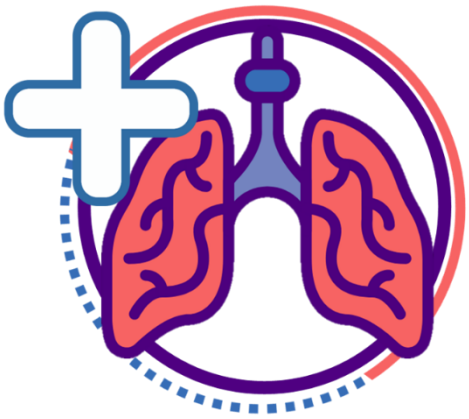

RESPIRATORY SYSTEM

Physiology

Sheet Slide

Number:	-3
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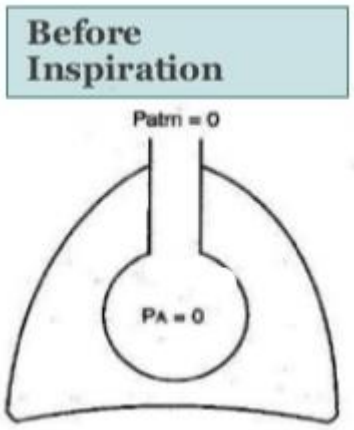
In the last lecture we talked about the ABGs, and we mentioned that we have too much lung than we need, so if a patient is presented with a respiratory symptoms, then he has a huge damage involving more than 2 thirds of his lungs.

The coming section discusses the lung mechanics, and answers the question:" How do we breathe?"

Air flows into and out of the lungs during the act of breathing, and this flow according to Ohm's Law: flow = pressure difference (driving force)/resistance. "pressure difference→ the difference between atmospheric and intra-alveolar pressure"

Before the inspiration, the pressure outside is atmospheric, and we take it as a reference having zero value (it is actually 760 mm Hg). Also the air inside the alveoli communicates and equilibrates with outside, so having a pressure of zero. See the figure here.



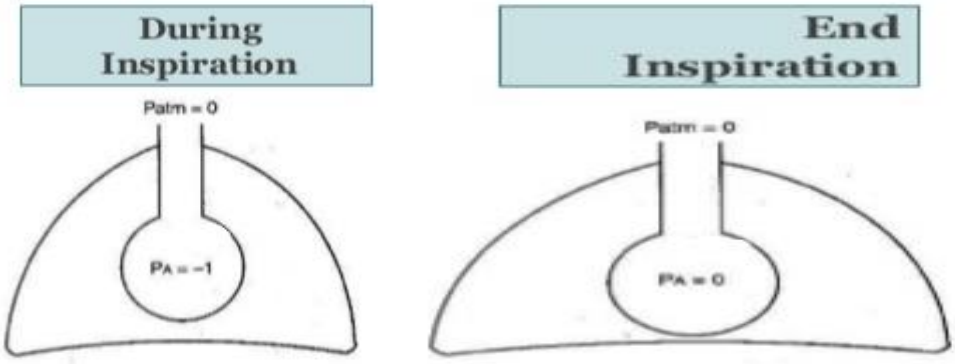
Under these conditions the pressure difference is zero ⇒there will be no flow.

According to Ohm's law, there must be a pressure difference to drive the air in and out the lungs. To drive it we have 2 options:

1-Making the atmospheric pressure > intra-alveolar pressure (+1>0): this type of breathing (positive pressure breathing) is not physiological, and is done only via an artificial external machine (ventilator or respirator). This machine has a tube which is inserted endotracheally to push (positive pressure) and pull (negative pressure) the air during the artificial inspiration and expiration respectively.

