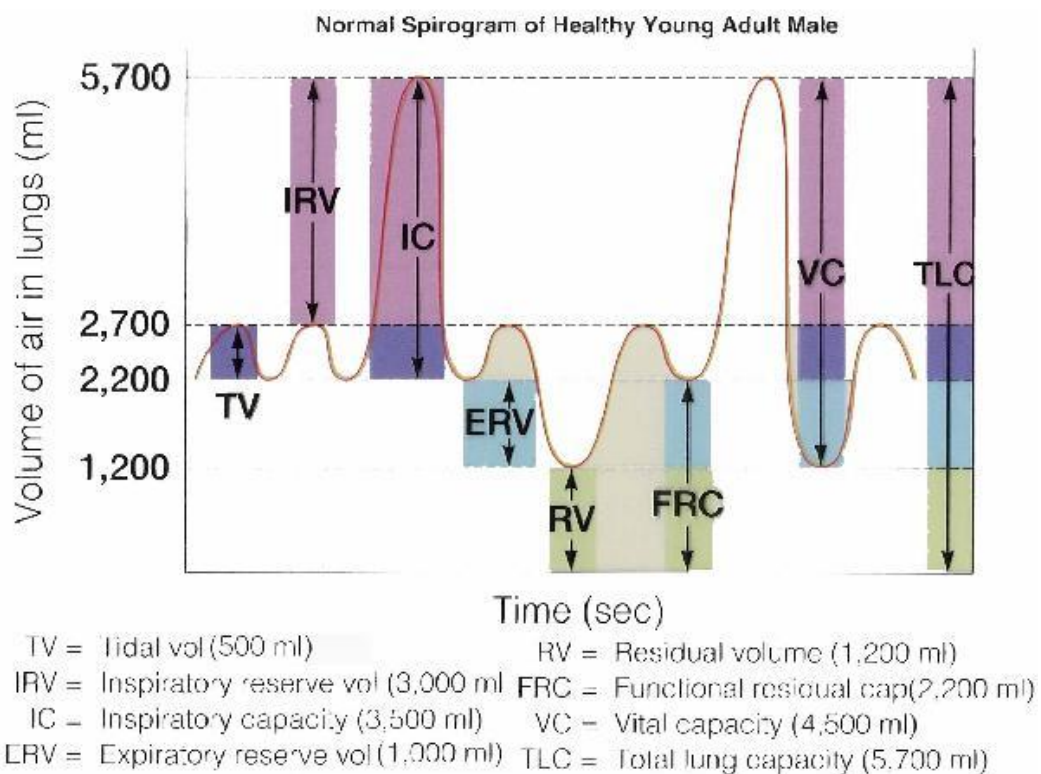


Physiology - lecture 3



- **Residual Volume (RV):** the amount of gas remaining in the lung at the end of a maximal exhalation
- **Tidal Volume (TV):** the volume of gas inhaled and exhaled during one respiratory cycle.
- **Inspiratory reserve volume (IRV):** the maximal amount of additional air that can be drawn into the lungs by determined effort after normal inspiration
- **Expiratory reserve volume (ERV):** the additional amount of air that can be expired from the lungs by determined effort after normal expiration
- **Vital capacity (VC):** the greatest volume of air that can be expelled from the lungs after taking the deepest possible breath.
- **Functional Residual Capacity (FRC):** is the volume of air present in the lungs at the end of passive expiration
- **The total lung capacity (TLC):** is the maximum amount of air that can fill the lungs
($TLC = TV + IRV + ERV + RV$)

Pulmonary function test:

- Firstly pulmonary function tests are used to help diagnose what type of disease a patient has, whether its obstructive or restrictive disease. However they are NOT diagnostic themselves
- It tells us what phase of a disease we are dealing with (ex. Mild, moderate or severe COPD)
- Helps following the progress of disease. To check whether the patient is responding to the treatment or not. (The test is done after giving the treatment)
- Monitor certain people with hazardous jobs to check if their respiratory system is affected.

The tool used in the test is a spirometer (to measure volume of air inhaled or exhaled)

The spirometer only measures the amount of air coming in and out of a person's mouth and cannot measure the volume that stays in the lung, hence the residual volume is not measured using a spirometer (since it remains in the lung)so you must use another indirect method for measurement of RV.

