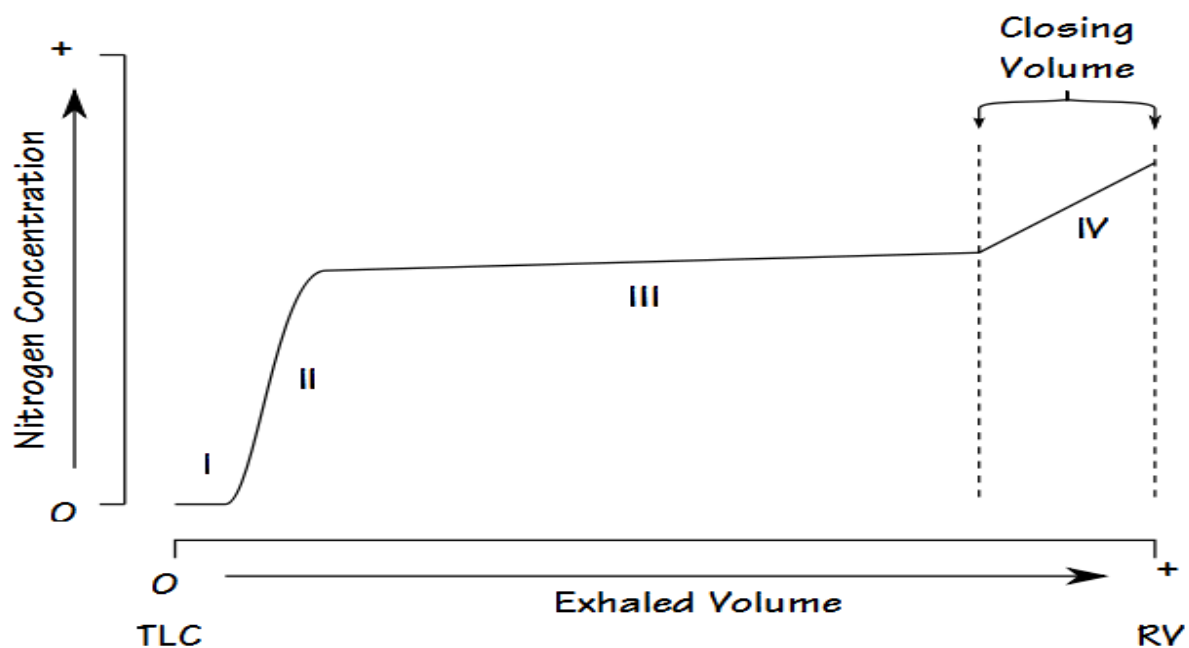
The trace is divided into four portions:

In **phase I** the expired air comes from the dead space regions of the respiratory passageways, where the air has been completely replaced by O2. Therefore, in the early part of the record, only O2 appears, and the nitrogen concentration is zero, but then it rises **slowly** that is because there is a transitional zone in the airways where minimal gas exchange occurs.

Phase II is when **alveolar air** begins to reach the nitrogen meter, the nitrogen concentration rises rapidly, because alveolar air containing large amounts of nitrogen begins to mix with the dead space air, so the recording will consist of mixture of airway and alveolar gas (from both apex and base alveoli).

Phase III is when all the dead space air has been washed from the passage and only alveolar air remains. Therefore, the recorded nitrogen concentration reaches a plateau level equal to its concentration in the alveoli (mixture of apex and base alveoli).

Phase IV is a terminal increase in the nitrogen concentration as expiration continues to residual volume, the expired nitrogen concentration rises abruptly because more and more of the expired gas is coming from the alveoli in the upper parts of the lungs. These upper alveoli have the highest nitrogen concentration. **Phase IV represents this airway closure**. The curve shows the sharp rise in nitrogen concentration when airway closures begin. The part following CV on the curve represents RV.

The junction of phase III and phase IV denotes the onset of the CV, at this point the base alveoli is closed and the exhaled air come from the apex only.