2-Making the intra-alveolar pressure < atmospheric pressure (-1<0): this type of breathing is physiological. To make the intra-alveolar pressure (which is normally= atmospheric pressure) negative. We apply the Boyle's law of gases that describes how the pressure of a gas tends to increase as the volume of the container decreases, and vice versa, so $V_1P_1=V_2P_2$. "pressure is inversely proportional to the volume"

So, we can manipulate the pressure easily by changing the volume of the alveoli. We said that we have a pressure of zero inside the alveoli, and by increasing their volume, the pressure decreases (becomes -1 or less < the atmospheric) driving the air into the alveoli. The air molecules keep accumulating until the pressure inside raises back to zero again at the end of inspiration (during the inspiration the intra-alveolar pressure < zero). Be careful, there are another factors playing around, and we will discuss them later in this sheet, just focus on the driving force.



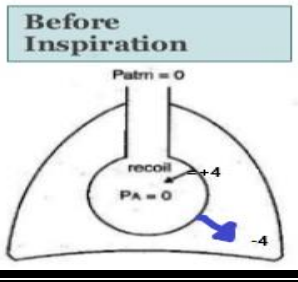
The question now is "How to change the volume of the lung (alveoli)?"

We know that pleural sac separates each lung from the thoracic wall and other surrounding structures. There is a pressure within the pleural sac called **intrapleural pressure** which is usually less than atmospheric pressure (having a pressure value of -4). This pressure acts to stretch (notice the direction-increasing volume-) the lungs, and works against another force that works in the opposite direction (to collapse the lung-decreasing volume-), the later force is called **Recoil force** and it results from the elastic properties of the lung tissue (we will discuss later the source of this force in details). So, lungs don't collapse because the intrapleural pressure overcomes the recoil force of the lungs.

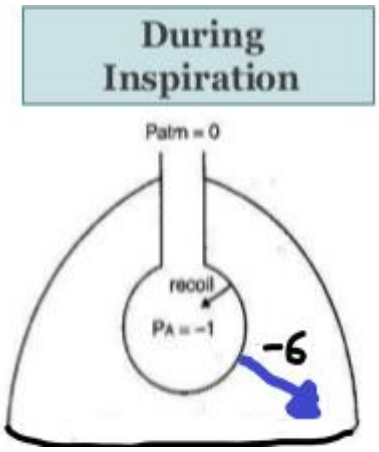
**The respiratory muscles (diaphragm mainly and the external intercostal muscles) work to increase the volume of the thoracic cavity.

The mechanism of respiration:

-Before inspiration, at the end of the preceding expiration, intra-alveolar pressure is equal to

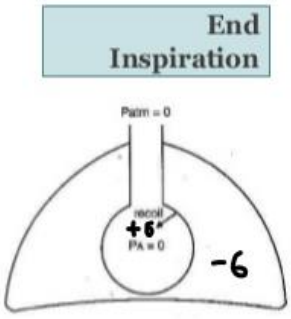


atmospheric pressure, and also the intrapleural pressure (-4) is equilibrated with the lung's recoiling force (+4), so no air is flowing into or out of the lungs.



- As the thoracic cavity enlarges during inspiration by the contraction of the diaphragm, the pleura is also forced to expand to fill the larger thoracic cavity so, decreasing the intrapleural pressure below -4 (let's say it will be -6). The intrapleural pressure will overcome the recoiling force of the alveoli resulting in their expansion (the volume increases and lungs inflate). According to Boyle's law, the pressure inside the alveoli decreases (becomes negative -1 or less) making a pressure deference which drives the air inside the lungs. (go back to the first page/second point).

**** So, the inflated lungs drive the air inside, and Not the air that inflates the lungs.**



- The air molecules keep accumulating until the pressure inside raises back to zero again (during the inspiration the intra-alveolar pressure < zero), and also the recoil force of the alveoli equilibrates again (becomes +6) with the intrapleural pressure at the end of inspiration "increasing in the recoil force during inspiration happens because it depends on the elastic properties of the lungs, and as lungs increase in volume during inspiration, as if you stretch a rubber band this leads to increase the tendency to recoil".

