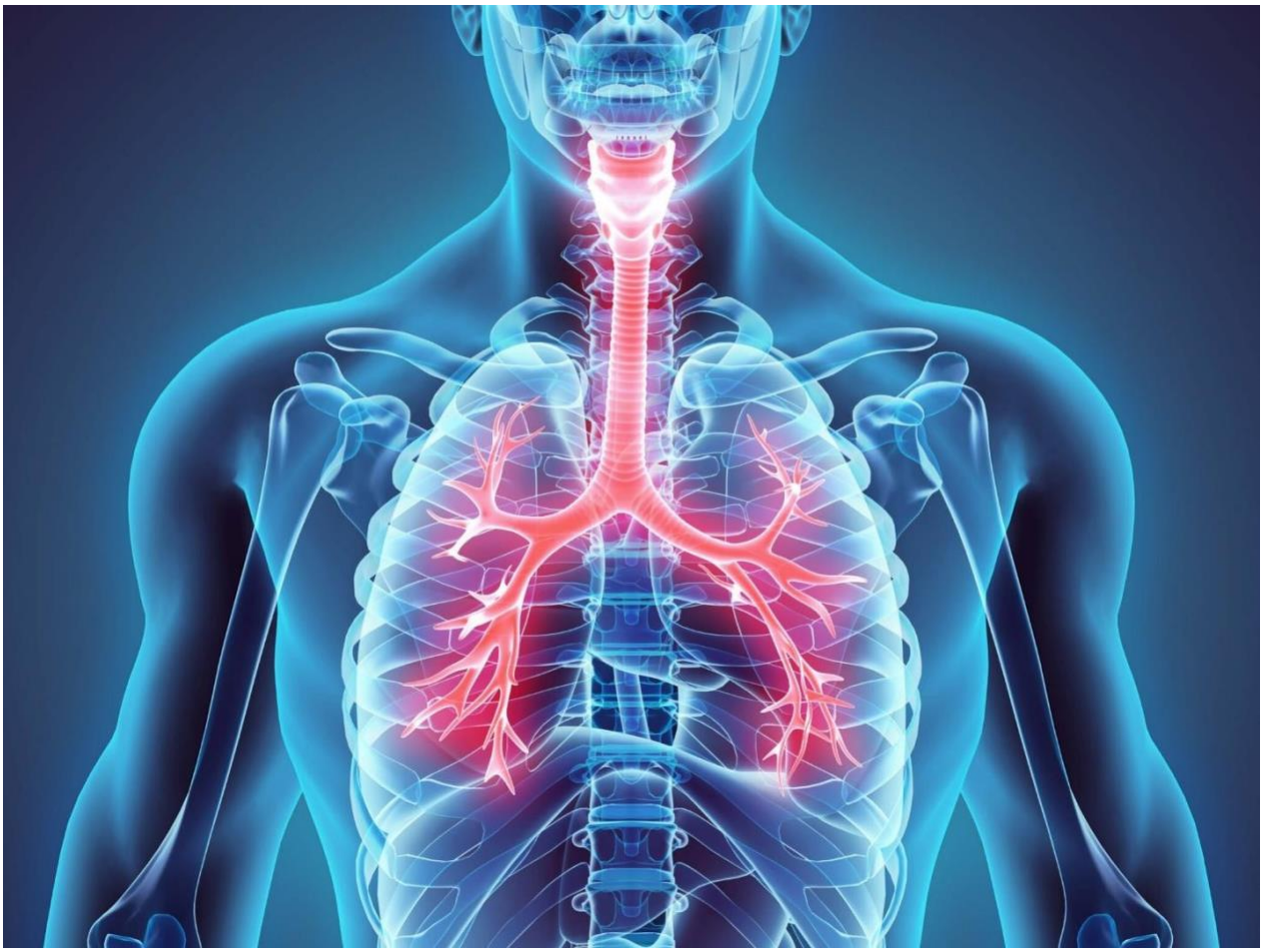


Respiratory system physiology

Doctor Yanal Shafagoj's notes

Written by Noor Mosleh, Shahed Nasser

Corrected by Dima ALrafaiah

• Mechanics of breathing (ventilation)

The movement of air in (inspiration-inhalation) or out (expiration-exhalation) is considered a flow.

Flow=difference in pressure/resistance (airway R)

- ✓ The pressure difference is measured between the atmospheric pressure (P_{atm}) and the alveolar pressure (P_A)
- ✓ we consider the atmospheric pressure at sea level (760 mmHg) as our **point zero**, anything above it is positive while anything below it is negative.

