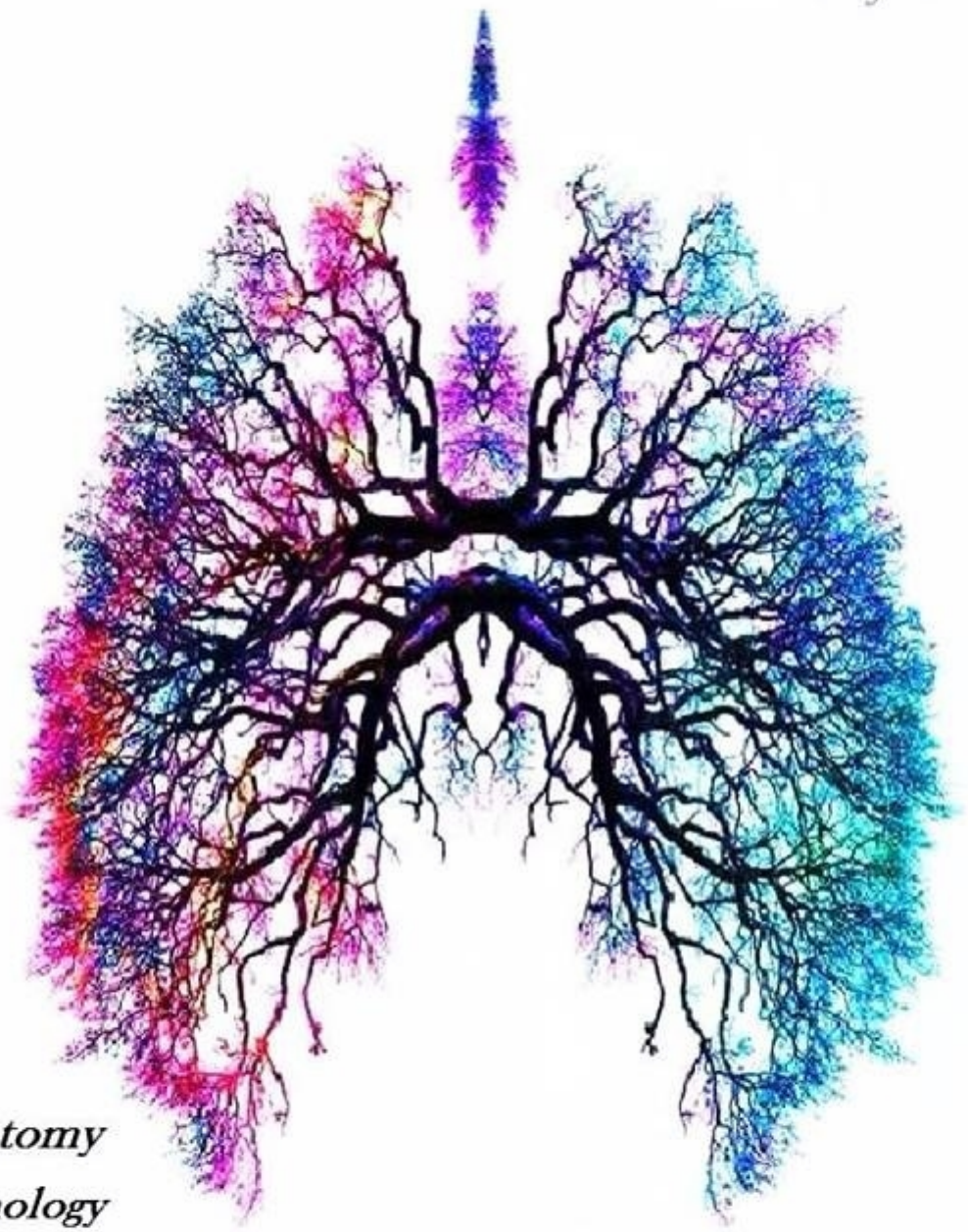
RESPIRATORY SYSTEM

Cover by: Aseil Khatib



- ○ Anatomy
- ○ Pathology
- ● Physiology
- ○ Pharmacology
- ○ Microbiology
- ○ PBL

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Lecture # 5
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Lung Compliance

As a general rule, if the elastic shape of an elastic structure is changed, it will have a tendency to go back to its resting state. Imagine a balloon as it's deflating, at a certain point it will cease to collapse and return to the shape it was in before it was inflated. The same idea can be applied to the lungs.

