RESPIRATORY SYSTEM

PHYSIOLOGY

HANDOUT NO. 4

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important

TOPICS WILL BE DISCUSSED:

1. **Spirometry**
2. **FRC**
3. **Pulmonary function test**
4. **COPD**
5. **Diagram**

▪ Spirometry

Spirometry Basics

- **Spirometer**: Instrument to measure breath (spiro = breath, meter = measurement).
- Pre-breathing volume: 2.2 Liters.
- **Tidal Volume (TV)**: 500 ml (volume of air moved per breath).

  (So it's added to the already existing 2.2 liters)

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 (active process). This volume of 1.1 liters is referred to as the (ERV), (2.2-1.1=1.1). However, the inspiration in this case will become passive. Remember the ticket, you pay it once.

In elderly, the expiratory muscles are weak, so the ERV is less than 1.1 L (could reach 1.2 L)

4. **Residual volume RV**: The remaining volume after forced exhalation is the

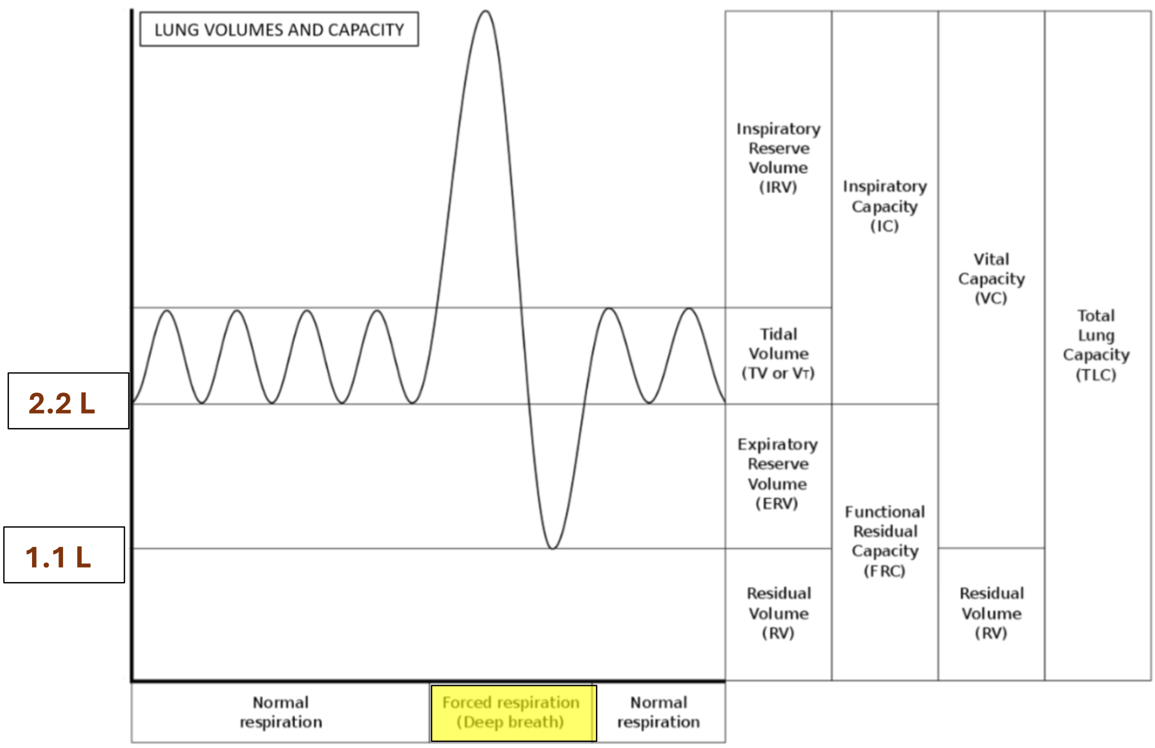
RV, it's about 1.1 L.