1. Inspiration (inward airflow)

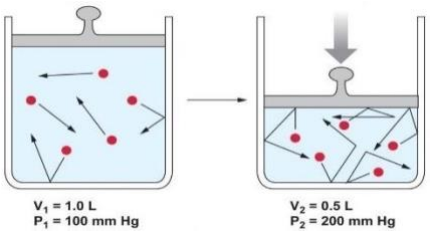
- If we assume P_{atm} = 760 mmHg = 0
- And P_A = 760 mmHg = 0

The net pressure difference would be zero, and the flow will equal zero too. So, we can conclude that if an **inward** flow is to be created you either need to:

- Increase the Patm, a process called **positive pressure breathing**. It's done when a patient is intubated in the ICU and connected to a respirator.
- Decrease the P_A, a process called **negative pressure breathing**. Which is the physiological way of breathing.

How is this negative pressure created, how to decrease alveolar pressure?

According to Boyle's law, an increase in volume results in a decrease in pressure. which makes sense because with a larger volume for the same amount of air, there is a reduced likelihood of air particles hitting the walls of the container and each other. Consequently, the pressure decreases. Simply put, to generate negative pressure; the lungs must be inflated.



Boyle's law: the pressure and volume of a gas in a system are inversely related if the temperature is kept constant

$$P_1 V_1 = P_2 V_2$$

But how do they get inflated?

The lung functions like an elastic balloon, always tends to collapse. Consequently, the pressure within the pleural space is negative, typically around -4 mmHg. This negative pressure serves as an **expansive force**, preventing the lungs from collapsing and pulling them outward. This pressure represents the counterforce against collapse; as the collapsing force increases, the intrapleural pressure must become more negative and vice versa.

The pressure that we are talking about here is called the **intrapleural pressure**, when it becomes more negative (from -4 to -6 for example) the lungs inflate. The reduction in intrapleural pressure is **done by the expansion of the thoracic cavity as the diaphragm descends down and the external intercostal muscles contract.**

Going over the sequence of events:

1. The diaphragm descends.
2. Increased size of the thoracic cavity.
3. More negative intrathoracic/intrapleural pressure.
4. Lungs inflate.
5. More negative P_A.
6. Flow of air inwards.

It's not the air that inflates the lungs, rather, an inflated lung is what pulls the air inwards.

This will make P_A= -1 while P_{atm}= 0 → inward air flow.

During inspiration, atmospheric pressure (Patm) is greater than alveolar pressure (PA). However, at the **end of inspiration**, they equalize, stopping the airflow. This happens because as air enters the lungs, it counteracts alveolar pressure (PA), bringing it back to zero.

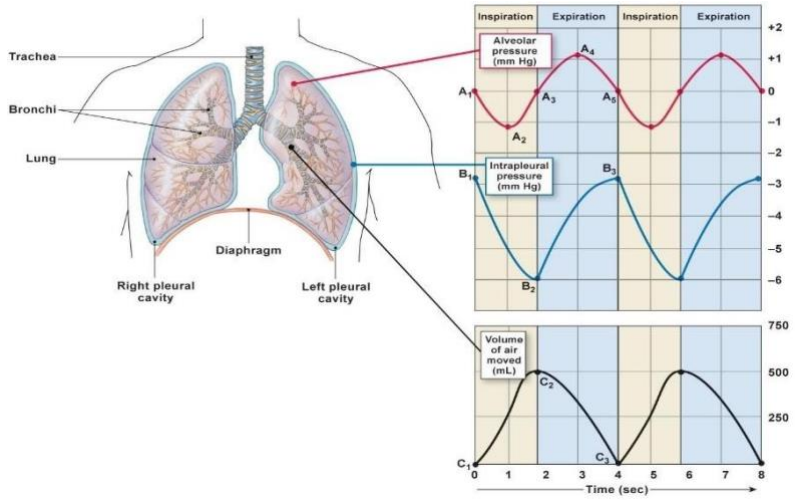
2. Expiration (outward airflow)

Towards the end of inspiration, we reach a point where Patm=PA=0. To initiate an outward flow, you can achieve this by either reducing Patm or increasing PA. Physiologically, increasing PA involves:

- Allowing more air to enter the lungs (initial lung volume: 2200ml, and after inhalation completion: 2700ml).
- Creating a less negative intrapleural pressure (from -6 back to -4) through the relaxation of the diaphragm and expiratory muscles

This makes P_A= +1 while P_{atm}= 0 → outward air flow.

During expiration, atmospheric pressure (Patm) is less than alveolar pressure (PA). However, by the **end of expiration**, they equalize, bringing the airflow to a stop. This equalization occurs as air exits the lungs, returning alveolar pressure (PA) back to zero.