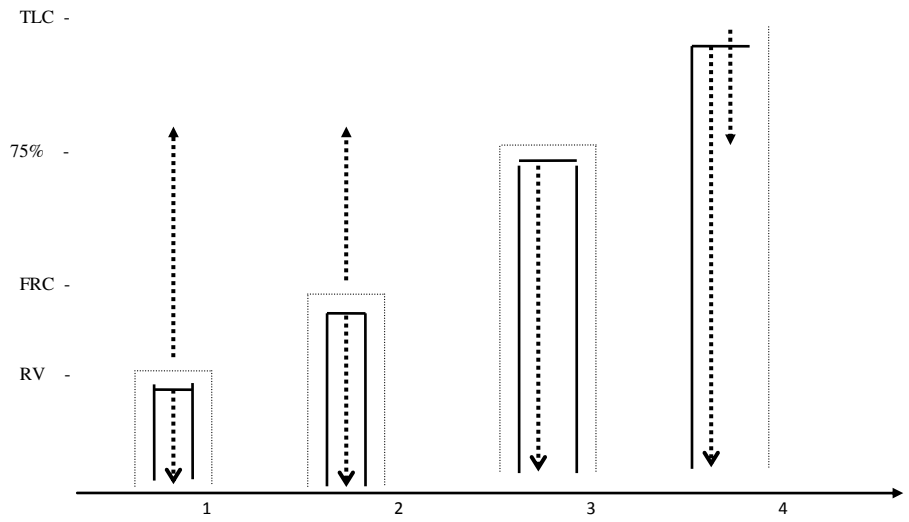
Each lung has a tendency to collapse until it reaches its resting volume (minimum volume) of 150ml. At this volume the lung has no more tendency to collapse and is at rest. However, the lung never reaches this volume because of the outward intrapleural (thorax) pressure of -4mmHg expanding the lungs preventing the lungs from ever reaching their state of rest.

In other words, the lung's tendency to collapse is counteracted by the thorax's tendency to expand.

Lungs and Thorax as a System

These opposing forces allow us to breathe with ease. As we said, the resting volume of the lungs is 150ml. In vivo, the lungs do not reach this resting state and always have a tendency to collapse. However, The resting volume of the thorax is 75% of the total lung capacity (total lung capacity is 6L and so the volume of the thorax would be 6 x 0.75 = 4.5L). This means the thorax has a tendency to expand during normal breathing. Keep in mind that when we go above the thorax's resting volume (75% of TLC / 4.5L), the thorax will have a tendency to collapse back to 4.5L.

At FRC (Functional Residual Capacity) the SYSTEM is at rest. The expanding force (of the thorax) is equal to the collapsing force. When we try to deviate from this, we need to use energy. On the way back however, it is a passive process. Columns 1,3, and 4 will passively return to the system's resting volume shown in column 2.



The previous chart shows different lung volumes and the direction of the forces. Before explaining each column, a general pattern can be seen. Starting with the collapsing pressure exerted inside the lungs, (represented as bottom arrows in the rectangles) the force is always downwards (collapsing) going to 150ml. We can never reach the low amount of 150ml of volume in a healthy person so the pressure is always collapsing. Looking at the thoracic pressure, you will notice the arrow going from the volume of the lungs at that particular time to 75% of the TLC. When the volume in the lungs is below 75% this is an expanding pressure, but when the volume is above that 75% mark, this becomes a collapsing pressure.

In column 1, at the RV (Residual volume: the volume of air remaining in the lungs after forceful expiration), expanding pressure of the thorax dominates and will return the system to equilibrium passively. In this case, the inspiration taken to return to FRC (column 2) will not use energy because these elastic forces of the system return it to equilibrium.

In column 2 the expanding and collapsing forces are equal and the system is at rest. Deviating from this volume will always need energy. However, when returning to FRC it will be done passively (Whether it is inspiration or expiration).

In column 3, we breathe until we reach 75% of the TLC and reach the thoraxes resting volume. At this instance the thorax has no tendency to collapse or expand. The thorax is at rest. The System, however, has a tendency to collapse because the lungs tendency to collapse is greater that the thoraxes tendency to expand (none) at this particular volume (75% TLC).

In column 4, we took a forceful inhalation and reached the TLC. This results in a huge collapsing force because of the summation of the lung's collapsing force and the thoraxes force (also a collapsing force above 75% TLC). Imagine yourself trying to take a deep breath and hold it in. While holding your breath, try to relax your muscles. This is very difficult because your system (lungs+ thorax) has a strong tendency to collapse.