- let's recap the story quickly:

Intra-alveolar pressure=atmospheric pressure (no flow)⇒contraction of the diaphragm ⇒thoracic cavity volume↑⇒ intrapleural pressure↓⇒lungs inflate(the alveolar volume↑)⇒intra-alveolar pressure ↓⇒the air enters.

The expiration occurs by the relaxation of the diaphragm ⇒thoracic cavity volume↓⇒ intrapleural pressure↑⇒lungs deflate (the alveolar volume↓)⇒intra-alveolar pressure↑ ⇒the air exits.

Some important notes regarding the lung mechanics:

- Normally, air does not enter the pleural cavity because there is no communication between the cavity and the atmosphere. However, if the chest wall is punctured (for example, by a stab wound), air flows down its pressure gradient from the higher atmospheric pressure and accumulates into the cavity (until the intrapleural pressure becomes zero or positive!). The abnormal condition of air in the pleural cavity is known as **pneumothorax.** The intrapleural pressure –as we said- opposes the recoil force of the lung which works to collapse the alveoli, so once we lose the stretching force(intrapleural) the lung collapses by the action of the recoil force.

-The inspiration is an active process, as the inspiratory muscles (mainly diaphragm. Others include external intercostal muscles) utilize ATP during their contraction. On the other hand, the expiration is a passive process, as it just requires relaxation of the diaphragm. The inspiratory muscles utilize only less than 5% of the total ATP consumption in our biological system leaving 95% for the rest of the body. However, if the expiration becomes active by the action of expiratory muscles, the body must pay for this, and sometimes it may utilize 20%, 30% or 40% of the total ATP consumption ending up with a fatigue (lake of ATP).

-**lung tissue is elastic, meaning that is has 2 characteristics: compliance(is a measure of the lung's ability to stretch) and recoil tendency(rebound of the lungs after having been stretched)** Compliance will be discussed later during this course in more details. I asked the doctor about this point and he said that" every elastic tissue must be compliant, but not every compliant tissue is elastic, but compliance and elasticity are completely different.

Recoil tendency is an intrinsic property due to the elasticity of the lung, for this reason, if you stretch the lung and remove the force, it will come back to its resting state(during the resting state the lung is neither collapsed nor stretched).

So, to change any elastic structure from its resting state, you need to pay for that (since the inspiration is active), but bringing it back is passive.

During the resting state, the lung are not empty (neither collapsed nor stretched), we can find 2.2 L of air (as the lungs are balanced during resting state by 2 forces (Intrapleural pressure & recoil force) giving them the volume of 2.2 L.

By this we have finished the pressure difference part of the flow law, and it is the time to discuss the second part(factor) of the law, which is the resistance.

The resistance of the Airway

-The resistance is very difficult to measure in the human body, but how can we do?

Indirectly, by knowing how much ΔP is needed. If the airway resistance is high, ΔP would be high too (to overcome it). We said that the pressure difference is just 1 mm Hg. It is minimal, and this indicates that the resistance must be very low (1 unite).

-In the CVS, total peripheral resistance is the sum of the resistance in arteries 15%, arterioles 45%, capillaries 20%, and (venules and veins) 20%. They are called resistances connected in series. Resistance is not calculated by adding the resistance of each part of the circulation. Just like in the respiratory system, resistance in the cardiovascular system is calculated by knowing how much ΔP is needed (in the cardiovascular system it is 100 mm Hg). "these percentages are calculated by knowing the pressure drop between each segment and the next one, e.g. between arteries and arterioles".

Vascular resistance is 100 times more than the airway resistance. Most of this resistance resides within the arterioles (not the capillaries), as the cross-sectional area of all capillaries (not a single capillary) is much more than the cross-sectional area of the arterioles and that's why arterioles are the major resistance vessels.