Notice how P_A in the red graph decreases during inspiration, goes back to zero then increases during expiration.

- **Ps. Inspiration is an active process, it requires ATP because it involves the contraction of the inspiratory muscles (the diaphragm and external intercostals). While the process of expiration is a passive one that requires the relaxation of the inspiratory muscles. With that being said, the respiratory machine is very efficient, as it only consumes 2% of energy expenditure, leaving 98% of ATP for the rest of the body. In respiratory distress syndrome the babies die from fatigue (not enough ATP) because the lungs are using 80% of ATP for inspiration.**

- ## Pulmonary function test

There are 4 pulmonary volumes and 4 pulmonary capacities, which are parts of the pulmonary function test.

We do PFT to:

1. Find the type of pulmonary disease (obstructive, restrictive or vascular)
2. Monitor how the patient is responding to treatment.
   And other reasons…

1.Pulmonary volumes

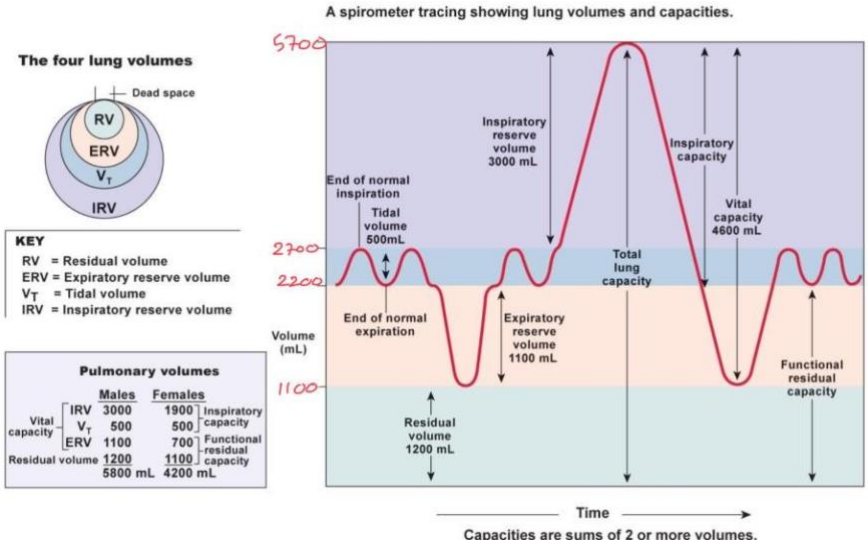
The volume of air in the lungs at rest is 2.2L.

1. **Tidal volume VT**: the volume of air that moves in and out with quiet breathing. For example, If the volume at rest is 2.2 L and becomes 2.7 L at the end of inspiration the tidal volume is 0.5 L.
2. **Inspiratory Reserve Volume IRV**: The extra air drawn **in** with force beyond VT, where lungs are filled to capacity. If the volume at the end of inspiration is 2.7L with quiet breathing, it can increase up to 5.7L by forced inhalation (using all inspiratory muscles). This additional volume of 3L is called IRV. (5.7-2.7=3)
3. **Expiratory Reserve Volume ERV**: the extra air pushed **out** with force beyond VT (residual volume remains in lungs). When the lung volume is at 2.2 liters, it's possible to achieve a volume of 1.1 liters through forced exhalation, utilizing all expiratory muscles. This volume of 1.1 liters is referred to as the (ERV), (2.2-1.1=1.1)
4. **Residual volume RV**: The remaining volume after forced exhalation is the RV, it’s about 1.1 L.

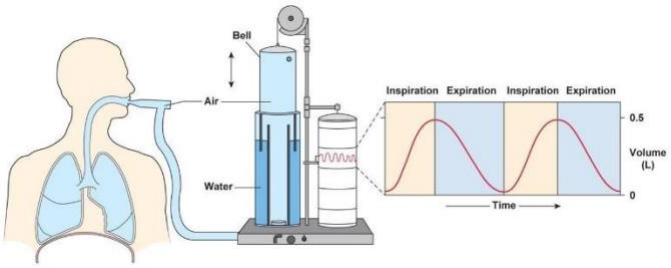
2. Pulmonary capacities (capacity=sum of two volumes)

They are obtained by adding pulmonary volumes.

