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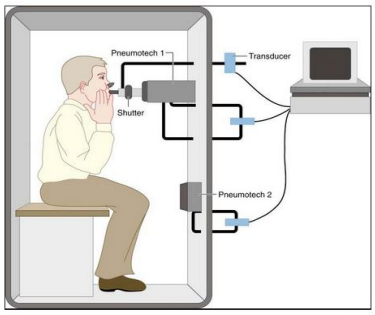
Physiology 4

We said in the last lecture that we can't measure the FRC (**Functional Residual Capacity**) directly and we use the **helium dilution method** for that.



**There are other methods for measuring FRC {a machine called plethesmograph .

Now, why the lung is tending to collapse?

We know that as a hollow elastic organ it will collapse .

- Collapsing forces in the lung:

Work of breathing = △P * △V

ΔP : refers to the transpulmonary pressure (the pressure difference between the plural cavity and the alveoli) , or to transthoracic (the difference between outside and the plural cavity) , or to transmural (the difference between outside the airways and inside)

i.e, the pressure difference across pulmonary structures.

1- Static / elastic forces

- 70% of total work of breathing.
- 2/3 of these elastic forces come from surface tension, 1/3 from elastic fibers.

2-Dynamic / non-elastic forces

- Manifested only during air flow.
- 80% of it is airway resistance and 20% tissue viscosity resistance.
- If there is no air flow >> Dynamic forces =Zero

- Surface tension: (present when there is liquid – air interference)

- Results from the attractive forces between liquid molecules lining the alveoli , trying to make these molecules closer to each other and as a result it creates a collapsing force (that's why air bubble is not stable because it will immediately collapse).
- Laplace's law :

  P= 2T/r

  Notice that: pressure P that tends to collapse the alveoli is directly proportional to surface tension T and inversely proportional to radius r.

P: collapsing pressure on alveolus

T: surface tension

r: radius of alveolus

- An alveolus lined inside with water only, needs an inflation pressure (-ve pressure) about -23 mmHg, if lined with interstitial fluid needs less, and if lined with surfactants it needs only -4 mmHg.

- Surfactants:

In the alveoli we have 2 types of cells, the majority of cells is type 1: squamous thin layer cells, they are thin to allow gas exchange, the minority is type 2 : columnar and they produce surfactants.

*Remember that the respiratory tract is formed of 23 branches : from 1-16 >> they follow the conducting portion of the RS

From 17-23 >> they follow the respiratory portion of the RS

No. 16 is called terminal bronchiole , No. 17 is called respiratory bronchiole .

- We might see some surfactants inside the respiratory bronchioles and the alveolar ducts but mainly they are in the alveoli.
- Surfactants are glycolipoproteins : 90% is lipid (different types of phospholipids)
  8% is protein
  2% is carbohydrates
  Because of the sophisticated mixture it's hard to manufacture the surfactants

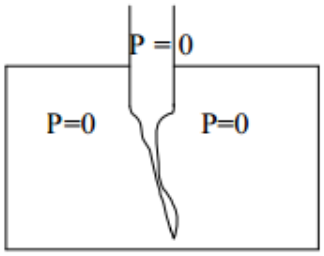
- Surfactants secretion starts at week 20 of gestation and ends at week 34.
  Before that time the lung is premature, prematurity of the lung means lack of surfactants.
  *babies that are born at week 31 are much better than those that are born at week 28.
  *babies that are born without surfactants face a major problem because their lungs will collapse almost to zero volume , each time these babies want to re-inflate their lungs they must put too much effort that they can't manage it most of the time, so the mortality rate is high.
  *between weeks 26 to 28 RDS (respiratory distress syndrome) risk is around 50% and between weeks 31 to 32 the incidence is 25%, {one extra day can make a difference}.
  *diabetic mothers have more chance to give birth to babies with RDS.
  *Males are more prone to RDS than females.

