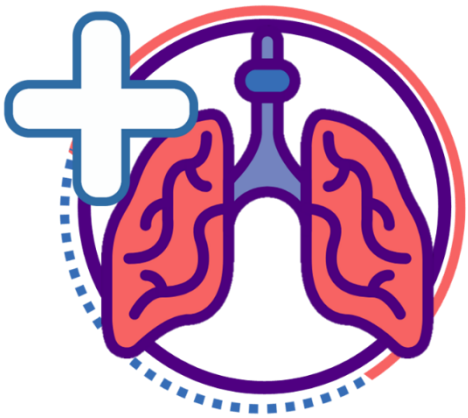


RESPIRATORY SYSTEM

Physiology

Sheet Slide

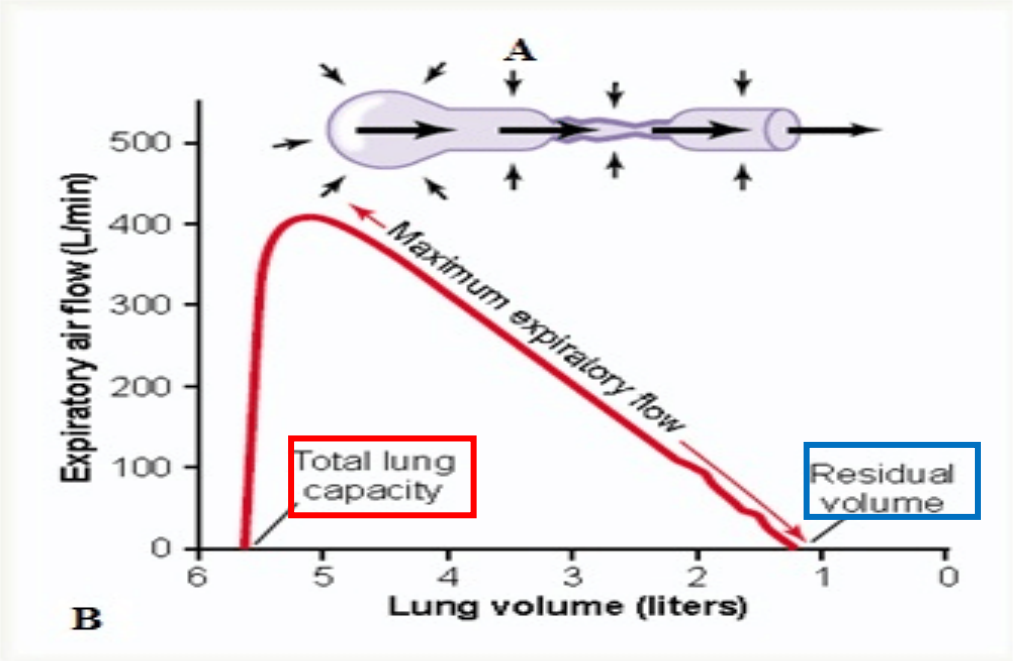
Number:	- 5
Done by:	- Ensherah Mokheemer
Corrected by:	- Rama Nada
Doctor:	- Yanal shafakoj

-we will continue talking about **obstructive pulmonary disease**:

Maximum expiratory flow rate:

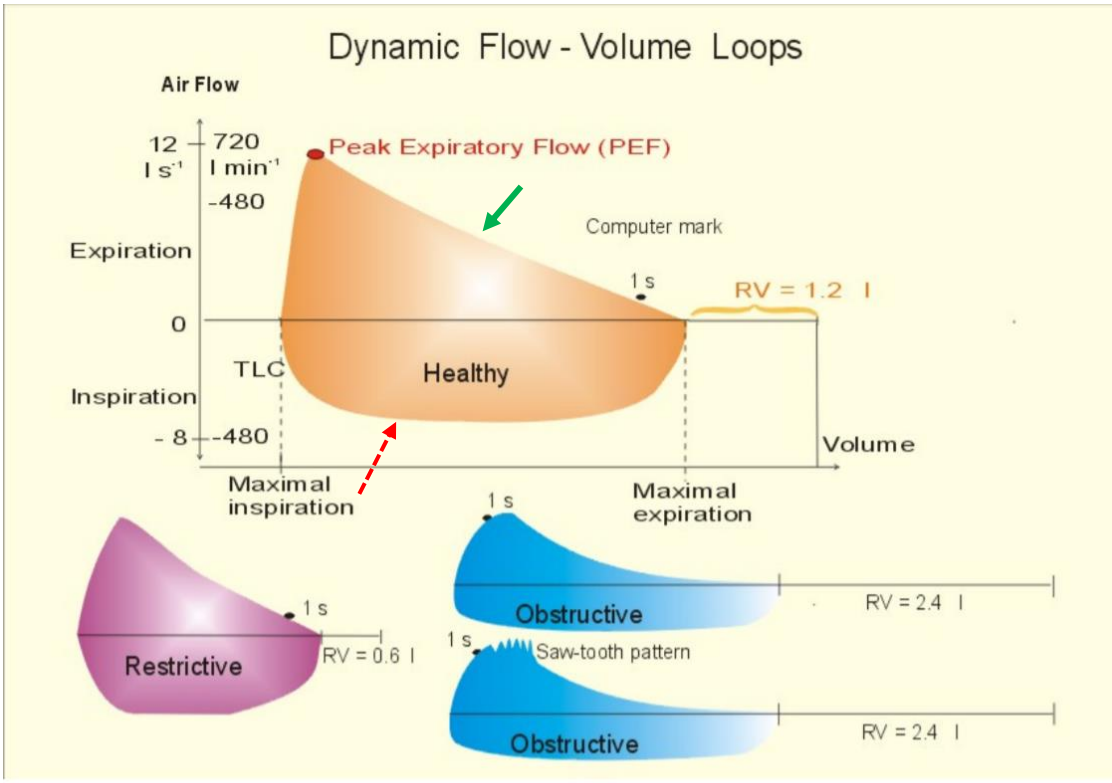
- To know whether the patient has obstruction or not, we measure **the <u>maximum</u> expiratory flow rate**. The patient is asked to inhale deeply to fill his lungs with air and then exhale forcefully and inhale forcefully again and so on. Maximum flow rate can reach (6-7L/s or 400-500L/min) per second.