1. **Inspiratory capacity**:
   - ✓ most air you can inspire (V_T+IRV) = 3.5L
2. **Functional residual capacity FRC**:
   - ✓ residual volume after quiet expiration (ERV+RV = 2.2L)
   - ✓ volume when the system is relaxed
   - ✓ point of equilibrium (chest wall pulling out = lungs pulling in)
3. **Vital capacity**:
   - ✓ The amount of air you can exhale forcefully following forced inspiration, by the contraction of your expiratory muscles (the internal intercostals and the muscles of the abdominal wall) (ERV+IRV+VT) = 4.6L
4. **Total lung capacity TLC**: IRV+V_T+ERV+RV = 5.7L
   - ✓ the volume of air both lungs can take.



- To measure pulmonary volumes, we use a **spirometer**. It measures the amount of **inspired or expired air.**
- However, **RV cannot be measured using a spirometer** because it only measures moving air (inspired or expired), while RV is always present in the lung therefore it cannot be measured. So, there must be another way to measure RV and capacities that involve it (FRC & TLC).



- One way is **helium dilution technique.**

In a respirometer, there is an initial known volume of air (V1) that contains a known concentration of helium (C1). The person using the respirometer is instructed to breathe until an equilibrium is established. During this process, the helium present in the initial volume gets mixed and diluted within the final volume (V2). As a result, a new concentration of helium (C2) is achieved in the final equilibrium state.

$$C1 \times V1 = C2 \times V2$$

C1: the concentration of helium in the respirometer at the beginning.

V1: the volume of air in the respirometer at the beginning

C2: the final concentration of helium

V2: the final volume which basically V1 + FRC (FRC is the amount of air in the lung initially)

$$C1 \times V1 = C2 \times (V1 + FRC)$$

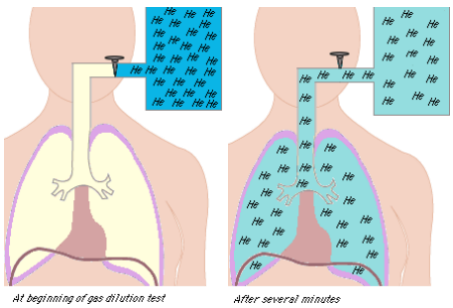
$$\mathbf{FRC = \frac{V1\ (C1 - C2)}{C2}}$$

V1 & C1 are known, C2 can be measured. We can find FRC.

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

We found FRC and we can get the value of ERV from the spirometer, finally we have RV.

- Why did we use helium? Because it's a non-absorbable gas.



• Minimal volume of the lung

If the lung is left in vitro outside the thorax, without the influence of the intrapleural pressure, it will naturally collapse on itself. Because, as mentioned earlier, the lung is an elastic ballon. In its natural resting state within the thorax, the lung volume is 2.2 L (this is the value of FRC). However, in vitro the lung collapses until it reaches a volume of 0.15 L. this **volume at which the lung has fully collapsed onto itself and no longer has a tendency to collapse, is called resting/minimal/unstressed lung volume.** (it's the smallest volume the lung can attain without external influences)

Application: minimal volume in medico legal purposes

- A dead baby is brought by its parents to the hospital, they claim that the baby was born dead. Forensic medicine can confirm their story by dissecting the lungs and putting them in a water bath. if they float, this means that they have a minimal volume, and the baby took a breath before dying meaning it was alive and died after birth. If they don't float, this means that they don't have a minimal volume and the baby was born dead.

*The lungs of any dead person that was once alive will have a minimal volume

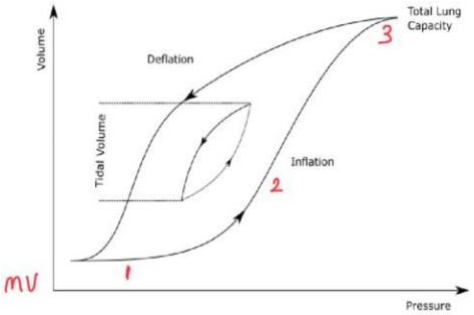
• Compliance curve of the lung

Remember that in order to inflate the elastic balloon (the lung) we need to create a negative intrapleural pressure, that will generate an outward inflation pressure; we will call this pressure **transpulmonary pressure (alveolar pressure – intrapleural pressure)**. It is a measure of how much force is needed to inflate the lung at a certain volume. So, if we draw a curve that illustrates the relationship between the inflation pressure and the volume of the lung, the slope of this curve $\Delta V/\Delta P$ would equal the **compliance**.