InCOPD, emphysema:

- RV is increased
- Functional residual capacity (FRC is increased)
- Total lung capacity is increased

In restrictive pulmonary disease all these values are decreased.

One way to measure RV is to measure FRC and we know that ERV can be measured by a spirometer.

$$\mathbf{FRC - ERV = RV}$$

How is FRC measured?

FRC cannot be measured directly; you cannot measure any volume or capacity directly if it includes residual volume (RV). This includes TLC and FRC.

We allow the person to breathe from a closed bag and we know the volume of air in the bag. Assume it is 10L, containing non-absorbable gas (helium). This gas enters the respiratory system and leaves without crossing the respiratory membrane and the total amount of helium remains the same.

Amount of helium = volume * concentration

We allow the person to breathe several times so that the air in lung mixes with the air in the bag until it reaches an equilibrium point where the concentration of helium outside and inside are the same. Then we calculate FRC using:

$V_2 = \text{Total gas volume (FRC + } V_1\text{)}$.

$V_1 = \text{Volume of gas in the bag}$.

$C_1 = \text{Initial (known) Helium Concentration}$.

$C_2 = \text{Final Helium concentration (after mixing)}$.

$C_1 \times V_1 = C_2 \times V_2$

$C_1 \times V_1 = C_2 \times (V_1 + \text{FRC})$

$\text{FRC} = ((C_1 \times V_1) / C_2) - V_1$

This is called **helium dilution method**

There is Conservation of mass since total helium remained the same.

Note: there are other pulmonary function tests that will be discussed later specific for each disease. The one we took is a general test.

In the graph on the first page $VC = 5.7 - 1.2 = 4.5L$, assume VC is 4L this doesn't mean that you are 80% of the normal. Before doing the test we take the name, age, height, gender, weight of the patient and according to the data there is a normal corresponding norm.

-If the normal Vital capacity for example is 4 liters according to his norm (called predicted value) and the observed value is 4 liter (after doing the experiment) then the ratio is 100%

-Females, children and thin individuals usually have lower VC

How do we normally breathe?

-Airflow is governed by ohm's law (flow is directly proportional to the driving force and inversely proportional to the airway resistance)

Flow= Δp /airway resistance

-The flow in respiratory system is approximately 5 liters
{Flow= 0.5(TV) *12(breaths per min) = 6 liters}

-The atmospheric pressure is 760 and we only need 1mm Δp to create flow. Hence a pressure of -1(inside the lung) is enough to drive air in. airway resistance is just 1% of vascular resistance since if you face too much resistance Δp must be higher to accomplish the same flow.

-To sum up airway resistance in the 23 divisions of respiratory system is almost negligible since the change in pressure needed to accomplish flow is very small.

- Two methods (which work in 2 different mechanisms) are used to drive air in:

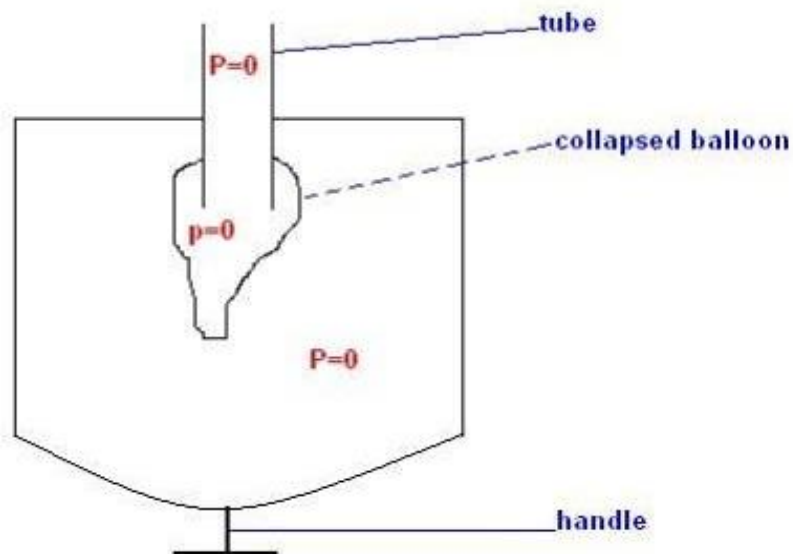
- 1- **First Method:** Making the pressure outside higher than that inside the lung (+1). This is called positive pressure breathing, which is an artificial type of breathing using a ventilator (an endotracheal tube attached to a machine) the pressure in the machine can be altered from positive (air moves in) to negative (air moves out) values. (Used in RDS)
- 2- **Second Method:** normally used, making the pressure in the alveoli less than that of atmospheric pressure (-1)
In order to reduce the intra-alveolar pressure from 0 \rightarrow -1 you must change the volume according to poiseuille's law.

