صدقة جارية عن المغفور له بإذن الله **عمر عطية** من دفعة 2023 – كلية الطب، الجامعة الأردنية.

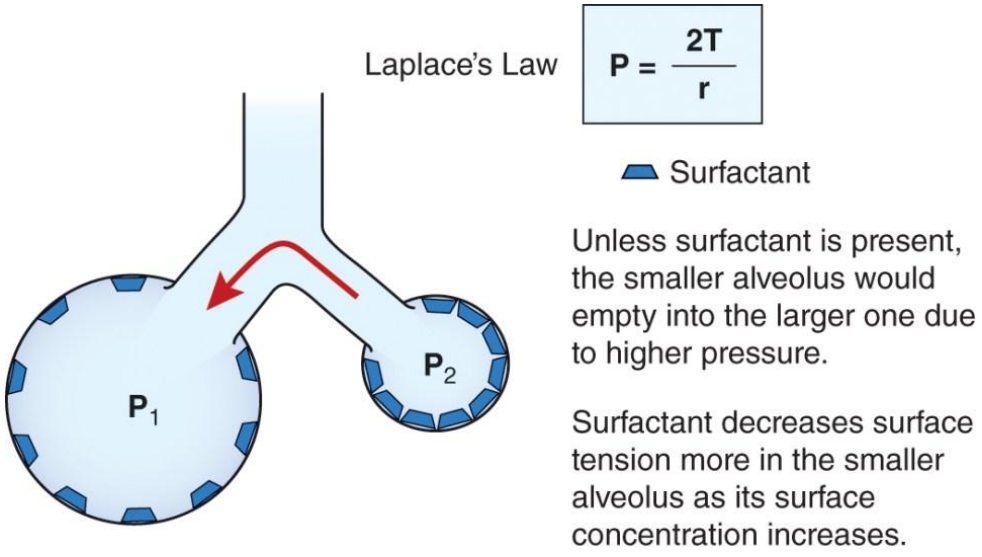
اللهم ارحمه واغفر له وأكرم نزله ووسع مدخله، لا تنسوه من دعائكم، إنا لله وإنا إليه راجعون.

#فريق_دوبامين_العلمي

Respiratory System Physiology

Comprehensive File 5 – V2

Dr. Yanal Shafagoj



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Lung Compliance

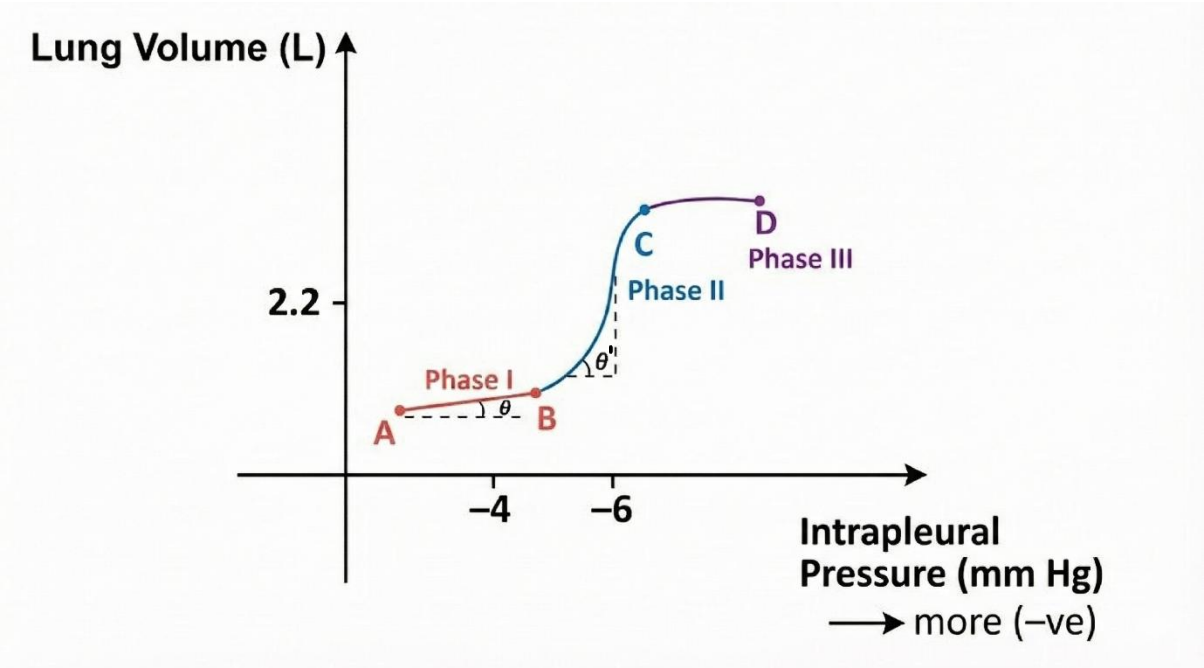
The lung is an elastic balloon, and when inflated, it has a tendency to collapse. This collapsing tendency is due to two forces: surface tension, which contributes for approximately two-thirds of the collapsing force, and the recoil of elongated elastic fibers, which contributes for the remaining one-third. To overcome these collapsing forces, a surrounding negative pressure of −4 mmHg in the thoracic cavity is required. Lung compliance should be maintained within a physiological range; if it is increased (as in emphysema) or decreased (as in pulmonary fibrosis), lung function will be compromised.