- ✓ **compliance** could be defined as how much change in volume can be achieved per unit pressure, how much force we need to expand the lung. C = **$\Delta V/\Delta P$**

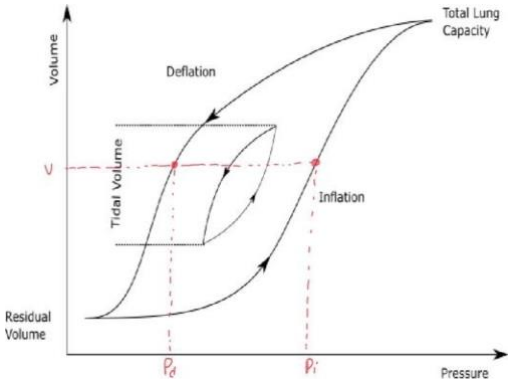
- ✓ a compliant lung requires small amount of diaphragm effort, generates small pressure change across lungs, accompanied with a large volume change and it's easy to move air in and out across it (stretchable).

➢ Inflation (inspiration) curve



- (phase 1) when inflation (inspiration) starts at the minimal volume MV, there will be **little change in volume opposed to the increase in pressure**. The lung is not compliant. The slope is almost 0.
- (phase 2) **the volume is increasing with increasing pressure**. The lung is most compliant here. The slope is positive.
- (phase 3) max volume is reached, and no more inflation can happen with increasing pressure. The lung is not compliant.

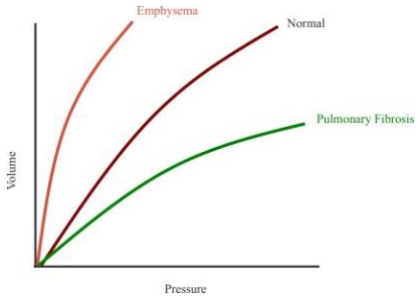
➢ Deflation (expiration) curve



If we look at the deflation (expiration) curve, we observe a difference: the pressure required to keep the lung inflated at a specific volume is less than that in the inflation curve. This disparity in the forward and backward processes is known as **hysteresis**.

- ✓ Hysteresis in the lung's pressure-volume curve is attributed to the influence of **surface tension**, a force acting at the air-liquid interface within the alveoli. **During inflation**, overcoming surface tension requires additional pressure, leading to a higher-pressure requirement. Conversely, **during deflation**, surface tension aids in maintaining alveolar patency, and pressure was to overcome the elastic fibers only. Resulting in a lower pressure requirement to keep the lung inflated at the same volume.

The optimal volume for the lung is during phase 2 of the inflation curve, as it represents the point of maximum compliance.



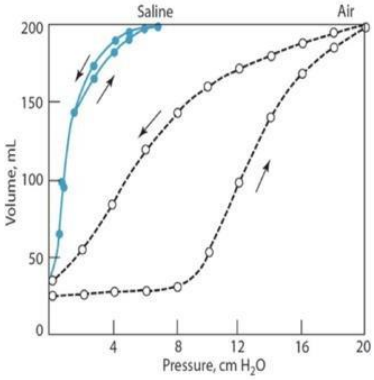
The deflation curve is often depicted as the compliance curve of the lung.

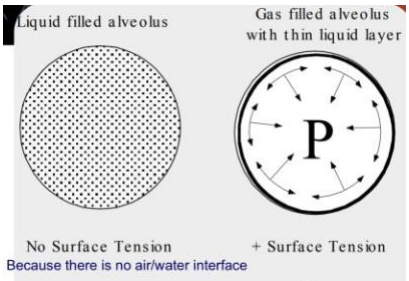
- It shifts to **the left in emphysema** (compliance increases) and **to the right in pulmonary fibrosis or RDS** (compliance decreases). The explanation lies in the factors influencing lung compliance, primarily the collapsing factors that act to reduce compliance;
  - ✓ Two-thirds of these forces are attributed to **surface tension**, an attractive (inward) force between water molecules.
  - ✓ One-third arises from **elastic fibers,** providing a recoil force.

As following..

- In emphysema, the destruction of elastic fibers reduces recoil, increasing compliance resulting in hyperinflation and increase in TLC, FRC, and RV. This is a bad thing because recoil is crucial for passive expiration. Without adequate recoil, the process of expiration becomes active.
- In fibrosis, there is limited lung stretchability, resulting in decreased compliance.
- In RDS, elevated surface tension, diminishes compliance.

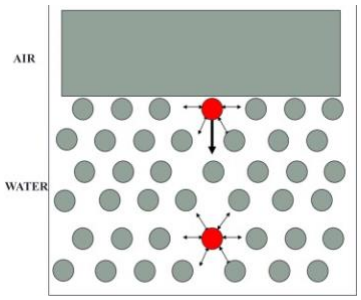
- We can cancel the surface tension by filling the lung with saline, replacing the air, so there's no air-water interface, no surface tension





- ## Surface tension
  - ✓ The alveoli are lined with a film of liquid, and the liquid-liquid forces tend to pull the surface area together and form a sphere, this liquid-liquid forces are called Surface Tension.
  - ✓ Surface Tension is a measure of cohesive forces among liquid molecules at a surface, an interaction between the thin layer of fluid lining the alveoli and the air.