  <u>The bigger the volume you start exhaling from, the faster the maximum expiratory rate.</u> To reach that, the person takes a **deep breath**; filling the lungs to their maximum (TLC).
  At the residual volume (the amount of air that remains in a person's lungs after fully exhaling) there will be no air to flow so the maximum expiratory flow rate will be zero.



** Notice that the x-axis values are in descending manner. Also notice that the starting x value is TLC, and the end x value is RV.

- Notice from the figure above that the maximum expiratory rate flow is highest "400L/min", when exhaling starts with The total lung capacity (Greatest volume), but when exhaling starts at lower volumes the maximum expiratory flow will decrease until it reaches Zero at the residual volume.



The expiratory flow rate.

The inspiratory flow rate.

- In COPD patients, **the maximum expiratory flow rate is lower** than normal because of the obstruction that will prevent the flow, and the **TLC (starting point) is higher than normal** because in case of obstruction it is easy to inflate the lung and it is more difficult to deflate the lung; so, the graph is **shifted to the left**. Note that the overall shape of the curve in this case differs than the normal curve "شكله مقعر للأسفل"

  Example: when there is emphysema, which is associated with loss of elastic fibres in the lungs, the compliance of the lungs increases. **EXTRA**→ As a result, at a given volume, **the collapsing (elastic recoil) force on the lungs is decreased**. At the original value for FRC, **the tendency of the lungs to collapse is less than the tendency of the chest wall to expand (It is easier to expand the lungs)**, and these opposing forces will no longer be balanced (the collapsing is less). For the opposing forces to be balanced, volume must be added to the lungs to increase their collapsing force by increasing the elastic force (elastic fibers). Thus, the combined lung and chest-wall system seeks **a new higher FRC**, where the two opposing

forces can be balanced.

* patient with emphysema is said to breathe at higher lung volumes (in recognition of the higher FRC) and will have a **barrel-shaped chest.**

- In restriction, however, **the starting point (TLC) is less than normal** because the problem is in inflating the lung with air, and the peak is lower than normal.

  Example: Fibrosis is associated with stiffening of lung tissues and decreased compliance. A decrease in lung compliance will make **the tendency of the lungs to collapse at the original FRC is greater than the tendency of the chest wall to expand** (Huge collapsing force) and the opposing forces will no longer be balanced. To re-establish balance, the lung and chest-wall system will seek a new lower FRC. And so, the patient with restriction would have higher expiratory rate than the normal expiratory rate at given lung volume (because of the huge collapsing force). **And the curve shape resembles the normal curve** and **shifted to the right**, with less TLC (starting point) due to the difficulty in inflating the lung, less RV (end point) which is due to **huge collapsing force** that will push more air out of the lung lowering the residual volume, **lower peak** and **higher-than-normal flow rate** at comparable volumes.

  ** Remember that Functional Residual Capacity (FRC) is the volume of air present in the lungs at the end of passive expiration.

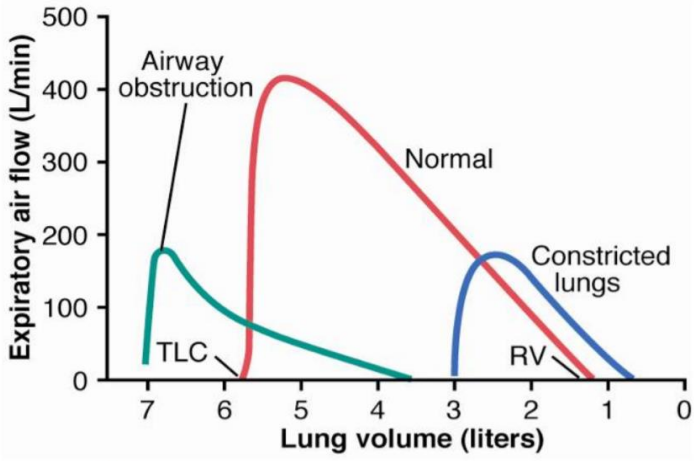


Figure 42-2

In conclusion:

- The Maximum Expiratory flow rate depends on the volume of air in the lung at the start of exhalation, the higher the volume the higher the Maximum Expiratory flow rate.
- The lung volume in litres is the x axis and it starts in a descending manner (7,6,5,4….). The expiratory flow rate is on the y axis and it is ascending (0,100,200,).
- **In case of obstruction pulmonary disease:**
    1- The compliance increases, and the lung is easier to inflate→ higher TLC.
    2- Due to the obstruction the flow in interrupted during exhalation → lower maximum expiratory rate.
    3- The shape of the curve is different than the normal مقعر.
    4- The curve is shifted to the left.
- **In case of restriction pulmonary disease**:
    1- The compliance decreases but the collapsing force increase → Lower residual volume.
    2- Inflation of the lung is difficult → Lower TLC.
    3- The shape of the curve is like the normal one.
    4- The curve is shifted to the right, with lower peak.