With aging the closing capacity* will increase in which it equals FRC in a 45-year-old in the supine position** and exceeds FRC in a 60-year-old in the erect position.

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*closing capacity (CC)= RV + CV

**supine positioning will decrease functional residual capacity (FRC) but has no effect on closing capacity.

A mnemonic for factors increasing closing capacity is ACLS-S: Age, Chronic bronchitis, LV failure, Smoking, Surgery.

what is the main role of the lung?

To maintain normal ABG; PO2=100 mmHg, PCO2= 40 mmHg & PH= 7.4

So, the lung also participates in acid base balance.

The lung has respiratory functions (normal ABG) and non-respiratory functions, such as: to control blood pressure by converting angiotensin I to angiotensin II and the increase the venous return, but How?

If there is a deep chest wall injury and the intrapleural pressure get exposed to the atmospheric pressure the lung will collapse to its resting volume which is equal to its minimal volume, here the patient might die not because of hypoxia but due to the decreased venous return, you may ask yourself what is the relation?

During inspiration the pressure in your chest will become more negative, so the pressure gradient (the driving force) between the right atrium and the veins will increase thus the venous return will increase, so in each inspiration you actually return the blood to your heart.

In case of pneumothorax when the pressure become positive the driving force will decrease and there will be no VR & no CO.

The immediate cause of death in pneumothorax is the decrease in VR and the subsequent decrease in the CO and not hypoxia.

If you measure the ABG and found that the arterial PO2 is 95 mmHg, then its normal although we said previously that it equals 100 mmHg, the important thing is that the different shouldn't exceed 5 mmHg.

The PO2 pressure in the apex alveoli is 130 mmHg while its 90 mmHg for the basal alveoli, so we say that the alveolar PO2 is 100 by mixing 1 part from the apex with 3 parts from the base (as the ventilation in the base is more and also perfusion from the base is higher), so the PO2 alveolar= (130+90+90+90)/ 4= 100 mmHg so we conclude that the high O2 from the apex was able to correct the low O2 form the base when mixture, but for the arterial PO2 it equals 95%, why? That is mainly because of venous admixture, and the sources of admixture are:

1- About 98 percent of the blood that enters the left atrium from the lungs has just passed through the alveolar capillaries and has become oxygenated up to a PO2 of about 104 mm Hg. Another 2

percent of the blood has passed from the aorta through the bronchial circulation, which supplies mainly the deep tissues of the lungs and is not exposed to lung air. This blood flow is called "shunt flow," meaning that blood is shunted past the gas exchange areas. Upon leaving the lungs, the PO_2 of the shunted blood is approximately that of normal systemic venous blood— about 40 mm Hg. When this blood combines in the pulmonary veins with the oxygenated blood from the alveolar capillaries, this so-called venous admixture of blood causes the PO_2 of the blood entering the left heart and pumped into the aorta to fall to about 95 mm Hg. (physiological shunt)

2- Additionally, there are some cardial veins empty directly in the left atrium. (cardial circulation)

3- BRONCHIAL, PLEURAL, and THEBESIAN veins which flow into the Pulmonary veins that then flow into the Left Atrium. (bronchial circulation)

So, in the arteries the hyperventilated blood is unable to correct the hypoventilated blood, unlike the CO_2 which is able to correct itself so the PCO_2 in the alveoli = PCO_2 in the arteries = 40 mmHg.

The main idea is to transport O2 from the **atmosphere** to the **arterial blood**, we discuss the inspiration, the airways and the problems related to them now we reach the ***respiratory membrane*** at which the O2 is passed from the alveoli to the pulmonary capillaries.

People who works in the field of phosphate mines are exposed to phosphate dust which increase the thickness of the respiratory membrane, do you think we should wait until these people suffer from dyspnea or we should discover any thickening on the respiratory membrane before the symptoms appear and to change their work from the field to the office for example? Its better discover any change in the membrane thickening as early as we can by doing periodic examination for how much respiratory membrane they have.