– Law of Laplace is an equation that is used to determine the collapsing pressure of the alveoli that we need to overcome, and it's related to surface tension.



$$\text{Collapsing Pressure} = \frac{2 * (\text{surface tension})}{\text{radius}}$$

– Collapsing pressure is the forces that tend to collapse the alveoli, low collapsing force means there are relatively few forces trying to collapse the alveoli and it's easy for an alveolus to remain open (less opposing negative pressure is needed). In contrast, high collapsing pressure means it's difficult for alveolus to remain open (more work, more ATP, fatigue).

– The law of Laplace has important implication for our lungs since they contain many small alveoli with **a very low radius** (a very high collapsing pressure). So in order to balance out the small radius and keep our alveoli open, we need to have **really low surface tension**, and that's what surfactant does!

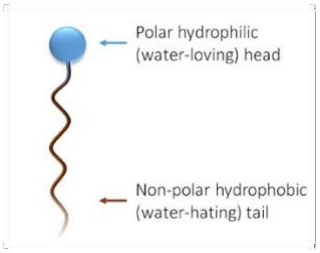
– **Surfactants**

✓ Prevents collapse of alveoli during exhalation, by reducing surface tension. thus, reducing collapsing pressure.

✓ Increase lungs compliance and maintain their elasticity making them less stiff. Which in turn, increases the efficiency of gas exchange.

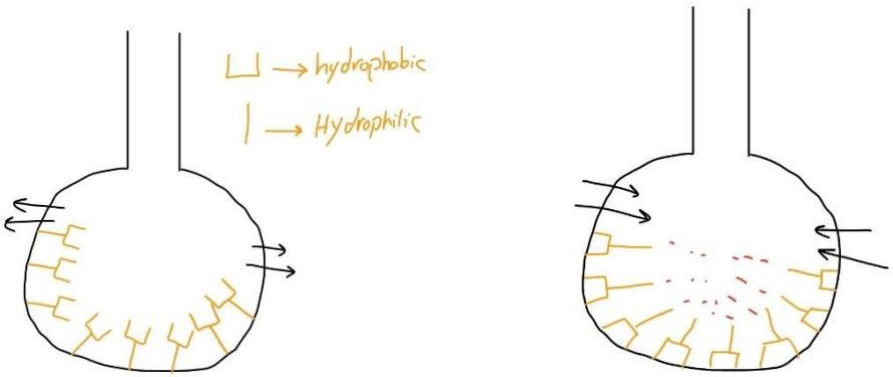
- ✓ Secreted by type 2 pneumocytes, a mixture of lipids and proteins (glycolipoprotein), lipids (90%), glyco (2%), protein (8%) and calcium ions.

Primarily composed of **phospholipids**, which consist of:

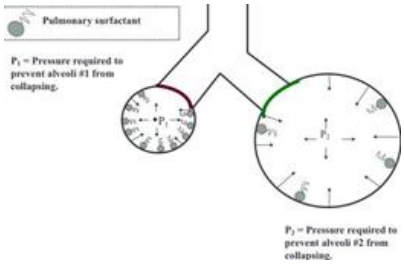


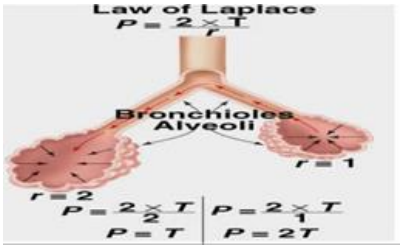
1. Glycerol (polar hydrophilic head)
2. 2 fatty acid chains (non-polar hydrophobic tail)

- ✓ The surfactants align themselves at the Air-Liquid interface, in which their hydrophobic tails are oriented inward toward the air, and their hydrophilic heads are oriented outward toward the alveolar fluid. This orientation creates a barrier that reduces attractive forces between water molecules reducing surface tension.



If we could have a large alveolus with a large radius that would be the most perfect case, because we'll have a low collapsing pressure. Unfortunately, we don't, we have millions of small alveoli (to make for the large surface area needed for gas exchange) that tend to collapse. But if we add surfactant and break up those liquid-liquid forces surrounding the alveoli, we can convert the high collapsing pressure into a low one, and that's what our lungs do. another advantage of surfactants is **alveolar stability, which means that the presence of surfactant makes it possible for small alveoli to coexist with large alveoli**. Since small alveoli have a smaller radius they would collapse because they have much more collapsing forces than those with a larger radius, the solution lies in the fact that smaller alveoli have more concentration of surfactant which decreases the surface tension to a point where it balances out the small radius, which allows these smaller alveoli to have equal collapsing forces to the larger alveoli making it possible for them to coexist.Another factor that contributes to stability is the attraction forces between adjacent alveoli.