-So, Airway resistance is very small (only one unite) and negligible because we need very small driving force to overcome it. And this resistance is distributed along the airways (which extend from the trachea 0 to the 23rd generation of the airways till reaching the alveoli:

a. 40% of resistance is above the larynx. (nose, mouth, and pharynx).
b. 40% resistance is in the first 7th generations of the respiratory tree.
c. 20% resistance is in the following 7th generations (8-14) of the respiratory tree (but from the 15th generation and beyond there(23rd) is almost zero resistance, due to the huge cross sectional area of these generations).
- Therefore, under physiological conditions most of the airway resistance resides in the large airways.

1st take home message: "Airway resistance is very small and negligible because we need very small driving force to overcome it".

2nd take home message: Physiologically, Because of the huge cross sectional area of the 15th generation and beyond, the airway resistance in them is almost zero, and most of the resistance resides in the largest airways.

- If we face more airway resistance, the negative pressure inside the alveoli must become more negative to drive air in (increase pressure gradient).
This increase in the resistance comes from small airways because the large airways are supported by cartilage which prevents them from collapsing. The cartilage is present in the first 10th generations in the respiratory tree. The bronchioles after the 10th generation are not covered with cartilage.
Small bronchioles (generation 10th- 23rd) are not supported by cartilage "collapsible". And they have smooth muscles surrounding them. Contraction of the smooth muscles causes bronchoconstriction, which closes them.

Bronchioles (which have a very small diameter- 1 mm-x) are lined with goblet cells so, any mucus plugs can close them. Mucus Plug can't obstruct the entire lumen of the trachea.

3rd take home message: In pathological condition airway resistance increases, and this increase comes from the small

airways because the large airways are supported by cartilage which makes them non collapsible.

-Conductance is the measure of how easily a material flows along a certain path, and conductance is considered the opposite of resistance. In terms of resistance and conductance, the reciprocal relationship between the two can be expressed through the following equation: R = 1/G, G=1/R; where R equals resistance and G equals conduction.

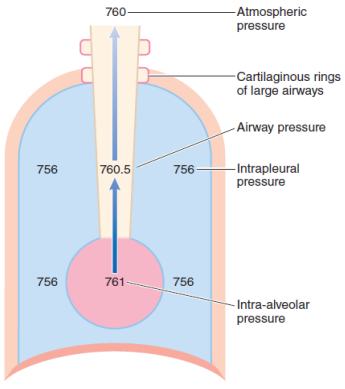
-We said that pulmonary diseases can be classified into 3 entities:
1- Obstructive diseases: difficulty in expiration; 70% of respiratory diseases.
2- Restrictive diseases: difficulty in inspiration; accounting for 20-25%.
3- Vascular; problem in oxygen diffusion across the respiratory membrane: 5-10% of respiratory diseases.

-In the obstructive diseases, the resistance of the small airways increases, and this results in difficulty in expiration (not inspiration).Why?!

- normally the the alveoli are in resting state (neither collapsed nor stretched)

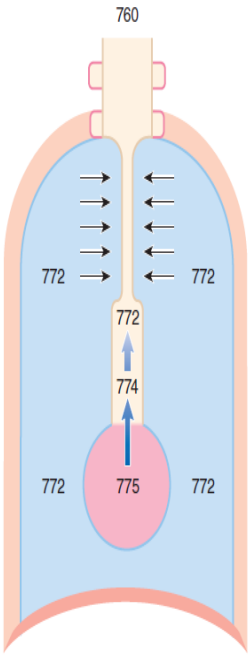
-We said previously in this sheet that: during inspiration, intrapleural pressure becomes more negative thus causes the opening of the bronchioles making the alveolar pressure (-1) which enables the inward movement of air.