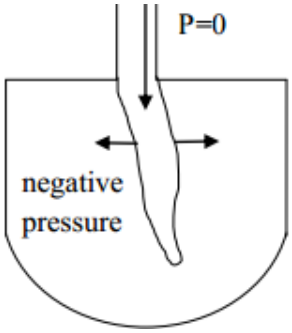
- **Now how do we know that 2/3 of the elastic forces come from surface tension and 1/3 from elastic fibers? We are going to do the following experiment :**

we bring a lung that is totally collapsed with a pressure of 0 inside and outside (starting from minimal volume and not from residual volume) and then we start changing the surrounding pressure (-1) then a second step (-2) by changing the volume until reaching -30.

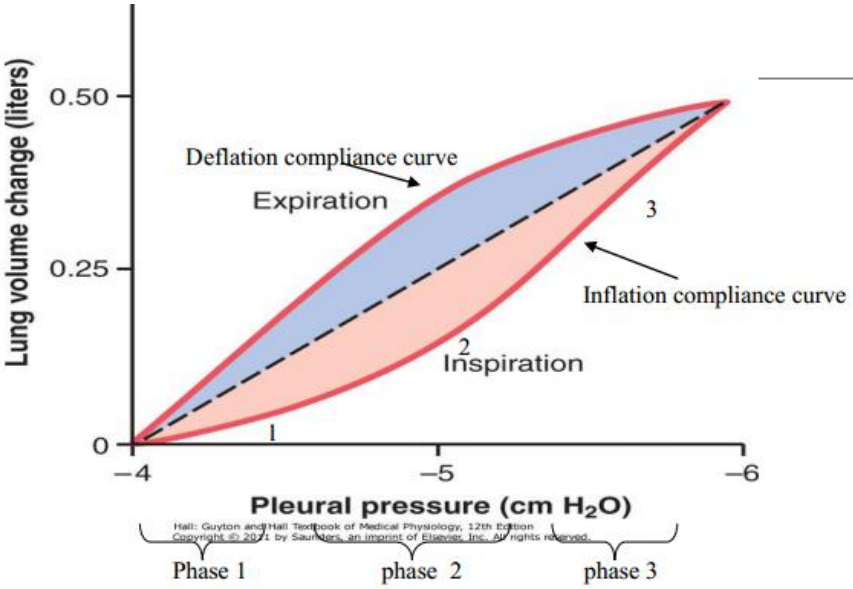
As we know **<u>compliance(C) = △V / △P (how much change of volume you get per unit change in force)</u>**

*force is directly proportional to negative pressure.





In the graph the x-axis is negative change in pressure and y-axis is volume.



- *<u>Compliance is the slope of the curve =(y2-y1)/(x2-x1)</u>*
- More negative pressure means more force.
- You need too much pressure (too much work ,too much ATP and oxygen consumption) before you make a noticeable change in the volume in **<u>phase 1</u>** and here the lung is incompliant or stiff , it doesn't respond to your force.
  * It's like a balloon, when you first blow into it, it doesn't inflate then it becomes easier.
- **<u>Phase 2</u>** : critical opening pressure or pop opening pressure (as in popcorn) any increase in pressure is followed by an increase in volume. Here the slope of the curve becomes high.
  →the lung is very compliant.

- When you reach the maximum volume and you can't stretch the lung anymore you reach **<u>phase 3,</u>** you apply too much force and you get little change in volume so it's again not compliant, so it's not wise to inflate completely collapsed alveoli, and it's not wise to inflate already inflated alveoli (here the lung in both phases is not compliant)
  For example if we take 500 ml where would they go to the apex or to the base?

It depends on FRC, we see the condition or situation of the basal and apical alveoli, basal alveoli are partially inflated and the apical alveoli are already inflated so most of the air goes to the basal alveoli and a very little portion goes to the apex.
*ventilation at the base is more than the ventilation at the apex.