5. **Minute ventilation or RMV**: Total amount of air moved into

and out of respiratory system per minute

6. **Respiratory rate or frequency RR:** Number of breaths taken

per minute



Volumes that get out and in are measured by a **spirometer**, but there are some volumes that can't be measured because they don't get out or in, like Residual Volume. Residual Volume RV is the volume that resides in the lungs following forced expiration.

- Normally, People even using all their forces to expire the air in their lungs, can't reach to a volume of zero but they would reach a certain volume, called residual volume.
- Spirometer can't measure RV but can measure IRV, VT, ERV
- If you add 2 volumes together you get capacity. (4 capacities)

➢ **inspiratory capacity:** IC=IRV+VT

➢ **functional residual capacity:** (volume of air present in the lungs before breathing and taking VT) FRC=ERV + RV

➢ **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

➢ **Total lung capacity TLC:**

✓ IRV+VT+ERV+RV = 5.7L

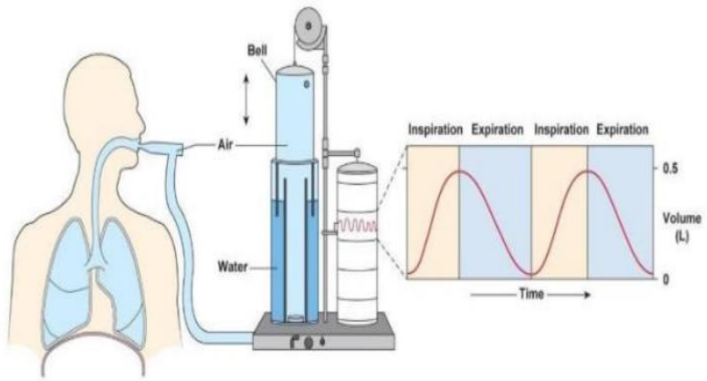
✓ the volume of air both lungs can take.

(All capacities that include RV can't be measured by the spirometer, like TLC+FRC)

FRC (HOW to calculate it?!)

➢ Helium dilution technique

To measure Functional Residual Capacity (FRC), we allow the patient to breathe from a closed bag filled with helium (He), a non-absorbable gas that cannot cross the respiratory membrane. (So it's like we're creating a closed chamber for He that can't exit by absorption through capillarie, and its mass is conserved) For instance, suppose the initial volume of the



bag is 10 L, and the initial concentration of He is 10 mol/L. We let the patient breathe in and out from the bag until equilibrium is achieved. While the amount/mass of He remains unchanged because it does not diffuse into the bloodstream, the final volume(V2) will be the sum of the bag's volume and the volume of the lungs (FRC), effectively diluting the helium, and the final concentration of He can be easily calculated.

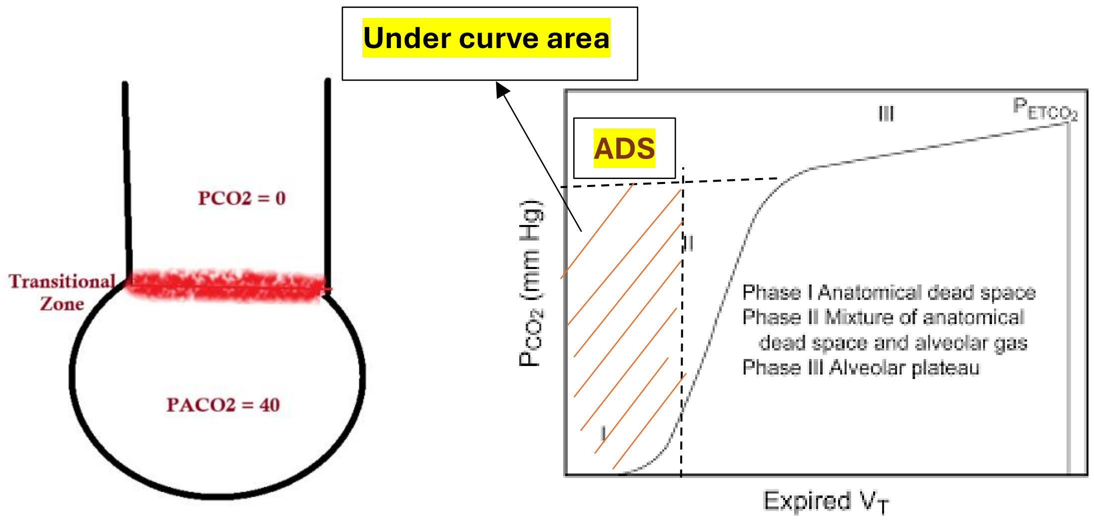
Law/principle of conservation of mass:

$$C_i\,V_i = C_f\,V_f$$

$$C_i\,V_i = C_f\,(V_i + FRC)$$

$$FRC = \frac{V_i\,(C_i - C_f)}{C_f}$$

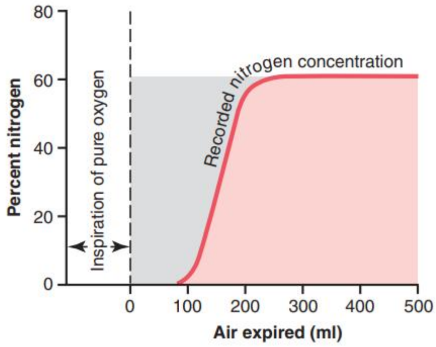
ADS (Anatomic Dead Space)



- When we measure the volume and CO_2 percentage during expiration, the CO_2 at the end of inspiration in the anatomical dead space (ADS) would be zero, as it aligns with atmospheric levels. While PCO_2 in the alveoli is 40 mmHg due to gas exchange with the capillaries. However, there exists a transitional zone between the alveoli and the ADS, where some CO_2 can diffuse from it. Additionally, a mixture of gases is present between the ADS and the alveolar volume.

- In the accompanying graph, as the patient exhales, we will not detect any CO_2 until the ADS has been fully evacuated; after that, the CO_2 level will gradually rise from the alveoli, ultimately reaching a plateau. It is essential to note that this gradual increase in CO_2 percentage is a result of the transitional zone.

The measurement of ADS is determined by calculating the area under the curve, but we must subtract specific areas to exclude the alveolar air.



In another experiment, we let the patient take one full breath of pure oxygen and then measure the percentage of nitrogen (N_2). In this case, the N_2 level would be zero in the ADS because, as previously stated, the patient inhaled pure O_2 along with some water vapor. Consequently, any nitrogen detected must have originated from the alveoli, leading to a similar graph.

PDSV (Physiological Dead Space Volume)

➢ VQ ratio:

Remember! We have a total of 500 VT, 150 of which is in the ADS while the rest 350 is distributed between **alveolar volume** and **wasted volume**. Wasted volume is when air is delivered to a part of the lung but the perfusion (blood supply) to that part is defected due to some pathological condition, so the gas that enters is not being exchanged with the blood leading to alveolar gases partial pressures similar to those in the atmosphere in the defected area ($PCO_2=0$, $PO_2=150$). This low perfusion is more likely to be to areas next to the apex of the lung than the base where it is harder for the heart to deliver blood to them. This case leads to a V/Q (ventilation to perfusion ratio) of **infinity** (as perfusion =0, and when we divide any number by zero we get infinity as an answer).

Concept of VQ ratio: (Ventilation to perfusion ratio V/Q)

- ✓ V/Q ratio: alveolar ventilation/ pulmonary blood flow
- ✓ is a measure used to assess the matching of ventilation (the amount of air reaching the alveoli) to prefusion (the blood flow reaching the alveoli) in the

lungs, reflecting the harmony by which respiratory & cardiovascular systems are working.