-While During expiration, intrapleural pressure becomes less negative thus causing a little collapse of the bronchioles making the alveolar pressure (+1) which enables the outward movement of air.(see the figure and notice that the pressure difference is only =1)



During expiration, the intrapleural pressure increases to become less negative, so it's overcame by the recoil force of the alveoli. By that, the lung collapses till the forces are balanced again. During the whole process of normal inspiration and expiration, the intrapleural pressure ranges between negative values

(stretching forces). But if it becomes positive -due to some reasons- it will act as a collapsing force (aiding the lung recoil force to collapse the alveoli). Now let's apply this clinically:



(d) In obstructive lung disease

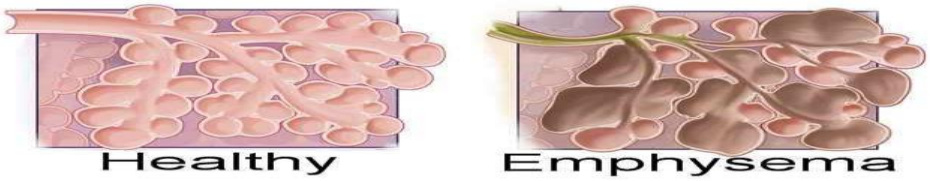
- If bronchioles are partially obstructed(resistance↑), more effort is needed for expiration by increasing the intrapleural pressure to less negative values (less negative than -4) to maintain the pressure difference (effort is done by the expiratory muscles to increase the pressure inside the alveoli for expiration). The patient will produce wheezing sounds due to turbulence in the obstructed bronchioles. (notice the figure here, notice that the pressure difference is increased very much, and the black arrows showing the active expiration)
-If the resistance increases 10X, pressure difference must also increase 10X to maintain constant flow. So, intrapleural pressure now becomes positive (in order to increase the intra-alveolar pressure) which compresses on the lung "the increment in intrapleural pressure was to increase the alveolar pressure and aids in expiration of air through constricted bronchioles; but at the same time increasing intrapleural pressure causes more pressure on the bronchioles, thus patient starts wheezing during expiration and not during inspiration". Positive intrapleural pressure in expiration is a closing pressure the partially closed airways will be fully closed in expiration.
-Since resistance increases in obstructive diseases, expiration becomes an active process (see the beginning of the sheet). So sleeping is affected, because the patient needs to be awake while breathing.
-The patients may also need to narrow their lips while exhaling; because closing the lips elevates the pressure backward which aids in expiration of the too much accumulated air inside the chest (Barrel chest).

4th take home message: Patients with partially obstructed lungs face more difficulty during expiration.

We will discuss 2 COPD diseases (asthma sometimes may be chronic, but in 90% of patients it is reversible especially in children, so we won't discuss it here):

1- **Emphysema:**

- Emphysema is also irreversible
- Most commonly, emphysema results from excessive release of protein-digesting enzymes such as trypsin from alveolar macrophages as a defence mechanism in response to chronic exposure to inhaled **cigarette smoke** or other irritants. The lungs are normally protected from damage by these enzymes by antitrypsin, a protein that inhibits trypsin.
- This leads to the digestion of the elastic fibres (by the action of proteases-they are no longer under the control of the antiproteases), which results in collapse (loss of the cartilaginous support). Elastic fibres in the bronchioles keep the airways open. In emphysema, elastic fibres are destroyed so the airways close(collapse). This is an example of obstruction from the outside.
- Walls of alveoli are also destructed so surface area for diffusion will decrease.



- Destruction of alveoli is followed by the destruction of the pulmonary capillaries, which will result in a decrease of capillary beds.

    - The pressure in the pulmonary artery ranges from 8-25 mmHg. The mean pulmonary arterial pressure is 15 mmHg. This is considered to be the after-load to the right ventricle. When 50% of the capillary veins are destroyed, the area is decreased so the resistance will increase. There will be increased pulmonary vascular resistance due to smoking. This is referred to as pulmonary hypertension.

-Pulmonary hypertension will result in dilatation of the right ventricle and eventually right heart failure due to increased load on the right ventricle. Therefore, emphysema is associated with right heart failure, this is called **Cor Pulmonale** (is right ventricular dilatation +/- right ventricular failure due to lung disease).