- Now we move to the deflation (expiration), we deflate the lung by changing the surrounding pressure making it less negative (more positive), you can see that the deflation curve follows a different path so the backward process is faster than the forward one, this is called ***hysteresis.***
  *Hysteresis means that the backward process is not the same as the forward one.

- If you look at the graph, you can see that for a given volume (which is controlled by the radius as in Laplace's law) for an alveoli, the pressure is different in inflation from deflation even though the surfactant concentration is the same during both processes.
  *so it is much easier to hold your breath while expiration than inspiration.
  - y3ni same volume and same concentration of surfactant but not the same efficacy, (during inspiration surfactant is not as effective as in expiration)

- Some notes:

- Surfactants reduce the surface tension.
- Surfactants make surface tension volume dependent.
  - When radius is decreased, surfactant becomes more concentrated and reduces surface tension, and when you increase radius you decrease concentration of surfactant and that makes surface tension high.
  - So according to Laplace's law, since decrease or increase in radius is accompanied by decrease or increase in surface tension T respectively, pressure P will remain constant and that allows alveolar stability.
    * alveolar stability means small alveoli can coexist with large alveoli at the same region.{ lungs of people with RDS don't contain small and large alveoli together ,you find hyper inflated alveoli with totally collapsed ones}

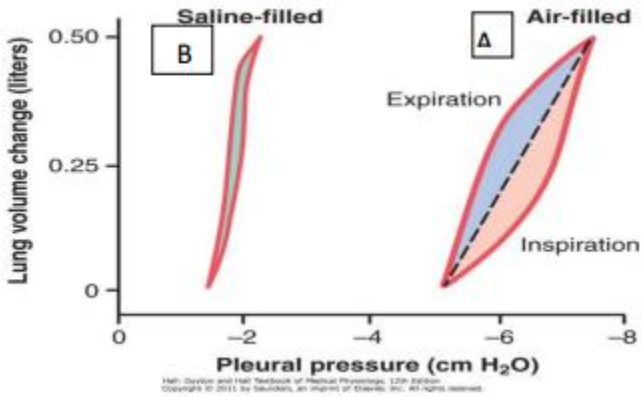
Laplace's law:

P=2T/r

- The best way of orientation of surfactants is the hyrdrophobic tails facing the air and the hydrophilic heads facing the epithelium.
- Surfactant behaves differently while inflating (spreading) or deflating (Compressing) the alveoli.
  - While spreading surfactant (inspiration), it becomes oriented in a non proper way (hydrophobic tails not facing the air) which means surface tension is high, surfactant is not doing its job properly by reducing surface tension(not effective).
  - During compression of surfactant, surfactant is oriented in a proper way, which means surface tension is low.
- The inflation curve is not purely complaint, it is complicated by other phenomena like what's so called alveolar recruitment { at a certain point the alveoli start to

recruit each other and become more effective like a positive feedback mechanism and so the surface tension starts to decrease}.

- By filling the lung with saline you cancel the surface tension , shifting the curve to the left with no hysteresis.
- This means that at any volume the pressure we need is just to over come the elastic fibers and no surface tension is present



- Microcirculation in the lung:

- Between arterial, capillary and venous parts
- Starling forces are 4 :
    1. the pressure in the capillary is(7-10)mmHg (filtration pressure)
    2. the pressure in the interstitium is -5 mmHg (also a driving force from inside to outside because it's negative)
    3. colloid osmotic pressure is 28mmHg (oppose the filtration force)
    4. colloid osmotic pressure of the interstitium is 14mmHg

So the net force is : (10+14+5)-28 = +1mmHg

Outward forces (filtration) | Inward force

The net pressure across the pulmonary capillary is a filtration force, so we have more filtration than absorption this means that fluid will accumulate and cause edema. We must keep our lungs dry and this is done by the lymphatics. Lungs are drained by the right lymphatic duct with the exception of the left apex which is drained by the thoracic duct, so these lymphatics maintain the negative pressure.