-How can you change the volume?

The lung is surrounded by 2 membranes with a potential space in-between them (pleural cavity). The pressure in the

pleural cavity is -4; if this pressure becomes -6 then the lung is forced to expand.

This is illustrated in the experiment



-Pulling the handle downwards increase the volume surrounding the balloon, therefore the pressure inside the box becomes -1. This forces the balloon to inflate causing a reduction in the pressure inside the balloon, which in turn forces air to enter. When enough molecules (nitrogen and oxygen) have entered the force increases bringing the pressure back to zero, hence no more airflow.

Since: $\text{pressure} = \frac{\text{force}}{\text{Area}}$,

And force is caused by the action of the molecules (the more the molecules the greater the force)

-So at the end of inspiration intra-alveolar pressure goes back to zero.

-During inspiration the pressure inside the box is less than zero (sub-atmospheric). Once the alveolar pressure becomes zero, there is no more inspiration, because there is no driving force.

-The inflated lung drives air in; it is not the air, which inflates the lung.

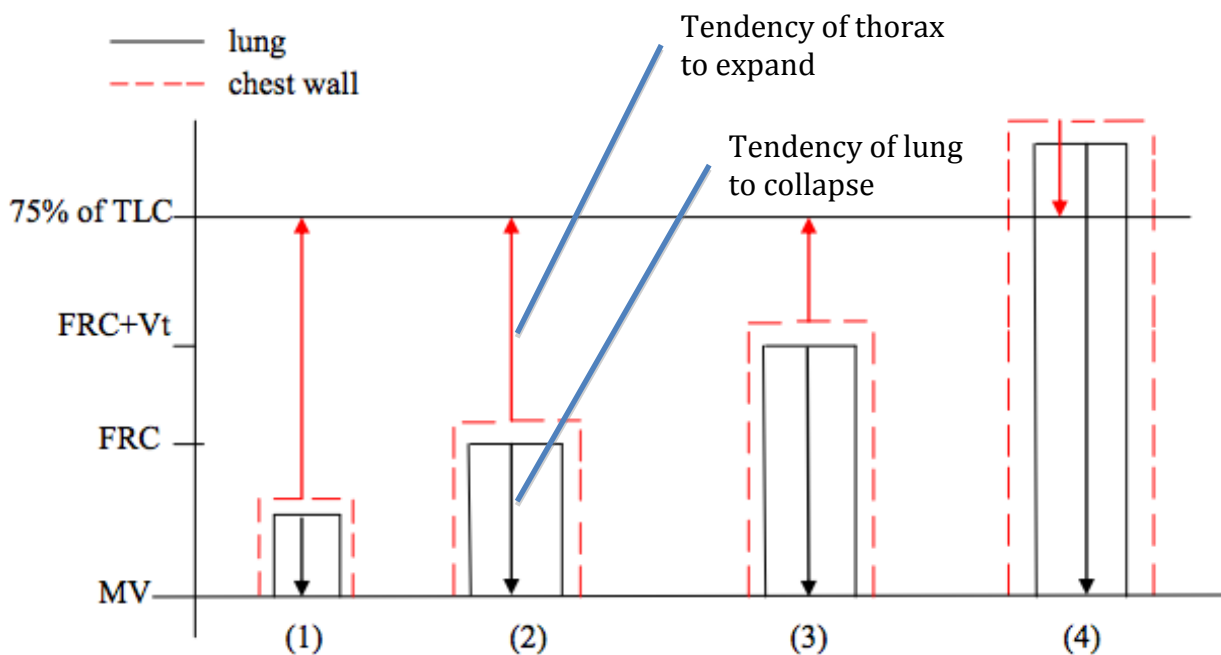
-This is the normal breathing pattern that is usually observed.

-The lung is like a balloon and a balloon is an elastic structure, if allowed it will deflate to zero volume.

-So what makes the lung inflated with 2.2 liters (which is the FRC)?