> The area of the respiratory membrane is ranging from 50 to 100 m2, and in case of membrane thickening or destruction there will be less available membrane.

Imagine that a marathon runner visits your clinic and tell you that to be able to run a certain distance he must have VO2max* = 5 L/min, and he ask you to know if his lung is able to give this amount per minute, then what you should do?

before knowing the answer let us learn some principles

why do we need to examine the respiratory membrane?

To detect any airway changes before the symptoms appear, because when the symptoms appear we will be very late, (as the lung reserve is high and we only use one third of the lung, so the symptoms will appear after the usage of the remaining two thirds and this is too late).

Do you remember ohms low :p?

It states that the flow equals the driving force divided by the resistance.

REMEMBER: resistance is a vague expression tells you how difficult this process is going to occur, and its inversely proportional to the permeability (k)

So, R= 1/k & flow= DF * k

So, we can end up that the permeability k= flow/ ΔP

Flow means how much oxygen diffuses form the lung to the blood per minute.

Permeability (k)= <u>the surface area of the membrane</u> * <u>solubility</u>

             The thickness of the membrane   Square root of the molecular weight

Permeability is directly proportional to the surface area and inversely proportional to the thickness These are intrinsic prosperities to the membrane and can't be measured	These are known as Diffusion Coefficient, and they are available information, note that the molecular weight is the least affecting factor as we take the square root (small number)

So, as we can't measure the thickness and the area directly, we use another way to measure the permeability using Ohms low; k= Flow/DF

*VO2max is the maximum oxygen consumption, and it equals 250 ml O2/ min in resting state, so the runner in the previous case need O2 six times more than the resting state (250*6=5000 ml = 5 L)

Thus, the factors that affect the permeability are:

(1) the thickness of the membrane

(2) the surface area of the membrane

(3) the diffusion coefficient of the gas in the substance of the membrane

(4) the partial pressure difference of the gas between the two sides of the membrane.

DIFFUSING CAPACITY OF THE RESPIRATORY MEMBRANE:

The ability of the respiratory membrane to exchange a gas between the alveoli and the pulmonary blood is expressed in quantitative terms by the respiratory membrane's diffusing capacity, which is defined as the volume of a gas that will diffuse through the membrane each minute for a partial pressure difference of 1 mm Hg. All the factors discussed earlier that affect diffusion through the respiratory membrane can affect this diffusing capacity.

The doctor asked a question which is why do we detect the lung diffusing capacity for O2? The answer is the early detection of any pathological airway changes before the symptoms appear because if symptoms appear it would be too late.

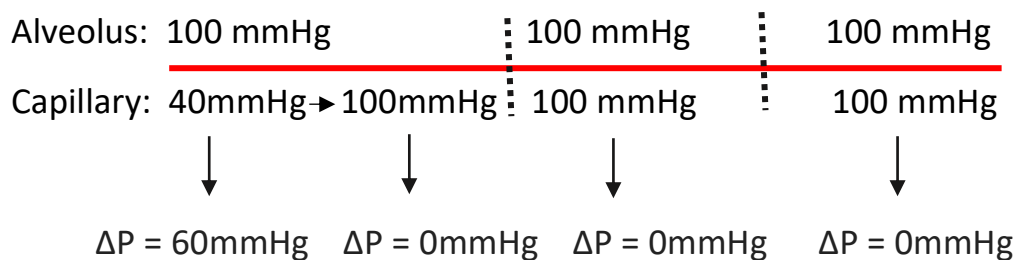**Now we are going to dig deeper in ohms low and the measurements of the diffusion capacity using it:**

Remember that: k= flow/ ΔP

1- The Flow can be measured easily by knowing how much O2 diffuses from the lung to the capillaries per minute (you ask the patient to breath in a closed page contains known amount of O2 for a certain period of time then measure the amount that he consumed and divide it over the time; example: if the page contains 1000 ml O2 initially, then after 5 minutes the remaining O2 is 200ml, so the flow will equal (1000-200)/5).