Lung Compliance

Last time we said that the **work of breathing** is overcome two types of forces:

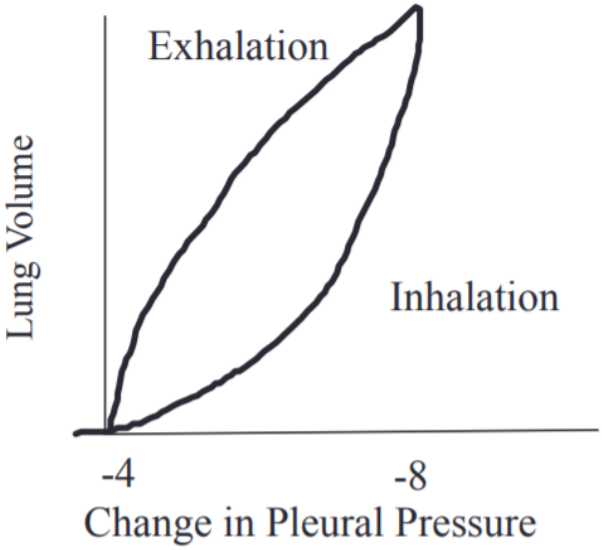
A) Elastic forces: 70%:
(not dynamic, the force of bringing anything back to its original state).
- 2/3 Surface tension.
- 1/3 elastic fibres.

B) Non-elastic forces: 30%:

- Airway resistance 80% (manifested only during air movement, that's why it's considered dynamic).

- Viscosity of tissues 20% (the interstitial tissue opposes the movement during expiration and inspiration {just like the gum oppose your motion when you try to change its shape}).

- remember that in order to inflate the lung, we needed to change the pleural pressure and make it **more negative in order to expand the lung** (inflation pressure)**.** <u>At the beginning</u> of the inflation, too much driving force (Change in pressure) is needed to achieve little change in the lung volume. So, if we tried to inflate a totally collapsed lung, we will have to put too much force to have little change in volume, at this phase we can consider the lung **uncompliant** غير مطاوعة→ (**phase1)**.



But then suddenly the lung become **compliant (phase 2)** meaning that little change in pressure (little force), will achieve great change in volume. But after that the lungs become **uncompliant** again **(phase 3).**

Example: when you want to inflate a balloon, at first you will face difficulty and you will need too much force to inflate it but then once it's a little bit inflated, things will become much easier and you can continue inflating with lesser force, but once you have almost fully inflate the balloon you will again have to put too much force to inflate it more.

So, compliance means how much the volume changes per a unit change in pressure, and from the curve you can measure the slop for each stage by dividing the change in volume over the change in pressure (Y/X), the result is equal to the tan of the angle of the slop (in phase 1 it's small, in phase 2 it's high and in phase 3 it returns small)

Take home message: - It is unwise, each time you exhale you go to zero volume because to re-inflate totally collapsed lung is

very difficult and you will have to put too much pressure → too much work → too much ATP!!

! Respiratory takes less than 5% of the ATP in our bodies but in this case, it might consume up to 20-30 % of our ATP which is too much.

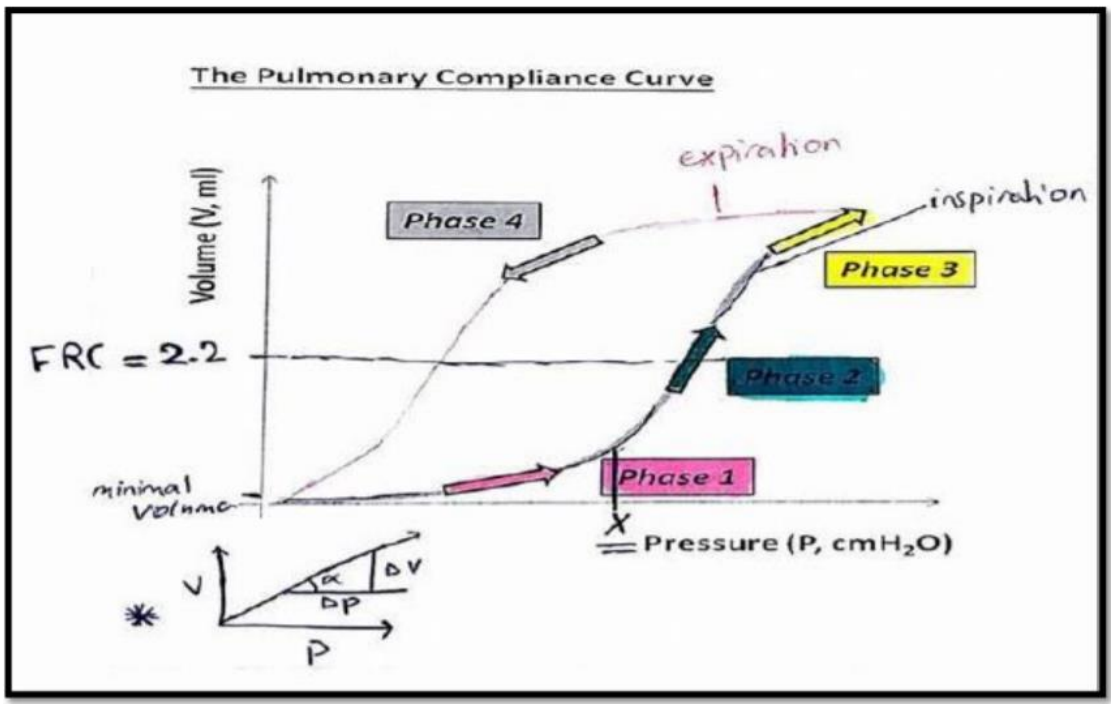
Also, it's very difficult to inflate already inflated alveoli (in phase3), because it will take too much effort (not compliant)