- ✓ This ratio is crucial for efficient gas exchange, ensuring that oxygen is delivered to the blood and carbon dioxide is removed.
- ✓ Normal V/Q ratio = 1 and it yields normal PaO2 (100 mmHg) and PaCO2 (40 mmHg).
- ✓ So, if ventilation and perfusion become off, these numbers might not be achieved, also there might be wasted ventilation or perfusion if they were mismatched.
- ✓ just like ventilation and perfusion vary as you go from the base to the apex of the lung, so does the ventilation to perfusion ratio. Heart finds it hard to pump blood to apex more than the base, perfusion in apex would be lesser than base.

Question: If we have V/Q is infinity, What would be PAO2 = ?

Ans: 150 same as the ADS.

The relationship can be summarized as follows:

- ADS + wasted volume = physiological dead space (PDS)

To measure the PDS, we can determine the ADS using nitrogen (N2) or carbon dioxide (CO2) washout techniques. To calculate wasted volume, we use the following equation:

$$PDSV = \frac{VT\ X\ (P_A CO2 - P_{\hat{E}} CO2)}{P_A CO2} = 500\ X\ \frac{40-28}{40} = 150$$

Extra: How did we measure 28?

$P_{\hat{E}}CO2$ is the expired Co2 from the lungs, contains 350 ml aleovli + 150 ml ADS:

$$P_{\hat{E}}CO2 = \frac{Alev\ X\ P_A CO2 + ADS\ X\ atm\ Co2}{VT} = \frac{350\ X\ 40 + (150\ X\ 0)}{500} = \mathbf{28}$$

In healthy individuals, PDSV is equal to ADS. However, if there is wasted volume, the partial pressure of carbon dioxide (PCO2) would be zero, which reduces $P_{\hat{E}}CO2$ and thus increases PDSv.

Example: if we have a $P_{\hat{E}}CO2$ of 20mmHg, (500 X (40-20)/40=250, the new PDSV), so the wasted volume in this case: 250-150=100 (150 is the ADSV which doesn't change)

▪ Pulmonary Function Test

Slides:

Work in the respiratory system is of 2 major types (discussed in the previous lecture):

1. Work to overcome elastic forces (70%): that required to expand the lungs against the lung and chest elastic forces. Two third is duo to surface tension and one third is duo to elastic fibers.

2. Work to overcome non-elastic forces (30%): that required to overcome:
1. The viscosity of the lung and chest wall structures (20%).

2. Airway resistance work (80%): that required to overcome airway resistance to movement of air into the lungs.

Cor pulmonale:

In emphysema, the surface area available for diffusion gets pretty limited and could drop to much less than the normal values of 50-100mm2! This decline leads to higher pulmonary vascular resistance due to the destruction of capillaries. Since those capillaries are arranged in a parallel distribution, as they are lost, the overall resistance goes up. And in order to keep the blood flow almost constant, the pressure should rise in the pulmonary arteries (remember: flow = ΔP/R), imposing an increase in the afterload that affects the right ventricle leading to its dilatation and possible failure (Cor pulomonale).

Extra: How destroying small resistance causes high resistance ?

Imagine with me that you have 4 roads (capillaries) of traffic leading to the same destination, with multiple cars travelling on each road (blood flow).

- If 1 of the 4 roads has been blocked or there’s a car accident, the total number of cars traveling decreases because the remaining roads can’t handle more cars.

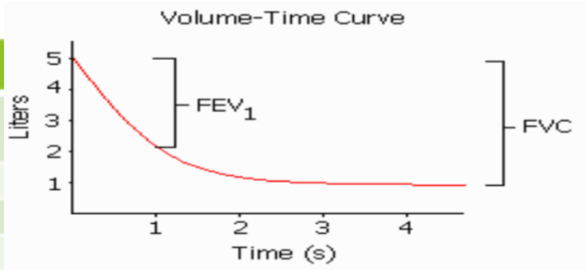
Parallel Resistor Equation

$$\frac{1}{R_T} = \frac{1}{R_1} + \frac{1}{R_2} + \frac{1}{R_3} \ldots\ldots + \frac{1}{R_n} \text{ etc}$$

FEV1 & FVC:

FEV1/FVC -- This is the percentage of the vital capacity which is expired in the first second of maximal expiration. In healthy patients the FEV1/FVC is usually around 80%. In patients with obstructive lung disease FEV1/FVC decreases and can be as low as 20-30% in severe obstructive airway disease. Restrictive disorders have a near normal FEV1/FVC or sometimes more than normal.