AGAIN, At FRC (Functional Residual Capacity), the SYSTEM is at rest. The expanding force is equal to the collapsing force. When we try to deviate from this, we need to use energy. On the way back however, it is a passiveprocess. Columns 1,3, and 4 will passively return to the systems resting volume shown in column 2.

You can think of the thorax like a spring, when it's below 75% TLC it is compressed and wants to expand. If you remove the compression it will expand.

Now we ask ourselves, why are the lungs trying to collapse? What is the nature of the collapsing forces of the lungs? This brings us to the concept of the work of breathing.

Work of breathing

$W = \Delta V \times \Delta P$

W= Work of breathing

ΔV is the change in volume (Tidal Volume)

ΔP = Change in pressure

At rest, the body uses energy to inhale and doesn't when exhaling. This typically is a very energy efficient system and only uses about 5% of the total ATP usage in a typical person. However, in some pathological conditions where the respiratory system is involved, this percentage can increase to much higher values resulting in fatigue and even death.

The work needed to breathe in a normal breath can be calculated by seeing how much we must change the pressure to get the volume change of 0.5L (tidal volume). The higher the pressure, the greater the amount of work required. What exactly do we need to work (expend energy) to breathe? We need energy to overcome two types of forces.

1) Non-Elastic forces

2) Elastic forces

1) Non-Elastic Forces:

Non-Elastic forces are responsible for 30% of the work of breathing. This is a dynamic force; this force only needs to be overcome when there is airflow (during inspiration). For example, airway resistance isn't faced when there is no inspiration or expiration.

Non-Elastic forces consist of…

-Airway Resistance (Contributes about 80% of the force.)

-Tissue Viscosity: Resistance is due to the non-elastic parenchyma of the lung. They will resist movement during inspiration and expiration. This tissue is not elastic. (Contributes about 20% of the force.)

2) Elastic Forces:

Elastic forces are responsible for 70% of the force needed to overcome while breathing. This is a static force; it still exists even when we are not breathing.

1) Surface tension - 2/3 of the elastic force we must overcome.

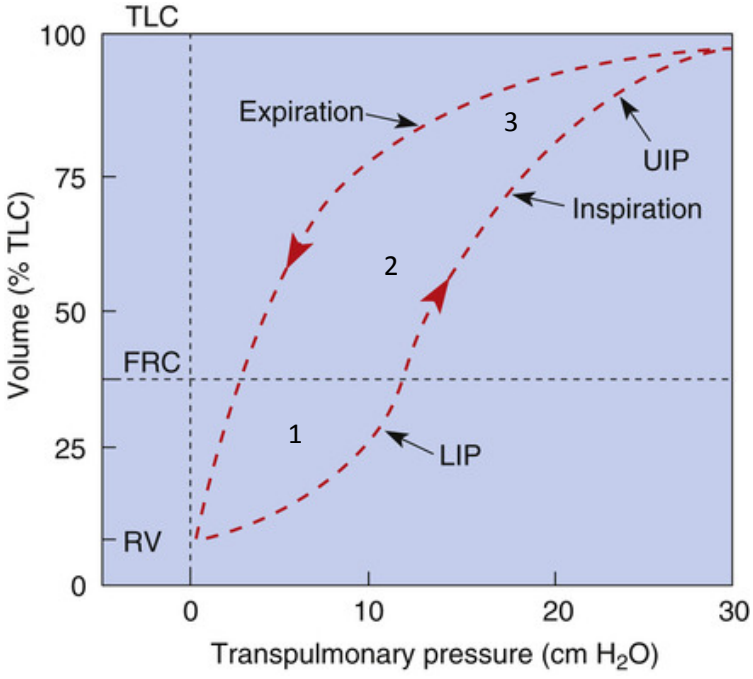
2) Elastic fibers (Elastin and collagen) - 1/3 of the elastic force we must overcome.

Inspiration Curve

Remember, The slope of this curve equals compliance (ΔV/ΔP)

Looking at the graph, we can divide the inspiration curve into three phases.

In the **first** phase, you will notice the pressure change from 0 to 10 takes a lot of force (large change in pressure) for a little change in volume. At first it is very difficult to inflate our lungs. And then all of a sudden, at the critical opening pressure(Labeled LIP on this particular graph), the lung compliance sharply increases.And this is the



beginning of phase **two**. So what happened?Alveoli recruitment. The alveoli recruit each other and it becomes easier to inflate the lungs (higher compliance).