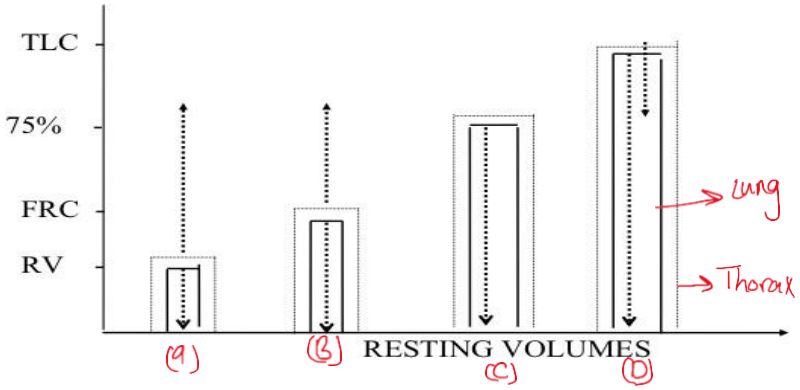




- **The lung – thorax system dynamics**
  - Is comprised of two balloons: the external one being the thorax, which tends to expand, and the internal one being the lung, which tends to collapse.

  With changing volumes of both (lung & thorax), the balance between collapsing and expanding forces changes. For example:
  - There's a volume where these forces balance, and the lung no longer wants to collapse, THE Functional Residual Capacity. At this point **dynamic equilibrium is established where the tendency of the lung to collapse is equal to the tendency of the thorax to expand.**
  - While the volume at which the thoracic cavity loses its tendency to expand is equivalent to 75% of Total Lung Capacity (TLC), which is 4.5 liters out of 6 liters.

- ❖ **The compliance of the combined lung-thorax system** (in vivo) is almost exactly **one-half** that of the lungs alone (in vitro).
- ✓ measuring **100 milliliters of volume per centimeter of water pressure** forthe combined system, compared to **200 ml/cm** for the lungs alone (in vitro). But why?
- ✓ In vivo, you are dealing with two balloons being filled, not just one as in vitro. Additionally, the lung in vitro is not surrounded by negative intrapleural pressure, whereas in vivo, it is located within the chest cavity.



B) Inspiration from Functional Residual Capacity (FRC):

Normally, inspiration initiates from the Functional Residual Capacity (FRC) level, approximately 2.2 liters. At this point, the lungs are partially inflated and highly compliant, signifying the system's resting state. The **collapsing tendency of the lung is counterbalanced by the expanding tendency of the thorax, establishing equilibrium and a state of rest**.

A) Below FRC - System Tends to Expand:

If the volume is below FRC, the system leans toward expansion, leading to the intake of air into the lungs. Since the system is leaning towards expansion, **inspiration at this volume is passive** and requires no effort (try to forcefully exhale then relax, you notice that air gets in without effort)

C) Volume Higher Than FRC (75% of TLC):

When the volume is higher than FRC, specifically at 75% of Total Lung Capacity (TLC), the thorax loses its tendency to expand, combined with the increased

collapsing tendency of the lung, **results in an overall inclination of the system to collapse.** Since the system is leaning towards collapse, **expiration is passive** at this volume. When one takes a breath normally, they bring the volume of their lungs to 75% of TLC, this is why we said earlier that expiration is passive, but as we noted in the previous point this is not always the case, but it is the case with normal respiration.

D) Total Lung Capacity (TLC):

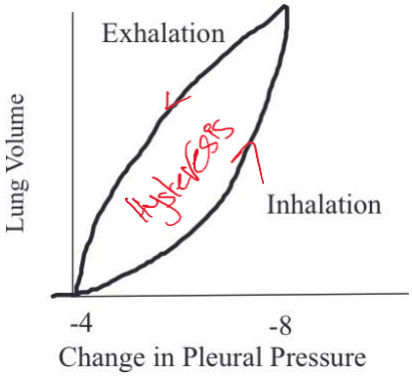
Upon reaching Total Lung Capacity (TLC), **both the lung and the thorax exhibit a significant inclination to collapse**.

- To maximize lung capacity, closing your mouth and nose while relaxing the muscles is possible, though it proves to be a challenging task.