- It is wise to inflate partially inflated lung, and it is not wise to inflate an already inflated lung.
- So when you breath you are taking the tidal volume on top of a pre-existing FRC in your lung (partially inflated lung) which makes your lung in the high compliance phase (phase 2), so you don't need too much change in pressure thus not too much ATP is required.

*Inflation of totally collapsed lung represents phase 1 → uncompliant lung (difficult phase)

*Inflation of partially inflated lung is phase 2 → compliant lung.

*Inflation of already inflated lung is phase 3 → uncompliant lung.



-This curve is the inflation-compliance curve.

- Notice that as we move to the right on X axis, the pressure becomes more negative.

In inflation:
So, we start decreasing the pressure around the lungs ((by increasing the volume in the thorax)), and we monitor the change in the volume of the lung, and we will have the following:

1- At the first the curve is barely elevated, too little change in volume for a huge change in pressure and a lot of ATP consumption; not compliant (Phase 1).
2- At critical pressure, the lung will become very compliant, then if we apply little force, we will get huge change in volume; compliant (Phase 2).
3- At the end of the curve; you cannot inflate already inflated lung (This is the Maximal point); not compliant (Phase 3).

Normally we start our inspiration at the level of the FRC (2.2L), at a partially inflated lung → very compliant lung.

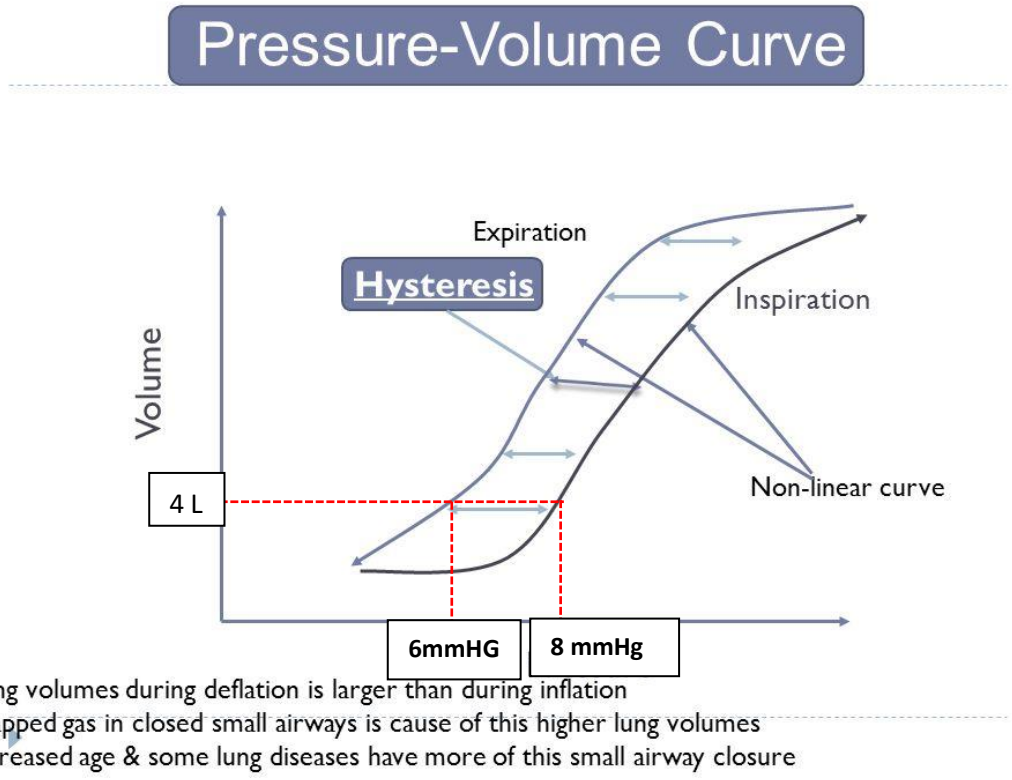
Now during **deflation**:

- In order to deflate the lung, we need less negative pressure (positive pressure) around the lung.
- The deflation curve is different from the inflation curve, it follows a different pathway (the backward process doesn't follow the same forward process).

- Logically the inflation curve and the deflation curve should be similar to each other but that's is not the case here.
- For example, If you carry an object of 10 kg from the ground upward to the height of 1 meter above the ground the tension in your biceps will be 50 (static, without movement). On the other hand, if you carry down the same object from upward to the height of 1 meter above the ground the tension in your biceps will be 45 (also static, without movement). We notice a difference in tension even though the weight and the distance from the ground in both cases are the same. This is called **Hysteresis.**
- Another example of hysteresis: when we say the distance from the university to Sweileh صويلح is 5 km but from Sweileh to the university is 4 Km.