In some pathological conditions, the patient may exhale until reaching the resting lung volume of around 150 ml, which is very low. At this volume, the lungs will be no more tending to collapse. Such a patient will also have marked difficulty with inspiration, as the inspiration is starting from an abnormally low lung volume.

In other pathological conditions, some areas of the lung will be so much inflated and can't accept more air as they are no more compliant.

Inflation-Compliance Curve

Imagine the lungs surrounded by a closed cavity with a mobile floor. The pressure inside this cavity can be controlled by pulling or pushing the floor, thereby changing the volume, which in turn leads to a change in pressure according to Boyle's law (PV = C), plotting changes in volume against changes in pressure will give the following figure:



Compliance can be calculated from the figure, as it is represented by the slope of the volume–pressure curve.

$$Compliance = Slope = \frac{\Delta V}{\Delta P} = \tan\theta$$

Using the A–B segment (Phase I) as an example, it is difficult to inflate an initially deflated lung, similar to inflating a deflated balloon. In this phase, a relatively large change in intrapleural pressure produces only a small change in lung volume, indicating low compliance. This is reflected by the small angle (θ) of the slope.

Breathing in this phase requires high work for a small ΔV, which may lead to respiratory fatigue, since the work of breathing is proportional to the pressure–volume change, remember, $Work = \Delta P \times \Delta V$.

In premature babies, the amount of surfactant is minimal, resulting in high surface tension and a strong tendency for the lungs to collapse at low lung volumes. Consequently, during expiration, the lungs reach very low volumes, and the next inspiration requires a large pressure change to reopen the alveoli. This corresponds to Phase I of the volume–pressure curve, where compliance is very low. The increased work of breathing leads to high energy consumption, which may cause respiratory muscle fatigue and, if untreated, respiratory failure.