- In chronic bronchitis , due to smoking, the goblet cells are stimulated to produce more mucus and the movement of the cilia is impaired so mucus stays in the lung causing chronic infections(Notice that the obstruction here is from inside.)

- COPD has 3 forms: chronic bronchitis, emphysema and asthma. These forms are related; for example, most chronic bronchitis patients have a degree of emphysema, and most patients with emphysema have some sort of chronic bronchitis. Pure cases of these two forms comprise less than 1% of COPD cases. And some patients may have the 3 forms at the same time.

-Pulmonary function test is used to diagnose patients with different pulmonary diseases (vascular diseases are not diagnosed with it). It can also predict the prognosis and progression of the disease with time. This test is based on the lung volumes and capacities.

Lung volumes and capacities

First, you should differentiate between these terms:

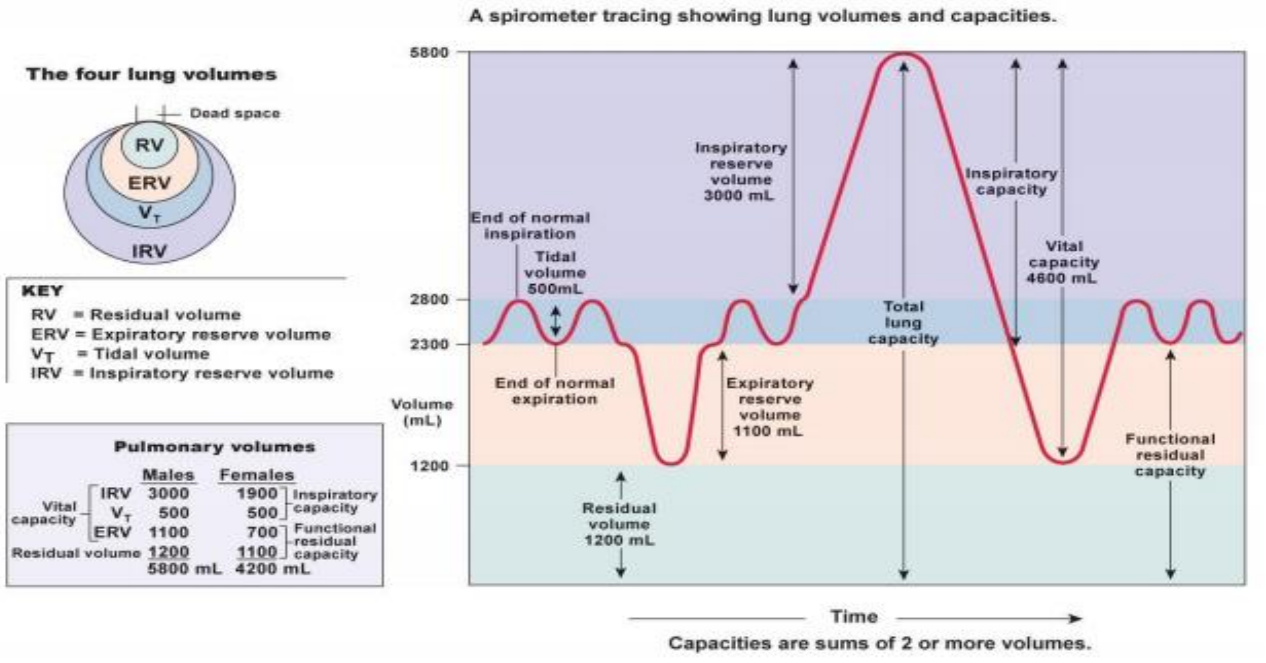
- Passive expiration: that happens from the relaxation of the diaphragm muscle (that contracts during inspiration) and due to the elastic recoil of the lungs. [no energy is needed]
- Active expiration: by the aid of Internal Intercostal Muscles and Abdominal Muscles. [with the use of energy]
- Inspiratory muscles: Diaphragm, external intercostal muscles and accessory muscles (sternocleidomastoid, trapezius & scalene).