	FEV_1 compared to predicted for age/ gender/ height
GOLD Stage I	$FEV_1 \geq 80\%$
GOLD Stage II	$50\% \leq FEV_1 < 80\%$
GOLD Stage III	$30\% \leq FEV_1 < 50\%$
GOLD Stage IV	$FEV_1 < 30\%$



Lung diseases are divided into 70% obstructive, 20% restritive and 10% vascular.

Obstructive diseases are manifested in exhalation; the patient faces problems in exhaling.

While in Restrictive, the problem resides in inhaling.

➢ Obstructive Disease

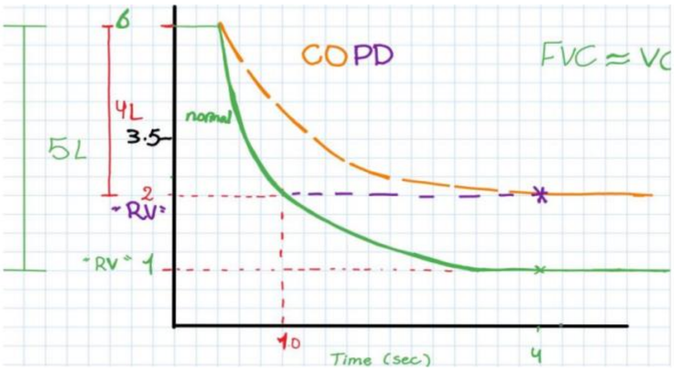
In obstructive diseases, it is easy to inhale and difficult to exhale, so the lungs are filled with air leading to high TLC, high FRC and high RV.

RV almost equals 1L in young healthy people but it's 1.5 in old adults; as their muscles are weak to force expiration. Similarly, patients suffering from problems in expiration (as is the case in obstructive diseases) have higher RV than normal people.

We measure the patient's anthropometric variables to asses his FEV_1 (Forced Expiratory Volume in one second) and his FVC.
FVC: Forced vital capacity, maximum capacity of air that a patient can forcefully exhale after maximum inspiration. Now, we can consider it ≈ VC, however FVC is slightly lower than VC. The reason behind that: when you expire forcefully using your muscles there is a chance that you close the bronchioles before exhaling the air residing in them → air trapping. In normal individuals, we consider VC = FVC.

For Example: in this graph, for a normal person FEV_1 = 4L FVC= 5L

$\frac{FEV_1}{FVC} X\ 100 = 80\%$



In normal people, 80 % of their VC is exhaled in the 1st second.

Now, we can use FEV_1 to classify the obstructive diseases (like COPD).

	FEV_1 compared to predicted for age/ gender/ height
GOLD Stage I	$FEV_1 \geq 80\%$
GOLD Stage II	$50\% \leq FEV_1 < 80\%$
GOLD Stage III	$30\% \leq FEV_1 < 50\%$
GOLD Stage IV	$FEV_1 < 30\%$

In obstructive diseases:

FEV_1 decreases

FVC could be normal or slightly decreased

But the ratio between them decreases (<80%)