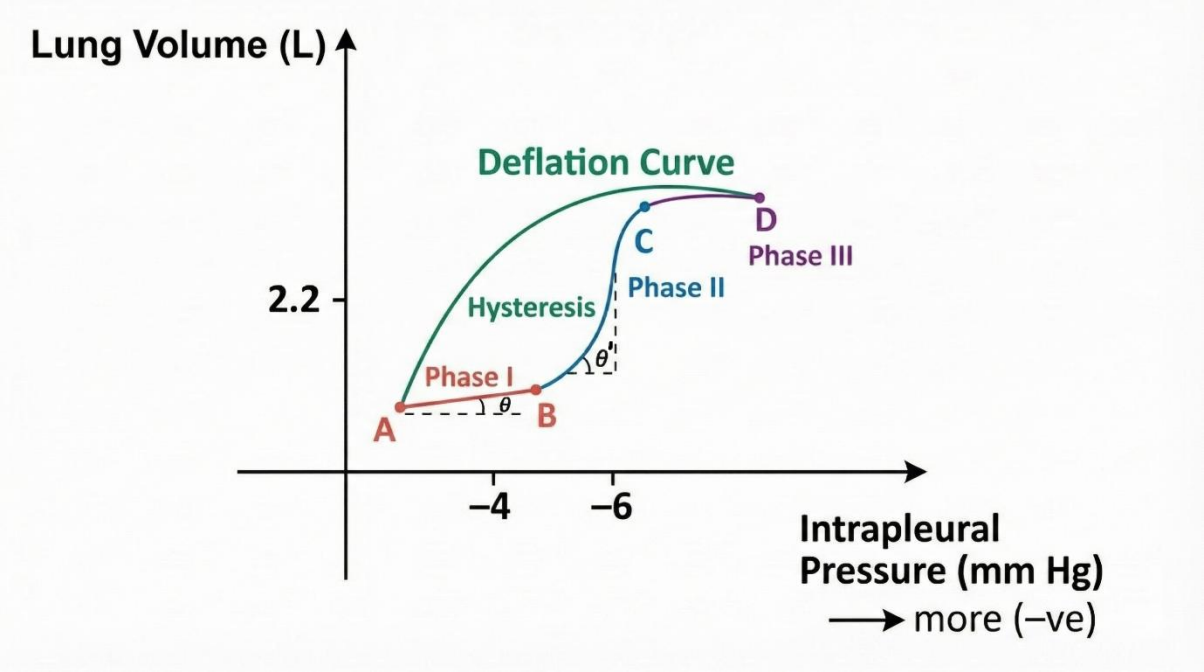
At point B, the compliance increases sharply, as this pressure represents the pop-opening pressure of the lung. Once this pressure is reached, the lung enters Phase II (B–C segment), which is a highly compliant phase. In this segment, a small change in intrapleural pressure produces a large increase in lung volume. Therefore, Phase II is the most efficient phase for tidal volume respiration, since the lung is most compliant in this region of the curve.

Phase III (C–D) occurs at high lung volumes, where the alveoli are already fully expanded. In this phase, compliance is low, so a large pressure change produces only a small increase in volume. As a result, breathing in Phase III requires more work and is inefficient for normal tidal respiration.

Note that the distribution of ventilation is not equal throughout the lung. At rest, the apical alveoli are already more inflated, whereas the basal alveoli are only partially inflated. As a result, during inspiration, more air is directed toward the basal alveoli, because they are more compliant and can accommodate a greater volume change.

This difference is due to regional variations in intrapleural pressure. The apical alveoli are surrounded by a more negative pleural pressure (approximately −8 mmHg), causing them to be already expanded, while the basal alveoli are surrounded by a less negative pressure (around −2 mmHg) and are therefore less inflated at rest. Consequently, most of the tidal volume preferentially enters the basal regions of the lung, which lie on the steeper (more compliant) portion of the volume–pressure curve.

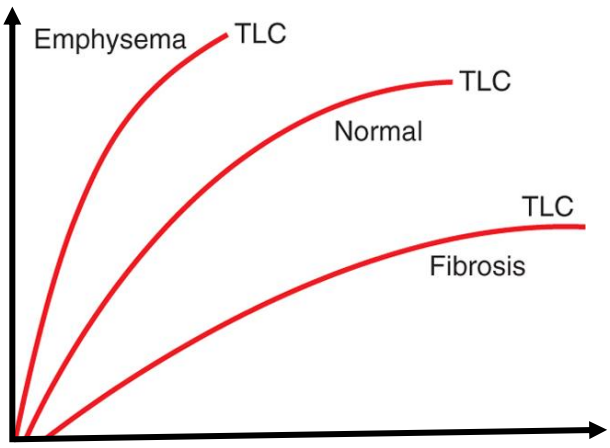
Deflation - Compliance Curve



During deflation, the pressure acting on the lung is a compression pressure, becoming less negative as we move from right to left on the x-axis. The curve shown in green represents the deflation curve. This curve does not retrace the inflation curve, a phenomenon known as hysteresis.

For example, to maintain a lung volume of 2.2 L, an intrapleural pressure of −4 mmHg is required during deflation, whereas during inflation, a more negative pressure (−6 mmHg) is needed to reach the same volume. This illustrates that less pressure is required to maintain lung volume than to initially inflate the lung.