2- The question here is how to measure the driving force which is the partial pressure difference of the gas between the alveolus and the lung capillary?

Before we learn how to measure it, study the following notes:

- The pressure difference across the respiratory membrane is the difference between the partial pressure of the gas in the alveoli and the partial pressure of the gas in the pulmonary capillary blood.
- When the partial pressure of a gas in the alveoli is greater than the pressure of the gas in the blood, as is true for O2, net diffusion from the alveoli into the blood occurs; when the pressure of the gas in the blood is greater than the partial pressure in the alveoli, as is true for CO2, net diffusion from the blood into the alveoli occurs.

Remember that when we discuss O2 diffusion from the alveoli to the capillaries we divide the capillary into three parts and we said that the O2 diffusion occurs in the first third so the difference in the pressure will decrease gradually as the following:

Alveolus: 100 mmHg   ┊ 100 mmHg   ┊   100 mmHg

Capillary: 40mmHg → 100mmHg ┊ 100 mmHg   ┊   100 mmHg

ΔP = 60mmHg   ΔP = 0mmHg   ΔP = 0mmHg   ΔP = 0mmHg

It's absolutely wrong to find the average of ΔP along the capillary, so we can't use O2 as we don't know at which point the equilibrium occur thus it won't give us a comprehensive view over the entire length. To overcome this problem, we use another gas which is CO (carbon monoxide), but How to do so?

The whole picture is discussed in the following paragraph:

Measurement of Diffusing Capacity—The Carbon Mono Oxide Method.
The O2 diffusing capacity can be calculated from measurements of:

(1) alveolar PO2

(2) PO2 in the pulmonary capillary blood   **ΔP = (1) − (2)**

(3) the rate of O2 uptake by the blood (the **Flow**).

However, measuring the PO2 in the pulmonary capillary blood is so difficult and imprecise that it is not practical to measure oxygen diffusing capacity by such a direct procedure, except on an experimental basis.

To obviate the difficulties encountered in measuring oxygen diffusing capacity directly, physiologists usually measure carbon monoxide (CO) diffusing capacity instead and then calculate the O2 diffusing capacity from this.

The principle of the CO method is the following: A small amount of CO is breathed into the alveoli, and the partial pressure of the CO in the alveoli is measured from appropriate alveolar air samples. The CO pressure in the blood is essentially zero because hemoglobin combines with this gas so rapidly that its pressure never has time to build up (250 times more than oxygen), **this is the reason behind using CO**.

To make it easier; CO binds hemoglobin rapidly, so all the CO molecules that cross the respiratory membrane will bind hemoglobin so PCO in the capillary will equal zero and therefore, the pressure difference of CO across the respiratory membrane is equal to its partial pressure in the alveolar air sample (ΔP= PCO in the alveolus).

Then, by measuring the volume of CO absorbed in a short period (the flow) and dividing this by the alveolar CO partial pressure (ΔP which is equal to PCO in the alveolus, we determine accurately the CO diffusing capacity (DLCO= 17 ml/min/mmHg).

DLCO is the diffusing capacity of the lungs for the carbon monoxide.

The number denoted that 17 ml CO crosses the respiratory membrane for each 1 mmHg pressure difference per minute.

We standardize that diffusion coefficient for O2 is our reference point, so it equals 1, based on it the diffusion coefficient for CO= 0.8 and for CO2 = 20.

So, to convert CO diffusing capacity to O2 diffusing capacity, the value is multiplied by a factor of 1.23 because the diffusion coefficient for O2 is 1.23* times that for CO. Thus, the average diffusing capacity for CO in healthy young men at rest is 17 ml/min/mm Hg, and the diffusing capacity for O2 is 1.23 times this, or 21 ml/min/mm Hg.

*we calculate this number by dividing the diffusion coefficient of O2 by the diffusion coefficient of CO; 1/0.813 equals 1.23

The End

This sheet was written from record 7/ section 1

Sorry for any mistake and best of luck