The negative pressure surrounding the lung. If the negative pressure surrounding the lung is removed, it will collapse to a minimal volume (150ml) the resting volume of the lung, hence the lung does not tend to collapse after the resting point.

The respiratory system includes 2 balloons, the thorax (outer balloon) and the lung (inner balloon). So when we inflate one balloon we inflate the second, this is harder than inflating only one balloon, thus we have to consider the thorax, lung and the thorax-lung system as one whole unit.



*Check the graph for the following points.

At FRC(2.2 liters) the lung has tendency to collapse, if you increase the volume of the lung to TLC the tendency to collapse increases and if you deflate the lung to RV the lung is still tending to collapse since its trying to reach its resting state. (RV is 1200ml while resting volume is 150ml)

What about the thorax, what is its resting volume?

If we open the chest, the thorax immediately expands trying to go back to its resting volume. The resting volume is equal to 75% of TLC (while FRC is 40% of TLC), which is around 4.5 L

Summary:How do we normally breathe in? We have the inspiratory muscles (diaphragm, external intercostal muscles) when they contract they increase the size of thorax → decrease the pressure in thorax → causes lung to inflate → reducing the pressure inside the lung thus creating a pressure gradient → air moves into lungs.(As in the example above)

Expiration is accomplished by relaxation of muscles, IPP of -6 becomes -4 during expiration this compresses the lung to its original volume increasing the pressure to +1

Inspiration is active; expiration is passive {free}

Any elastic structure to deform it you need a force but to bring it back to its resting state is free due to recoil tendency.

Inflating the balloon is active, deflating is passive

Column 2: At FRC (2.2 L)

- Lung is tending to collapse.
- Thorax is tending to expand
- These two forces are equal and opposite thus the lung-thorax system is at equilibrium (rest)

Recap: Resting volume of lung is the minimum volume which is equal to 150ml. Resting volume of the thorax is 75% of TLC which is about 4.5 L. Resting volume of the system is FRC which is 40% of TLC.

-FRC gives an idea about resting volume of the system hence if it is changed (increase or decrease) it indicates something pathological.

Column 3: at Tidal volume (2.7 L)

- The lung tendency to collapse is increased.
- The thorax tendency to expand is decreased
- The system is tending to collapse because the collapsing forces are more than the expanding forces.
- To move the graph upwards you need a force. (Since you're moving it from its resting state)
- Expiration is free in this case (without expiration there is no inspiration, you need to exhale in order to inhale)

Column 4: At TLC (5.7 L)

- The tendency of the lung to collapse is huge
- The thorax is also tending to collapse
- The system is largely tending to collapse
- This is the case when you take a deep breath and hold it in, relaxing the muscles becomes very hard due to the fact that the system tends to collapse.

Column 1: At RV (1.2 L)

- To reach residual volume you have to use the expiratory muscle (the abdominal and internal intercostal muscles which are usually resting) since expiration is usually passive, but in order to reach residual volume you're moving the system from its resting state hence force must be applied which comes from expiratory muscles.
- The lung is minimally tending to collapse
- The thorax is tending to expand more
- The system tends to expand
- Therefore, inspiration in this case is passive (free) since the system is trying to reach FRC

**We conclude that the lung is always tending to collapse.
(Unless at its resting volume)**

-If for example we are dealing with a disease that increases the tendency of lung to collapse (such as decreased surface tension and decreased surfactant production as in respiratory distress syndrome RDS), at FRC the tendency to collapse becomes twice as much (not normal) and tendency to expand is the same (since pathology is in the lung not the thorax) but the system is not resting (system always need equilibrium), so the lung curve shifts downwards trying to:

- 1) Make the tendency of lung to collapse less,
 - 2) And the tendency of the thorax to expand more.
- So we obtain a new FRC value. (Below the normal value)
- If your FRC is less than normal then the lung has higher tendency to collapse (pathological condition)

-If a disease decreases the tendency of the lung to collapse (disease discussed later) the graph moves upward trying to:

- 1) Increase the size of the lung in order to increase its tendency to collapse
- 2) Make the tendency of the thorax to expand less

-FRC is higher than normal.

-Pulmonary function test, lung volume and capacities help us in making a diagnosis, however they are not diagnostic by themselves. They help in staging of the disease, prognosis and monitoring people with certain hazardous jobs.

-Why does the lung tend to collapse, what are the collapsing forces and when are these forces increased or decreased?