- Now let's apply the term hysteresis to the inflation and deflation of lungs, we notice that the deflation (backward process) followed a different pathway from the inflation (forward process). What does that mean?
  If you look at the curve you will notice that to hold the lung un-collapsed at 4 L we need a pressure -8 mmHg during inflation, during deflation we needed -6mmHg.

So it's easier (need less pressure) to keep the lung inflated during deflation rather than during inflation at the same volume (4 litre in the previous example)

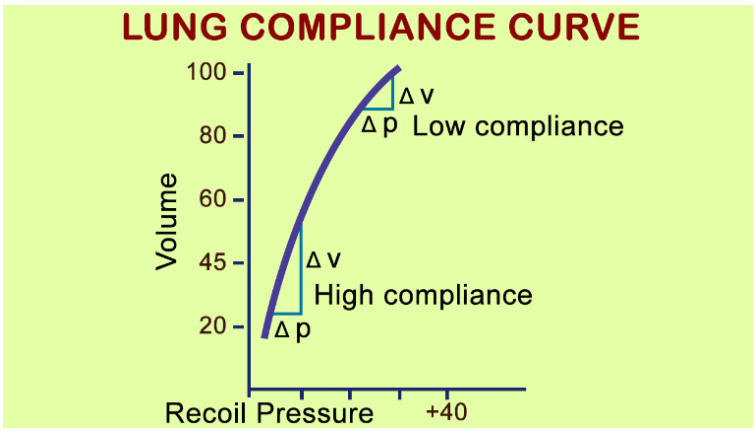


- Notes on the previous curve:
  - The X axis is the **negative pressure value,** the values of pressure are in the absolute form (without the minus sign) "The negative pressure is 6 mmHg= the pressure is -6mmHg).
  - The y axis is the volume (L).

- We notice hysteresis between the expiration and inspiration curves.

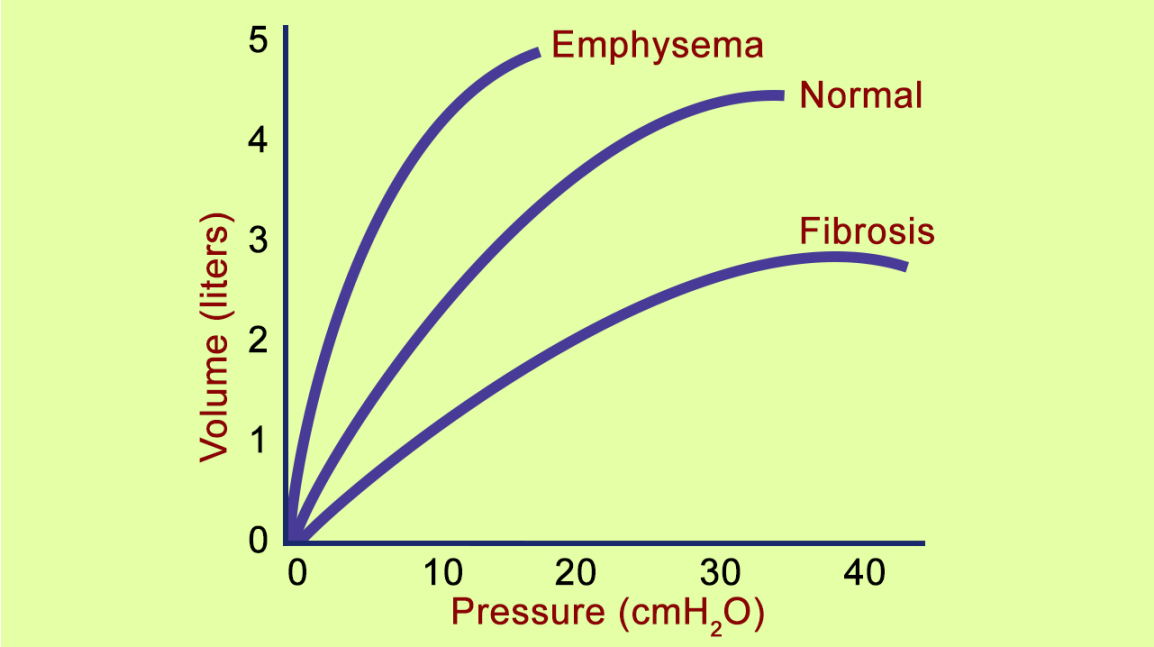
The inflation curve represents multiple phenomena called alveolar recruitment; that's mean the opening of one alveolus will help in the opening in the second alveolus (they help each other), in deflation there is no such thing.

Lung compliance curve:.



- When we say compliance curve of the lung, we mean **the deflation curve.** Compliance is the slope of the curve at any point, recall that the slope is $\frac{\Delta Y}{\Delta X}$ = **tan(θ)**

  -Compliance is how much volume change I can get per unit change in inflation pressure (the negative pressure).