At stage **three**, the lungs become stiff again, low compliance. As explained in lecture 4, this is the apical alveoli that are already inflated and their compliance is low. During tidal volume, most of the air goes to the base and not the apex because the apical alveoli are already inflated. (Explained in lecture 4)

By looking at the graph, we can see it is unwise to deflate our lungs to our residual volume (after forceful exhalation). Our lungs are not very compliant when we try to inflate it from this low volume. It is better to keep the alveoli inflated in order to keep them in a more compliant state and to preserve energy. If a patient had a disease where they go to minimum volume every time s/he exhales, we know this person will spend most of his/her energy to support the respiratory system and will suffer and possibly die from fatigue. That is why these balancing compression and expansion forces are so important.

In a resting state, we breathe at a very compliant state regarding the lung. On the graph, we can see the slope is very steep at the FRC volume and tidal wave volume.

Expiration Curve

Now lets talk about the expiration curve. The "deflation" curve follows a different pathway than inspiration. Whenever the forward process isn't the same at the backward process, we call this hysteresis.

It is much more efficient to leave the alveoli partially open rather than closing themevery time we breathe out. Now looking at the graph as a whole, the first thing we should notice is at the same volume, the pressure is different depending if we're inflating or deflating the lungs. By looking at both curves at FRC (2.2L), we notice the lungs at the same volume have different transpulmonary pressures comparing inspiration and expiration. To reach FRC from a higher volume by exhaling, we only need about -4 in pressure. However, when going to FRC from residual volume we could need -6.

If you are reaching the FRC by ascending, you'll need more pressure compared to descending.

Why is this?

Now, lets take the deflation curve only. The deflation curve only needs -4 pressure. What do we need the -4 pressure to overcome? Surface tension and elastic fibers (The elastic forces). This graph doesn't measure the amount of force needed to overcome

non-elastic forces because when we gather the data points for this curve we measure the volume and pressure when the lung is static, after the change of volume and pressure has taken place.We measure AFTER we change the volume, not during.

So we are left with these twoelastic forces (Surface tension and Elastic Fibers).

Surface Tension

Surface tension is the force at the water-air interface (a force resulting from water interaction with air). Water molecules are polar and are attracted to one another. Because of this, they will attempt to gather causing the alveoli to shrink. That is why surface tension is a collapsing force.

To prevent this from collapsing, we need an expanding force equal and opposite to it.

We can now apply law of Laplace. This law is able to determine the pressure needed to be exerted in order to keep the alveolus open.

P = Collapsing pressure on alveolus (AKA pressure required to keep alveolus open

T = Surface tension

R = Radius of alveolus

$P = (2T)/r$

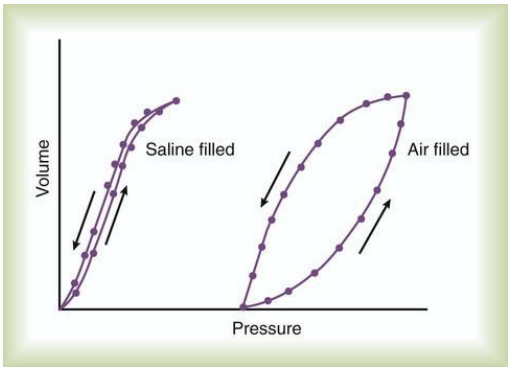
LAW OF LAPLACE

At FRC, the diameter of the alveolus is between 100-200 micrometers. However, if you are talking about a premature baby, the diameter of his/her alveolus is even smaller. According to the equation above, pressure and radius are inversely proportional. As a result, you will need a lot of pressure to overcome the surface tension.

What if a baby is suffering from increased surface tension due to surfactant deficiency? The pressure could now reach up to -30. This means we need muscle contractionsthat utilize ATP to overcome this collapsing force.

Elastic Fibers

We have two collapsing forces: surface tension and elastic fibers. How can we separate surface tension from elastic fiber forces so we can analyze themseparately?



We can fill the lung with saline solution 0.9% NaCl. By doing this, there is no surface tension and no water-air interface. Now the lung only needs to overcome the elastic fibers, not the surface tension, to inflate.

The curve with a saline solution filled lung is the curve on the left. In saline there is no hysteresis. We needed less pressure during inflation and deflation. So this graph shows the amount of pressure needed to overcome the elastic

fibers. The remaining force is to overcome the surface tension. This shows what we said earlier to betrue; elastic fibers contribute to 1/3 of the force and surface tension 2/3.