By convention, when we say compliance curve we mean the **deflation curve**.
When comparing pathological conditions to normal, the deflation curve is used.



Explaining the Paradoxical Behavior

As previously mentioned, surface tension accounts for approximately two-thirds of the collapsing forces of the lungs. This means that surface tension favors lung deflation rather than inflation. Therefore, during lung inflation, surface tension must be overcome, whereas during deflation, surface tension contributes to lung recoil and does not oppose it.

This difference in behavior during inflation and deflation explains why the inflation and deflation pressure–volume curves are not coincident – this is hysteresis.

To overcome the collapsing forces (including surface tension) during inflation, negative intrapleural pressure is needed. To be more context-oriented, the **inflation pressure (P)** needed to inflate the lungs is related to **surface tension (T)** and **alveolar radius (r)** by

Laplace's law:

$$P = \frac{2T}{r}$$

Approximate values for the alveolar radius are 300 μm in adults and 200 μm in newborns. In premature babies, due to reduced surfactant, surface tension is high. High surface tension combined with a small alveolar radius means that the pressure required to inflate the lungs is significantly increased.

As a result, premature infants require assisted respiration to prevent respiratory muscle fatigue and possible death.

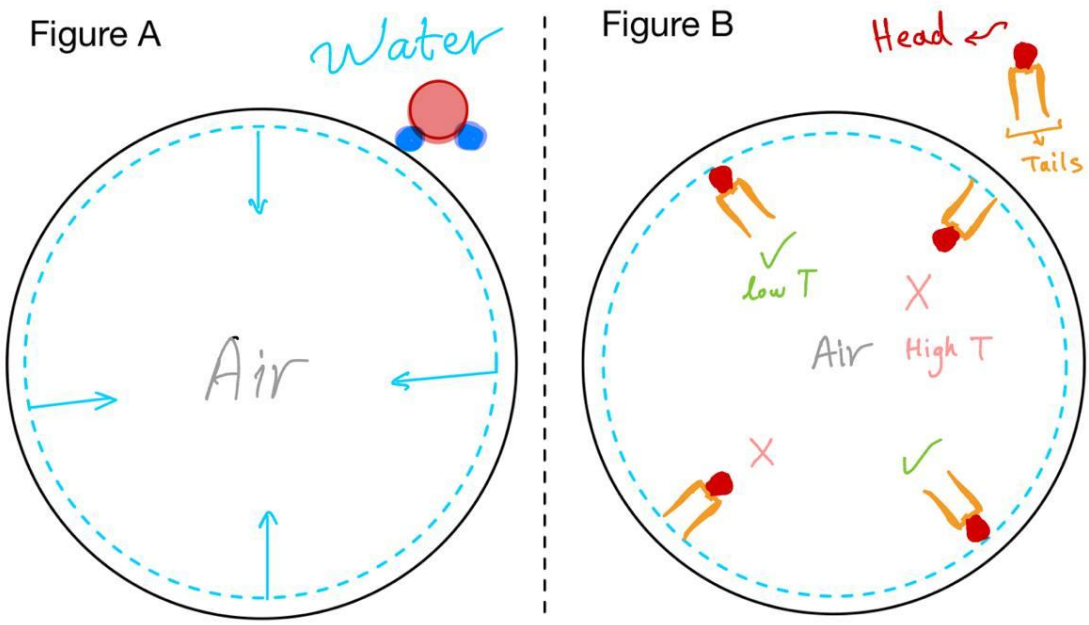
What exactly are surfactants?

Pulmonary surfactant forms a thin molecular film lining the air–liquid interface of the alveoli. Surface tension in the alveoli is generated by the **attractive forces between water molecules** lining the alveolar surface *(see figure A)*. These cohesive forces tend to **minimize surface area**, creating a collapsing force on the alveoli.

Surfactant composition is 2% carbohydrates, 8% proteins, and **90% phospholipids**, which is a complex composition that cannot be easily prepared.