*In left ventricular failure: left ventricle cannot pump blood and it will accumulate in it then it goes back to the left atrium then to the pulmonary veins and by that it increases the pressure inside the capillary within the lungs— the 10 mmHg will be 20mmHg and so the +1mmHg will be +11mmHg, this is called pulmonary edema certifactant Still the lymphatic drainage can take care of this.

*if there is no surfactant, the surface tension will increase and if I have a huge surface tension; I have a huge collapsing tendency, then I need a huge negative pressure, this negative pressure is the pressure surrounding the capillaries (-5mmHg will become -15 or -25 or -35mmHg) and so increasing the force that drives the fluid outside the capillaries and this will cause pulmonary edema, therefore surfactant prevent the occurrence of pulmonary edema.

- Respiratory distress syndrome (RDS):

- IRDS refers to infantile respiratory distress syndrome, while ARDS refers to acute and not adult respiratory distress syndrome (was called adult before).
- RDS baby has no surfactant so each time he exhales he empties his lungs (zero volume), it's very difficult to inflate them.
- RDS means no surfactant, means pulmonary edema and pulmonary edema means HYPOXIA.
- Hypoxia constricts pulmonary arteries and dilates systemic arteries.
- The pressure in the pulmonary artery fluctuates between systolic and diastolic (between contraction and relaxation).
  -The pressure in systole reaches 24mmHg and in diastole 8mmHg.
  -The mean pressure equals 2/3 of systolic + 1/3 of diastolic pressure so it's around 14mmHg.

When we have constriction in the pulmonary arteries, pulmonary vascular resistance will increase.
-as you know pulmonary vascular resistance is less than the systemic vascular resistance.

-The CO of right ventricle = CO of the left ventricle

so Q1 = Q2

Δp1/R pulmonary = Δp2(aorta - right atrium)/ TPR

14 / R pulmonary = 100 / TPR

so 14/100 is the pulmonary vascular resistance.

Poiseuille's Law

$$R = \frac{8\eta L}{\pi r^4}$$

- when we have constriction due to hypoxia we will have more resistance ,so you will have increase in the after load on the right ventricle

- RDS increases vascular resistance, when the vascular resistance increases the pressure in the right heart will increase and this will cause the foramen ovale to open thus shifting the blood from the right side to the left side (right - left shunt).
  -The duct between the pulmonary artery and the aorta re-open again this is called ⇒ patent ductus arteriosus ,now we will have mixing of arterial blood in this baby with venous blood, this makes hypoxia more sever.

- RDS premature baby suffers from :
  1. Very low compliant lungs.
  2. Right to left shunt.
  3. Pulmonary edema that makes oxygen availability less , the first organ will suffer is the

heart because less oxygen comes to the hear through coronary circulation so it will become weak therefore it will pump less blood → stasis of blood in the heart → increase pulmonary capillary pressure → more edema (so pulmonary edema leads to more pulmonary edema [positive feedback]) .

As a summary, what are the different functions of surfactants?

1. Reduce the surface tension
2. Make surface tension volume dependant.
3. Alveolar stability due to surfactants and alveolar traction (if one alveoli is blown off the other will tract it).
4. Prevent pulmonary edema.
5. Prevent hypoxia.
6. Prevent right to left shunt.

- What am I supposed to do if there's a history of premature labor from a mother?

- The most important thing is that this mother should give birth to her child in a hospital that has premature baby unit.
- Surfactant needs: thyroxin(T4), prolactin, estrogen(that's why females are more protected), glucocorticoids ;therefore I must give the mother glucocorticoids [specially dexamethasone] 2 injections This will increase the production of surfactants .
- We can give the mother surfactant inhaler.

- Definitely, the baby when is born needs help by CPAP {continuous positive air way pressure} or by PEEP {positive end-expiratory pressure} .

GOOD LUCK ☺

Your colleague: Leen Mismar
Special thanks for Deena Dari