"If the system tends to collapse, expiration is passive. Conversely, if the system tends to expand, inspiration is passive."

- ✓ Remember, when you want to stretch a rubber band, you need to apply force to change it from its resting state. To return it to its resting state, you only release the force.
- ✓ The same principle applies to any elastic tissue, including our lungs:

Moving any elastic structure from its resting state requires a driving force, an **active process during inhalation**. Bringing this elastic tissue back to its resting state is **passive due to the recoil tendency during exhalation**.



- **Work of breathing**
  - The work of breathing involves the consumption of ATP to expand both the thorax and lungs, resembling the inflation of two interconnected "balloons."
  - Roughly 50% of the work is dedicated to thorax expansion, while the remaining 50% is to lung inflation.
  - The work formula considers the difference in pressure (Δp) multiplied by the difference in volume (Δv).
  - Work in the respiratory system can be categorized into two major types:

✓ Work to Overcome **Elastic Forces (70%)** (Static): This type of work is required to expand the lungs against the elastic forces of the lung and chest. Approximately two-thirds of this work is due to surface tension, and one-third is due to elastic fibers.

✓ Work to Overcome **Non-elastic Forces (30%)** (Dynamic): This work is required to overcome: The viscosity of the lung and chest wall structures (20%).and Airway resistance to movement of air (80%).

- ## Infant Respiratory Distress Syndrome (IRDS)

1) Pathogenesis

✓ occurs in premature infants due to underdeveloped lungs and **insufficient surfactant production.**

✓ Surfactant, crucial for proper lung function, is lacking in premature babies, causing **elevated surface tension** and difficulty in maintaining lung inflation.

✓ Surfactant production typically begins around week 24 of gestation, reaching completion by weeks 34 to 36.

✓ infants may **have a rapid respiratory rate** (e.g., 60 breaths/minute compared to the normal 12-16), expending substantial ATP, risking fatigue and **shifting to anaerobic respiration**, possibly leading to **life-threatening lactic acidosis**.

2) Intervention

✓ involves CPAP (Continuous Positive Airway Pressure) or PEEP (Positive End-Expiratory Pressure) via a ventilator.

3) Risk factors for IRDS include;

✓ gestational age, maternal diabetes, and family history.

4) Lung maturity markers

✓ assessed by the lecithin/sphingomyelin ratio and surfactant/albumin ratio in amniotic fluid.

a. >55: mature lung

b. 35-55: intermediate

c. <35: immature

5) management

✓ Longer gestation lowers IRDS likelihood.

✓ Administering hormones like prolactin, estrogen, thyroxin, and glucocorticoids supports surfactant production.

✓ Postponing premature delivery, even by a day, improves surfactant production chances.

✓ Dexamethasone, a synthetic steroid, is given before premature delivery to enhance surfactant production.

- ## Acute Respiratory Distress Syndrome (ARDS)
  - ✓ Occurs in both adults and children.
  - ✓ Marked by bilateral lung inflammation visible in x-rays.
  - ✓ Pulmonary capillary wedge pressure less than 13mmHg.
  - ✓ Diagnosis depends on many criteria, one of them is the ratio of partial Pressure of oxygen in Arterial blood (PaO2) to (FiO2) Fraction of inspired air.

PaO2/ FiO2 ratio is a parameter used to assess the degree of hypoxemia, commonly used in the context of ARDS.

- FiO2 is the concentration of oxygen a patient is receiving through a ventilation device. Normally 0.21, maximum (pure oxygen) is 1.
- Normal PaO2 is 100 at FiO2 = 21%, so the ratio = 100/0.21= 475
- PaO2/ FiO2 ratio less than 200 indicates ARDS
- Reaching normal PaO2 (100mmHg) when FiO2 is 1 is not normal (ratio= 100/1 = 100, less than 200, sever ARDS)

	HEALTHY INDIVIDUAL	INDIVIDUAL w/ ARDS	
FiO_2	0.21	0.5	1
PaO_2	100 mmHg	100 mmHg	100 mmHg
$PaO_2 : FiO_2$	476	200	100

$PaO_2 : FiO_2$ → SEVERITY of ARDS, which CORRESPONDS to MORTALITY RATES

RATIO between 200 & 300 ↓ MILD

RATIO between 100 to 200 → MODERATE

RATIO < 100 ↓ SEVERE

Recommended videos:

https://youtu.be/7ZMweT5o3Io?si=00BZLnqBxV-K0pFw

https://youtu.be/AWKTCwmXopY?si=ac7r8so4QO7rw7jo

V2

-corrections highlighted in gray

V3

-corrections highlighted in yellow

V4

-correction highlighted in green