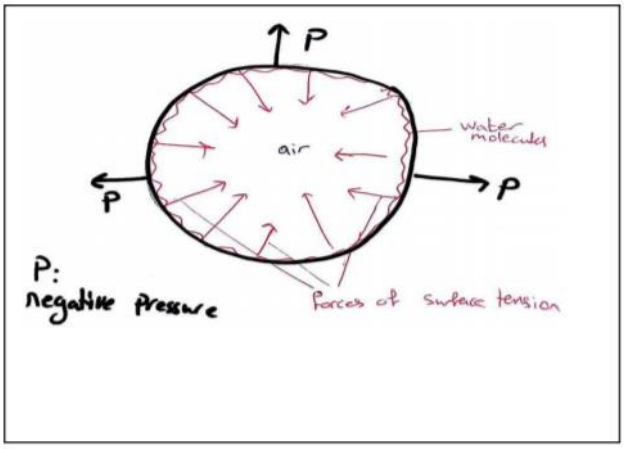
- This is the lung compliance curve for different cases:

1) In case of emphysema: the compliance increases (easily inflated) the curve is shifted to the left (the slop and the angel is higher than the normal).
2) In case of Fibrosis the compliance decreases (difficult to get inflated) and the curve is shifted to the right (the slop and the angel is lower than the normal).

Now let's ask ourselves what is the cause of hysteresis??

- **Surface tension: At water-air interfaces** there is the intermolecular attraction between water molecules (hydrogen bonds), the water molecules are attracted to each other to make the least surface area possible (toward the center), it is a collapsing force. At the surface of water it forms a membrane (بتمشي عليه البعوضة).
- Imagine we have an air bubble (walls are made by water molecules and inside is air) ("water-air interface"), the water molecules will try to come together bringing the bubble to the center causing it to collapse, surface tension is a collapsing force**.**
- **A) It is claimed that during inflation we have more surface tension and during deflation there is less surface tension:**
  The lungs are going to collapse due to collapsing forces unless there is an opposing pressure, and it is called inflation pressure, the amount of inflation pressure the lungs need to stay inflated (un collapsed) depends on how much collapsing forces are present, if the collapsing pressure is high, we need high inflation pressure to keep the lung un collapsed.
  The sources of collapsing forces are:

1) Surface tension: **Law of Laplace= ΔP = 2T / r**
   -T: tension (surface tension) -
   r: radius
   *the needed pressure is increased as we **increase the tension** and as we **decrease the radius,** because we're bringing water molecules closer to each other making the attraction easier.
   - explanation of Laplace law: in the alveoli, the wall is covered by water and in the center, there is air so there is surface tension



(collapsing force), in order to keep the lung inflated we need to overcome the collapsing force by an opposing force (negative pressure), the amount of the negative pressure is determined by:
1- the amount of surface tension.
2- how much is the radius, the smaller the radius the more pressure I need (more work → more ATP → fatigue).
As the radius decrease we need more pressure to keep it stable. In newborns the radius is small so they need too much pressure unless the surface tension decrease in the same proportion (if the radius is decreased half and the surface tension is decreased to half for example they'll need the same pressure as adults, and not higher). Imagine that the surface tension didn't decrease so they'll need more pressure to overcome the decrement in the radius and this is so difficult especially for newborns as they don't have strong muscles to apply more force.

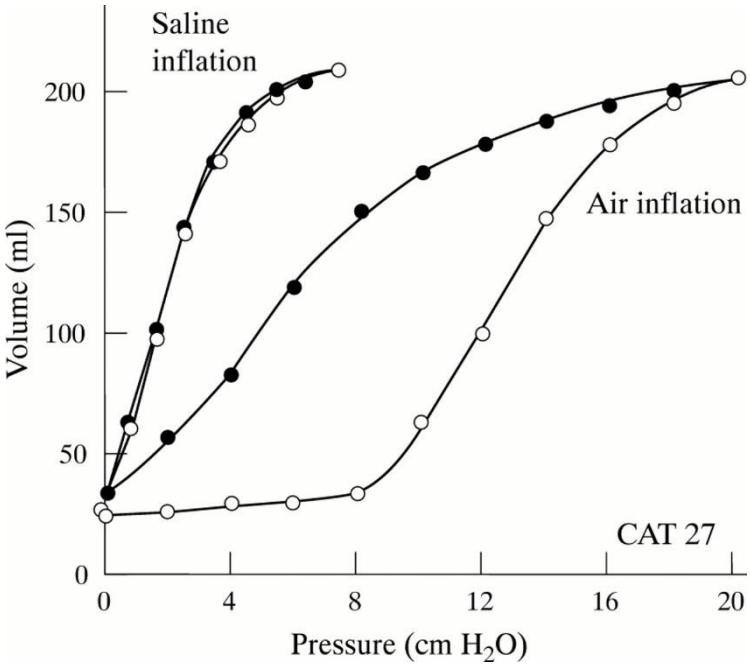
2) Elastic Fibers in the connective tissue of the lungs.

Previously we claimed that during inflation we have more surface tension and during deflation there is less surface tension:

How to prove that!!? We cancel the surface tension and then we see whether there is still hysteresis or not. If there is still hysteresis, then the surface tension was not the cause.

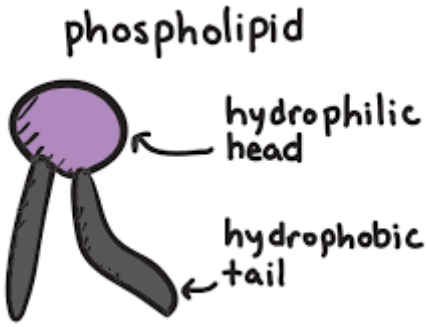
- Now in order to cancel the surface tension of fill the lung with **saline**, when the lung is filled with saline **the elastic fibers are stretched** (source of collapsing), however the saline replaced the air so there is **no water-air interface → no surface tension (We canceled the surface tension).**
- Normally when you fill your lungs with air there are two forces that you have to overcome which are the surface tension and the elastic fibers. When you fill your lungs with saline you will only have to overcome the elastic fibers because there is no surface tension. Let's draw the curves for both cases:

- Notice that in case of the saline inflation curve there is almost no hysteresis, which proves that our claiming is right, <u>during inflation we have more surface tension and during deflation there is less surface tension,</u> that is because when we removed the surface tension no hysteresis was present.