Surfactant molecules are surface-active phospholipids that insert themselves between water molecules at the air–liquid interface. Their presence disrupts the hydrogen bonding and cohesive forces between water molecules more effectively, leading to a greater reduction in surface tension *(see figure B)*.

Figure A *shows the air-water interface and cohesive forces between water molecules*.
Figure B *shows the orientation of the surfactant in the interface to minimize tension*.



How do surfactants contribute to hysteresis?

During deflation, when alveolar surface area decreases, surfactant molecules are compressed closer together. **This compression promotes better alignment** and more orderly orientation of phospholipids, with hydrophilic (glycerol-based) heads facing the aqueous lining fluid and hydrophobic tails facing the alveolar air. With correct molecular orientation and high surface density, surfactant maximally disrupts water–water cohesive forces, resulting in very low surface tension.

During inflation, when alveolar surface area increases, surfactant molecules are spread apart. They are therefore **less optimally oriented** at the air–liquid interface. Some molecules may tilt or fail to maintain ideal head–tail alignment, reducing their ability to disrupt water–water interactions. As a result, surfactant is less effective at lowering surface tension.

In the absence of surfactant, alveoli lined with water require a negative pressure of approximately -23 mmHg to inflate. If the alveoli are lined with plasma, surface tension is lower, so a smaller negative pressure of about -13 mmHg is sufficient.

In premature newborns, the alveolar radius is smaller (200 μm), which, according to Laplace's law, increases the inflation pressure. As a result, these infants require a negative pressure of around -30 mmHg to open the alveoli.

Because the surface tension is higher during inflation than during deflation at the same lung volume, the pressure–volume relationship differs between these two phases. This difference produces lung hysteresis.

Note that the orientation of surfactant is the main player, meaning that even if 2 alveoli have the same amount of surfactant, they can have different curves if the surfactant is, for any reason, well-oriented in one alveolus and poorly oriented in the other.

Moreover, the amount of surfactant in one alveolus is relatively constant throughout the breathing cycle, and it is the orientation that is changed between inflation and deflation.

An additional effect of **surfactant** is that it **prevents the occurrence of pulmonary edema** by decreasing the required intrapleural (and thus interstitial) pressure needed to inflate the lungs. This in turn decreases filtration and prevents edema formation. More on how edema forms is discussed in lecture 6.

Alveolar stability

Alveolar stability refers to the ability of alveoli to remain open and resist collapse, especially during expiration. Without stabilizing mechanisms, smaller alveoli would be prone to collapse into larger ones.

According to Laplace's law ($P = 2T/r$), the pressure required to keep an alveolus open is directly proportional to surface tension (T) and inversely proportional to alveolar radius (r). Thus, for the same surface tension, smaller alveoli require higher pressure to remain open and are more likely to collapse.

Pulmonary surfactant lowers surface tension, particularly in smaller alveoli where it is more concentrated, thereby reducing the pressure required to keep them open. By decreasing surface tension more in small alveoli than in large ones, surfactant equalizes pressures between alveoli of different sizes, preventing collapse and ensuring alveolar stability.

Alveolar stability makes possible the coexistence of different sizes of alveoli in proximity to each other. Although the pressure (*P*) surrounding them is similar, say -4 mmHg, they can coexist in stability without net air flowing between them. This means that the collapsing pressure must be similar between different alveoli in the same region.

Laplace's law assumes constant tension, but tension here must change because when '*P'* is constant and '*r'* changes, *'T'* must change to fit in the equation.

It is the physiological presence of **surfactant** that **makes surface tension volume-dependent**, and thus tension is dynamic, not constant.

How do we know that surface tension makes for 2/3 of the collapsing forces?

This conclusion comes from classic **pressure–volume (P–V) experiments** comparing air-filled lungs with saline-filled lungs.