-4 is the pressure used to overcome the collapsing forces. If IPP becomes -14 then the lung is facing stronger collapsing forces and so on.

More collapsing forces → more negative pressure → more muscle contraction → more oxygen consumption. (Oxygen consumption for the respiratory system is less than 5%)

- **Collapsing forces:**

Static forces: (70%)

- There is no air flow
- Force acting at FRC

- If you fill the lung and stop there, this is also static forces
- 2 types:
 - Surface tension(2/3)
 - Elastic fibers(1/3)

Dynamic forces: (30%)

- During air flow
- $W = \Delta P * \Delta V$ hence if the pressure needed to accomplish the same tidal volume is more then work of breathing is increased.
- 2 types:
 - Airway resistance (80%)
 - Tissue viscosity (20%)
 - To expand or collapse the tissue of the lung you need to pay for it by work.

-The negative IPP (-4) is called the inflation pressure. It is the pressure needed to overcome the collapsing forces.

-Surface tension:

-Diameter of the alveolus is 100micrometer at FRC but can reach up to 300 micrometers at TLC

-If we take an air bubble with a diameter of 100micrometer. The air bubble is composed of water (its wall) and air inside of it, any time there is water-air interface your are facing surface tension. Water is polar(hydrogen bonds) so water molecules are attracted to each other as if trying to bring both ends of the sphere together hence acting like a collapsing force. to prevent this you need an inflation pressure equal to the surface tension.

-Surface tension is defined as intermolecular attraction of water molecules.

-You can apply law of Laplace on the air bubble to indicate how much pressure you need to overcome collapsing forces.

Laplace's law: P (inflation pressure) = $2T/r$

Using the above example of the air bubble: $r = 50$ so the pressure needed is about -23 assuming T is equal to 1, this is a very high value

If you make the radius smaller then you increase this pressure
If you make the sphere from plasma (interstitial fluid), a pressure of -13 would be enough at this size.

In our lungs we only need -4, which is used to overcome surface tension in addition to the elastic fibers.

If the alveolus is lined with water vapor from inside this creates a major problem (since high negative pressures are needed to overcome the collapsing forces this is not practical)

Therefore it is lined with Phospholipid (fatty substance), which has a phosphate group (polar head) and glycerol backbone (hydrophobic tails)

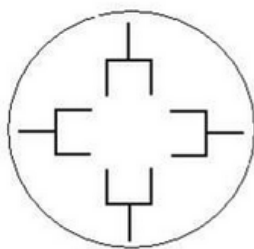


FIGURE 1

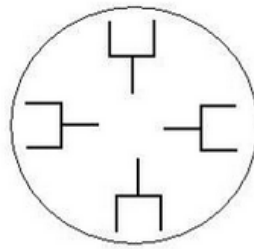
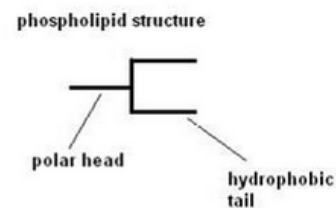


FIGURE 2



-In figure 1: air is facing non-polar tails, this there is no molecular attraction towards each other. This is efficient

-In figure 2: polar heads are facing each other, hydrogen bonds form and this is not efficient (collapsing forces are present).

This fatty substance is called a surfactant (surface active agent) mainly phospholipid, it reduces surface tension hence inflation pressure needed is less.

Without surfactant:

-If you have 2 alveoli close to each other, one slightly smaller than the other. The smaller one is going to collapse and empty its contents in the bigger one. Under the microscope you are going to

find totally collapsed alveoli and hyper-inflated alveoli in the same region, this means that you don't have a surfactant (Small and large alveoli cannot coexist in the same area)

-When the radius is decreased we said that pressure is going to increase according to Laplace's law ($P=2T/r$). However, when the radius decreases the concentration of surfactant increases, reducing surface tension at the same time, keeping the pressure needed the same.

Note: there are regional differences in IPP between base and apex

-With the presence of a surfactant, small and large alveoli can co-exist in the same area. This is called alveolar stability

-Consequently surfactant has 2 main functions:

- Reducing the surface tension
- Alveolar stability

In addition to Making surface tension volume dependent, the less the volume the less the surface tension since there is more surfactant concentration and thus making the pressure needed constant.

Good luck 😊

Luai Madanat