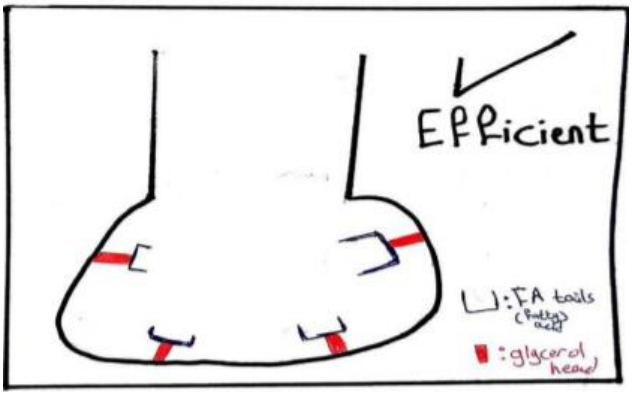
- In case of air inflation curve: (the number are from the doctor's curve not from the above):
  - During deflation for example we needed -2 mmHg pressure in order to keep the lung inflated at (4 L volume), this pressure was to overcome the ***elastic fibers*** only because the surface tension during deflation is low.
  - During inflation we needed pressure of -6 mmHg to keep the lung inflated at the same volume (4L), this increase in pressure was since during inflation we have to overcome ***both elastic fibers and surface tension,*** "increased collapsing force→ need more inflation pressure to overcome it".
    By finding the difference we find that we needed -4 pressure to overcome the surface tension.
    Overall, we needed -6 mmHg (Static Elastic forces)
    1/3 was for the elastic fibers → -2
    2/3 were for the surface tension→ -4
- The alveolus (with radius equal to 100 micrometer at FRC) is lined with water the pressure that is needed to keep them inflated in -21 mmHg, if it is lined with interstitial fluid 'plasma= (water +lipid +other), the pressure needed will be equal to -13 mmHg (less pressure). However, if we lined it **with surfactant** the pressure we need will become less and less and it will reach **-4 mmHg.** ***<u>The surfactant lowers the surface tension.</u>***

- **Surfactant** (surface active agent): Glycolipoprotien (90% lipids, 2% carbohydrates, 8% proteins)→ we are mainly concerned with lipids.
- The type of lipid that is present in the surfactant if phospholipid which consists of:
  a) Glycerol→ hydrophilic charged
  b) 2 fatty acids chain → hydrophobic, not charged.

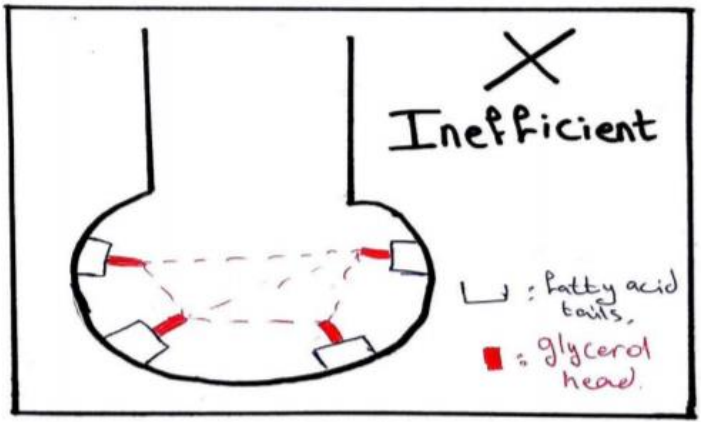


We can orient the surfactant molecules in two different ways:

1- Hydrophobic portion directed toward the air, so there will be no intermolecular attraction between the surfactant molecules→ no collapsing force→ less surface tension (efficient).



2- The hydrophilic portion is directed toward the air, there will be intermolecular attraction between the surfactant molecules→ collapsing forces→ surface tension. So, the surfactant is there but it is not efficient.



- **It's not only the concentration of surfactant that matters but also the orientation of it.**

- So, when I start inflating the lung from zero volume, I'm spreading the surfactant, and this spreading will make some of the surfactant molecules not oriented in a proper way, so it is there but it is not reducing the surface tension, so we need too much pressure to inflate from zero. During deflation we are compressing the lungs and thus we are forcing the surfactant to orient in the proper way, so the surface tension will decrease, that's why there is Hysteresis.
  Concentration= amount/area
  The concentration of the surfactant is constant (amount is the same and the area is the same) what differs between inflation and deflation is not the concentration it is the orientation
- The surfactant is considered extremely important because it reduces the negative pressure needed to overcome the tension, thus saving us a lot of ATP. Need an explanation? Keep reading…
  **As we've said before, work = ΔP * ΔV
  ΔV: Tidal volume
  ΔP: The pressure we need to overcome.
- **so, surfactant decreases the pressure needed to inflate the lungs, as a result decreases the work (decreasing oxygen and ATP consumption). And that's the reason why the lung is considered an efficient machine, as it only consumes 2-3% of the oxygen it produces. If the surfactant was deficient Oxygen consumption will increase up to 20-50% leaving small amount to other tissues resulting in muscle fatigue and death.
  Take home message: when the surfactant is absent the surface tension increases → collapsing force also increases→ each time you exhale you will go back to zero volume.