- Expiratory muscles: Internal intercostal [push the lung to inside] and abdominal muscles [raise the diaphragm up and decrease vertical diameter of lungs].

Let's suppose that a person had a resting volume of 2.2 L in his lungs after a passive expiration → he made a normal inspiration and got additional volume of 0.5 L to have a total volume of 2.7 L → he still have a capacity to inhale additional 3 L (they are needed while exercising) → a passive expiration process then took place and returned his lung's volume back to 2.2 L → an active expiration (forced expiration) could happen and reduce the volume into 1.1 L.

Now we will define each volume we've mentioned above:

1) Tidal Volume (T.V): is the volume we got after the normal inspiration. It is also the volume that we will exhale with passive



expiration so collectively; it is the normal volume of air displaced between normal inhalation and exhalation when extra effort is not applied. It's 0.5 L in our example.

2) Inspiration reserve volume (I.R.V): is the extra volume we can inhale above the tidal volume to get fully occupied lungs. That is the 3 L in the example. " muscles of inhalation are: mainly the diaphragm, to lesser extent external intercostal, and neck muscles are accessory"

- It is called reserve because we don't use it normally while we are resting.

3) Expiration reserve volume (E.R.V): is the volume that we exhale with a forced expiration (after exhaling the tidal). It is 1.1 L regarding our example. "expiratory muscles are abdominal muscles and internal intercostal, normally we don't use them"
4) Residual volume (R.V): is the minimum volume we can have in our lungs that couldn't be exchanged. The remaining 1.1 L.
   - With aging E.R.V decreases & R.V increases. [There is trapping in the lungs].

Lung capacities:

Lung capacity is the sum of two or more lung volumes.

1- Functional residual capacity (F.R.C): is the volume in the lungs before we inhale the tidal volume. F.R.C = E.R.V + R.V. so it is the volume after passive expiration.
2- Inspiratory capacity (I.C): the maximum air volume we can inhale after a passive expiration. I.C = T.V + I.R.V
3- Vital capacity (V.C): the total air we can inhale after an active exhalation. V.C = E.R.V + T.V + I.R.V
   In other words, the volume of air which one can exhale forcefully following forced inspiration.
4- Total lung capacity (T.L.C): is the sum of all volumes and this represents the maximum volume of air both lungs can take. T.C E. = R.V + I.R.V + T.V + R.V

- Study the figure above and notice how the four volumes don't overlap.
- Lung volumes are easily measured by a spirometer. Except the residual Volume and everything associated with it (FRC and TLC), which needs another method because it resides inside the lungs and spirometer measures only what enters and exits the lungs.

Pulmonary diseases are:

1) Obtrusive (the most common)
2) Restrictive
3) Vascular (the least common)

To determine what type of pulmonary diseases the patient has, we should do pulmonary tests by using spirometer and Helium dilution method.

In order to measure RV, we use the Helium dilution method as follows:

1- Before inhaling, the volume of the lung is equal to the (FRC which we are looking for). The person is asked to breath from a closed bag with a known volume. This bag contains a known concentration of Helium gas. The amount of Helium present equals (the volume of the bag x He concentration). Notice that we use the Helium as is not absorbable; it cannot penetrate the respiratory membrane. Thus, the amount of Helium is constant throughout the process.

2- After certain numbers of breaths, Helium is said to be distributed equally in the bag and in the respiratory system(equilibrium). The total amount of Helium is not changed (measurement is made after a normal tidal volume is expired):

$V_1C_1 = V_2C_2$ (conservation of mass)

Where V_1 is the volume of the bag; C_1 is the initial concentration of He in the bag; ($V_2 = V_1 + FRC$); and C_2 is the final concentration of He.

3- We calculate FRC and RV:

$V_1C_1 = V_2C_2$

$V_1C_1 = C_2 (V_1 + FRC)$

$FRC = V_1 (C_1 - C_2)/ C_2$

RV = FRC (calculated) –ERV