Surfactant

Surfactant deals with surface tension.

$P = (2T)/r$

Again, surface tension is a collapsing force. To overcome this we need the expanding force of the negative intrapleural pressure. How much exactly? We need to apply the Law of Laplace.

If the alveolus is lined form the inside with water, applying the Law of Laplace, we need about -21mmHg of inflation pressure.

If the alveolus is lined with interstitial fluid (like plasma), not water, we need only -13mmHg. Less force is needed. This indicates plasma has a lower surface tension than water.

If we line the alveolus with surfactant, "Surface active agent", then we only need -4mmHg of pressure. Surfactant lowers surface tension. How does surfactant do this?We should first look at its composition:

Glycolipoprotein + calcium ions

2% carbohydrates

90% lipids

8% protein

The lipid portion is a phospholipid. The phospholipids have a charged glycerol backbone (head) and 2 non-polar fatty acid tails. This is secreted by Type II alveolar cells and coats the inner wall of the alveoli.

The best orientation of the surfactant is having the non-polar tails facing the air (lumen) and polar end facing the alveolar cells. If they are flipped and the fatty acid tails are facing the alveolar cells and the polar backbone heads are facing the lumen, this is an ineffective orientation for surfactant.

This can be explained by….

When I start inflating my lungs, I start with very small alveolus(to the point the walls are touching each other). Each alveolus, regardless of size, has about the same amount of surfactant. So if we decrease the surface area, the concentration of surfactant per area in the alveolus will be higher than when it

is expanded. The total amount of surfactant stays the same, but the concentration changes. Now during inflation, the surfactant will spread and they will be in an improper orientation. Again, the improper way is when the hydrophilic portion is facing the air (lumen). So this makes the surface tension higher. However, when coming from a low concentration per area to a higher concentration (in deflation), it seems they are oriented correctly. So this will make the surface tension less during exhalation.

Now, type 2 alveolar cells make surfactant,sometimes, after week 20 of gestation. At week 34 of gestation, the lungs are almost mature and have a proper amount of surfactant.

When a premature baby is born, we are afraid of the baby not having enough surfactant and thus having too much surface tension in the alveoli. Also, the radius of the alveoli is small. This results in a very high pressure making it difficult for the baby to breathe. So with each inhalation, the baby will expend a lot of energy and have trouble breathing. The respiratory rate could rise to about 60. The baby will suffer from dyspnea. This will lead to Infant Respiratory Distress Syndrome.

IRDS

-Infant Respiratory Distress Syndrome

-Mortality rate very high

-Highest cause of death in western countries, not in developing countries.

-More prominent in diabetic mothers to give birth to premature babies

-Lungs are immature

-We can give the mother two shots of glucocorticoids (Cortisone); this will stimulate the production of surfactant. Surfactant needs thyroxin, prolactin, estrogen, etc.

-Deficiency in any of these will cause problems (especially in glucocorticoids).

Treatment:

We can try to delay the pregnancy; Delaying birth for one day could make a difference. But it could be life threatening to the mother, especially if she has eclampsia.

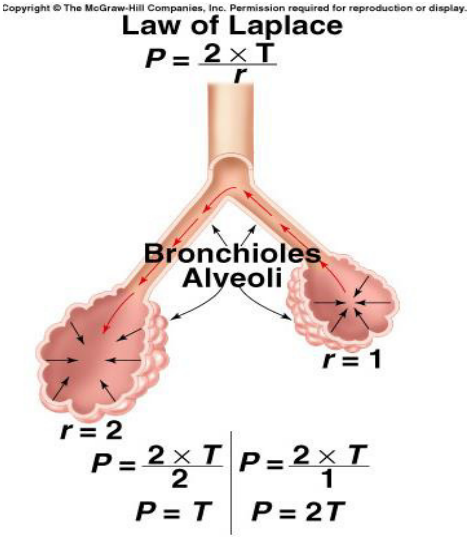
We know whether or not to treat the pregnant women by counting the number of weeks from the last menstrual cycle.If she is currently under 30 weeks, we give her a dose of glucocorticoids immediately.