  Infant respiratory distress syndrome:
  In premature babies, their lungs are still premature, and their type 2 cells are still not well developed so there will be NO production of surfactant (surfactant secretion starts at week 8 and completes around week 34 -36), and so each time these babies exhale they will

go back to zero volume. According to Laplace law= **ΔP = 2T / r,** The surface tension is high due to the absence of the surfactant and the radius is very small in infants, so these babies will need huge amount of pressure to inflate their lungs from zero and each time they exhale they will go back to zero.

IRDS means that the lung is premature it does not make surfactant.

- During the gestation period, the baby needs; prolactin, estrogen, thyroxin (T4) and glucocorticoids (cortisone) in order to produce surfactant.
- Baby to diabetic mother has higher probability to develop IRDS, and if the first baby has IRDS the chance for the second baby to have IRDS is high.
- The more the gestational age the less the probability for the baby to have IRDS.
- So, if there is threaten abortion, if we can delay the delivery by one day, we could make a difference, we will give the type 2 cell more chance to produce surfactant.
- We can predict the lung maturity via using lung markers, which could be taken from the amniotic fluid (by amniocentesis), and then we can decide the maturity of the lung depending on the marker ratio such as:

  1) **Lecithin to sphingomyelin ratio** If > 2; the lung is mature

  2**) Phosphatidylglycerol** If present→ the lung is mature.

  3) **Surfactant to albumin ratio; this is the most important lung marker**. Surfactant (mg) / albumin (g)

  a- If > 55; the lung is mature.

  b- 35 – 55(intermediate).

  c- If < 35; the lung is immature.
- If the lung is not mature, I will try to delay the delivery as far as I can (even one day makes a different).
- Before delivering premature baby, we give **two shots** of **dexamethasone (in two days)** whether we took an amniotic fluid sample, or we did not.
- Dexamethasone will increase the production of surfactants. Dexamethasone is a corticosteroid which has 22 carbon atoms, which mean that it's a synthetic steroid.

Recall that: **Naturally** occurring steroids in human bodies are of three categories:

① C18: has 18 carbon atoms (like estrogen)

② C19: has 19 carbon atoms (like testosterone)

③ C21: has 21 carbon atoms (like aldosterone and cortisone)

- Advise this mother to deliver in a very advance center where they can take care of this premature baby.

Actually, this baby has many problems such as pulmonary hypertension; because of hypoxemia that induce vasoconstriction in the pulmonary arteries , and this hypertension will lead to open of Ductus arteriosus (between the aorta and the pulmonary artery), so we will have mixing of venous and arterial blood >>more hypoxemia and acidosis (because of shifting from aerobic respiration to anaerobic due to hypoxia, which leads to accumulation of lactic acids>>acidosis)

→All these problems will make his respiratory rate 60 breath/min, so he will be fighting for air and he will die after few hours, unless we interfere, but how?

①We provide the baby with CPAP (Continuous Positive Airway Pressure)

②We provide the baby with PEEP (Positive End-Expiratory Pressure); we connect the baby to a ventilator.

-The baby will be kept on the PEEP method (maybe for two weeks, three weeks, or even more; depending on the case), until his condition improves, and surfactant becomes enough.

- The importance of surfactant:

Normally, we have filtration and reabsorption happened at the wall of capillaries, and these events is controlled by what we called starling forces

- Starling forces are 4 forces, and they are:

1- **Pc**; Capillary Hydrostatic pressure - a filtration force (pushes fluid outside the capillary)

it equals (-10 mmHg) in pulmonary capillaries

2-**πc;** osmotic force due to plasma protein concentration – a reabsorption force,

*it equals (28mmhg) in all capillaries of the body

3-**Pi**; interstitial fluid Hydrostatic pressure – it's variable but ranges from zero to slightly negative.
*it equals (-5mmgh) in the lungs >>represent the intra-pleural pressure

4-**πi**; osmotic force due to interstitial fluid protein concentration - a filtration force. *it equals (-14 mmHg**).**

- The forces if negative, it's a filtration force, and if positive, it's a reabsorption force.

- **The summation of these forces:**
  10+14+5= 29 (filtration force→ outward) "due to proteins"→ negative.
  28 → inside (reabsorption force)→ Positive.
  So, there is a difference of 1 between filtration and reabsorption.
  So, there is a little filtration which is taken up by lymphatic system (scavengers of our bodies).
- If the interstitial fluid Hydrostatic pressure becomes -21mmHg instead of -5 mmHg the extra filtration will become -16 so more fluid filtration→ edema.
  The lung should always be dry, we cannot tolerate pulmonary edema→ top medical emergency (threating situation).
- However, the lung is full of lymphatics and can take care of the excess filtrated fluids and edema does not occur. (This is called pulmonary edema safety factor) → **In acute cases** -like MI: even if Pc increases and reaches up to 30 mmHg, lymphatics can still take care of the extra filtered fluid.
  In chronic conditions -like chronic left heart failure: even if Pc reaches 40 mmHg, lymphatics can still take care of the extra filtered fluid. Which means that if a person developed pulmonary edema, his situation must have been severe (and his body has undergone severe damage).

The End
Good luck

Sorry for any mistake.