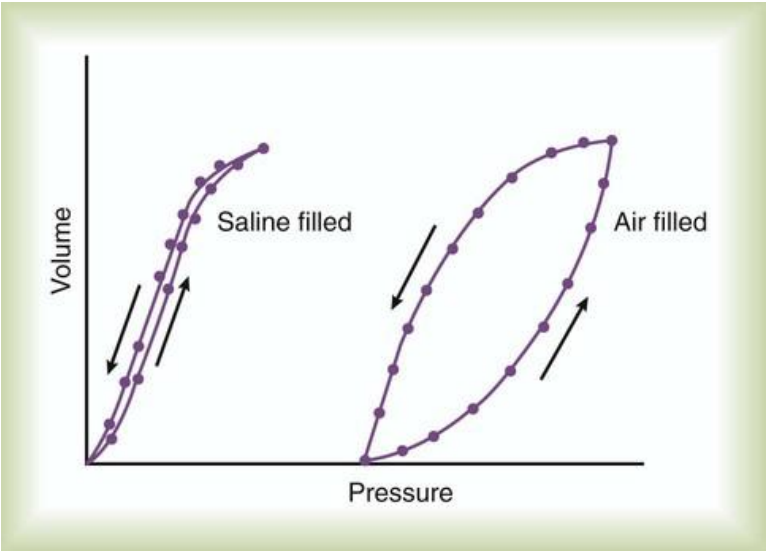
When lungs are **inflated with air**, the measured elastic recoil (collapsing force) reflects two components:

1. **Tissue elasticity**
2. **Surface tension** at the air–liquid interface lining the alveoli.

When the **same lungs are filled with saline**, the air–liquid interface is eliminated. As a result, **surface tension is abolished**, and the remaining recoil represents **pure tissue elasticity** only.

Experimentally, it is found that:

- The recoil pressure of **saline-filled lungs is about one-third** of that of air-filled lungs at the same lung volume.
- Therefore, the **remaining two-thirds of the collapsing force** present in air-filled lungs must be due to **surface tension**.
- Saline-filled lungs show **much greater compliance** and **minimal hysteresis**, indicating that surface forces (not tissue fibers) account for most of the resistance to inflation.



Notice how the saline-filled curve has narrower width (minimal hysteresis).

In summary: By removing the air–liquid interface with saline and observing that recoil falls to roughly one-third, we infer that **≈ two-thirds of lung elastic recoil is due to surface tension**, and **≈ one-third to tissue elasticity**.

How do we know if fetal lungs are mature or premature?

Amniotic fluid analysis is made. One of the most important markers for lung maturation is **surfactant to albumin ratio**.

- > 55% → mature lungs
- 35-55% → intermediate
- < 35% → premature lungs.

Antenatal Management of Infant Respiratory Distress Syndrome (IRDS)

Antenatal corticosteroids are given to the mother when preterm delivery is anticipated.

Normal surfactant production requires many hormones, including prolactin, thyroxine, estrogen, and glucocorticoids.

2 shots of **dexamethasone** (a 22-C potent synthetic glucocorticoid) are usually given to accelerate the production of surfactant in preterm cases.

Diagnosis of Acute Respiratory Distress Syndrome (ARDS)

ARDS is a progressive illness with a very high mortality rate. It mostly occurs in inpatient clinics, where patients suffer from other comorbidities, such as liver failure, kidney failure, heart failure, or septic shock.

Diagnosis of ARDS uses the following formula:

$$\frac{P_aO_2}{\%\ of\ O_2\ in\ inspired\ air}$$

A normal value would be around 500 = (100 / 21%).

In ARDS, this ratio falls **below 200**.

For example, in ARDS patients, pure oxygen inspiration only yields an arterial oxygen partial pressure of about 150 mmHg. Meaning that the ratio is 150 = (150 / 100%). Since this number is below 200, the patient is said to have ARDS.

Changes from VERSION 0 to VERSION 1:

- First paragraph (in page **4**):
  from "… becoming less negative as we move from left to right on the x-axis."
  to "… becoming less negative as we move from right to left on the x-axis."
- Fixed the quality of the images (page **2**; page **4** (**upper** one))

Changes from VERSION 1 to VERSION 2 (IMPORTANT):

1. **Pages 5-8 of V1 were dramatically changed (they are now pages 5-7}**
   - **The idea of changing surfactant concentration was removed.**
   - **The edema-protective effect of surfactant was added.**
   - **The order of paragraphs was changed.**

2. **Pages 8 & 9 were added from lecture 8 recording.**