If she surpassed the 30week mark, we aren't sure whether or not the lung has matured yet. We can run some test to determine that. We take a sample of the amniotic fluid surrounding the baby and test for markers. The first thing we can look for is the **Lecithin:Sphingomyelin** ratio. Normally, it should be 2:1. This reflects mature levels of surfactant. We can also look for the presence of **phosphatidylglycerol**:a sign of lung maturity. The most recent method being used is taking the **Surfactant:Albumin** ratio. Albumin is measured in grams and Surfactant is measured in milligrams. If the ratio is more that 55, it means the baby is producing enoughsurfactant for respiration. If it is between 35-55, this is the borderlinevalue, we would consider the test to be inconclusive. If it is below 35, the lung is definitely immature.

What is the significance of surfactant?

Lets talk about the alveoli at the apex of the lung.

The pressure to keep these alveoli open can be determined with the law of Laplace. The radius of one alveolusis small, meaning it needs more pressure to expand. And the other is larger. However, these two alveoli are surround by one expanding pressure. So automatically, the smaller one will collapse because it isn't surround by enough pressure and it will empty its contents into the neighboring alveoli. So we now have a completely collapsing alveoli and a hyper-inflated alveoli in the same region. This means that a small alveoli and large alveoli cannot coexist in the same region of the lung because of the law of Laplace. However, surfactant can help us change that. When the radius is small, the surfactant is more concentrated. It will be spread over a smaller area. So it makes surface tension smaller, keeping pressure constant. So -8 is enough to support the small and large one. This is called alveolar stability. This means small alveoli can coexist with large alveoli in the same region because of surfactant. Surfactant makes surface tension volume-dependent. More volume leads to more surface tension. Less volume leads to less surface tension.



So surfactant is very important! For a number of reasons….

1) Reduces surface tension

2) Makes surface tension volume-dependent

3) Promotes alveolar stability

4) Prevents occurrence of pulmonary edema (Discussed at the end of this sheet)

5) Decreases the work of breathing.

CPAP and PEEP

The decrease in pressure in the trachea follows a gradient. It slowly starts at -.25, then to -.5, to -1. When the baby is born, the cartilage is soft, and every time the baby breathes there is a risk that this negative pressure will collapse the trachea.

In this case, we will likely give the baby CPAP (Continuous positive airway pressure). For this to work he needs to breathe spontaneously. We keep the pressure in the airway positive in order to keep the respiratory tract and alveoli open. (Positive pressure inside helps with expansion).

PEEP (Positive End-respiratory pressure by incubation machine respirator)is the maintenance of positive pressure in the lungs even at the end of expiration. We do not want to make the pressure too positive because if we make it too positive we will obstruct the capillary blood flow and we will have wasted ventilation (No gas exchange).

Pulmonary Capillaries, Sterling Forces, and Lymph

This is the pulmonary capillary.

PC = -10, this is an outward force.

Pi C = 28, this is an inward force.

PI = -5, an outward force. Pi = -14, an outward force.

There are too many proteins here, they are leaky to proteins. So the outward forces is 10 + 5 + 14 = 29; the inward forces are only Pi C = 28, meaning we have more filtration than reabsorption. However, the lung must be kept 100% dry. Wet lungs are not tolerated because they would interfere with gas exchange. The lung is rich in lymphatics. The right lymphatic duct takes care

of the leaked proteins and the extra fluids present. Even if your PC rises to equal Pi C, pulmonary edema will still not occur because of right lymphatic duct. It takes care of most of the lymph in the lung. A small portion of the left apex drains into the thoracic duct. The thoracic duct is a major duct; it carries 100ml of lymph per hour to the subclavian vein, while the right lymphatic duct drains 20ml per hour. Sothere is 120ml of lymph being drained in total. So in 24 hours, around 3 liters is drained. That is what is filtered, not reabsorbed from the systemic capillaries. So here if there is no surfactant, that means intrapleural pressure becomes -30, it was -5 from starling forces. That means it increased by a value of 25, and the outside pressure increased to 26, this is too much, this baby will definitely suffer from pulmonary edema because the intrapleural is too negative and will suck out too much fluid from the capillaries to fill in the alveoli. The baby will die. What killed him? The pulmonary edema will cause hypoxia and lead to pulmonary hypertension. The increased pressure in the pulmonary trunk/artery (due to pulmonary hypertension) will open the ductusarteriosus leading to a right to left shunt and deoxygenated blood will go to the systemic blood. The foramen ovale may open also.

(The doctor was all over the place and wasn't very clear in this last section of the sheet. I think his main point was we have more filtration than reabsorption at the pulmonary capillaries and that without surfactant the lymphatic systemcan't keep up and keep the lungs dry, leading to pulmonary edema.)

The End