➢ Restrictive Disease

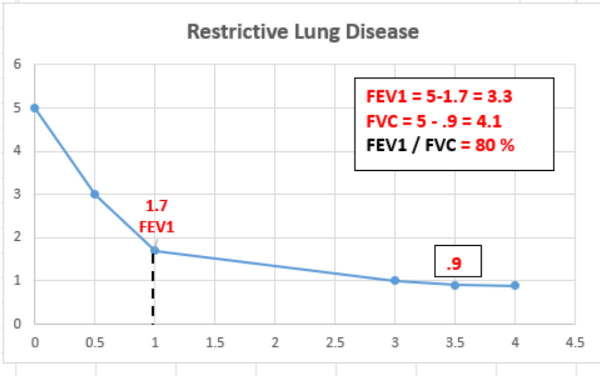
In restrictive disorders, patients typically experience a reduced volume of inhaled air. Unlike obstructive diseases, where patients struggle to exhale effectively, those with restrictive conditions have a notable decrease in forced vital capacity (FVC) as well, indicating lower lung volumes while maintaining a normal percentage of FEV1/FVC.

(This percentage is about how much of our inhaled air is exhaled in the first second, in restrictive conditions, it’s true that we inhale much less air volume but exhalation is normal, so we exhale a normal percentage of this low air volume we have in our lung)

In these cases, the forced expiratory volume in one second (FEV1) is low primarily because of difficulties in inhalation. Conversely, in obstructive diseases, FEV1 is reduced due to challenges in exhaling appropriately (in both cases FEV1 is reduced).

Additionally, total lung capacity (TLC), residual volume (RV), and functional residual capacity (FRC) are all diminished in restrictive disorders. Patients have a limited amount of inhaled oxygen in their lungs. The primary issue lies not in their ability to forcefully exhale air in the first second but rather in the insufficient air available for inhalation.

$$\frac{\downarrow FEV_1}{\downarrow \text{FVC}} X\ 100 \approx \text{ normal \% } (\geq 80\%)$$



➢ Summary:

Lung Disease Measurements

MEASUREMENT	RESTRICTIVE LUNG DISEASE	OBSTRUCTIVE LUNG DISEASE
TLC	↓	↑
RV	↓	↑
FEV_1	↓	↓
FVC	↓	↓
FEV_1/FVC (~80%)	Normal - ↑	↓

▪ Chronic Obstructive Pulmonary Disease (COPD)

As we learned in Lecture 3, COPD can be categorized into three groups (emphysema+chronic bronchitis +- asthma):

1- Emphysema:

- Pathological diagnosis
- Three types

2- Chronic Bronchitis

3- Asthma (with conditions):

- The classification depends on reversibility. If reversible, it is considered acute rather than chronic.

➢ Diagnostic Approach in asthma

In cases of suspected asthma:

1. **Measure FEV1.0** (Forced Expiratory Volume in one second) for the patient.
2. Administer **bronchodilators** such as Beta-2 agonists (e.g., Salbutamol, Albuterol).
3. Reassess FEV1.0 after inhalation of the bronchodilator. The results are interpreted as follows:
    - If FEV1.0 increases by **200 mL** or by **12%** of the original value, the condition is considered reversible.
    - If FEV1.0 does not meet these criteria, irreversibility is suspected.
4. If irreversibility is indicated, consider a course of **glucocorticoids** (anti-inflammatory treatment) for approximately two weeks.
5. Repeat the FEV1.0 test after the treatment to confirm chronicity, as distinguishing between acute and chronic conditions is critical for effective management.

Lung Mechanics and Compliance

Why is a negative pressure of -4 needed? This counteracts a collapsing force of +4.

The lung acts like an elastic balloon, and this Elastic nature has two main characteristics:

1. **Compliance**
2. **Recoil tendency**

When respiratory muscles (both expiratory and inspiratory) are relaxed, the lung has 2.2L. How is it inflated? Because it is surrounded by a negative pressure of -4.

If the lung is removed from the body (in vitro), it collapses because it is no longer surrounded by this negative pressure. It will collapse to the so called; minimal volume, but not to zero, as some air remains trapped in certain alveoli.

Minimal Volume (also called: **the resting volume):** This is the volume at which the lung loses its collapsing tendency, and where the structure neither tends to collapse nor expand.

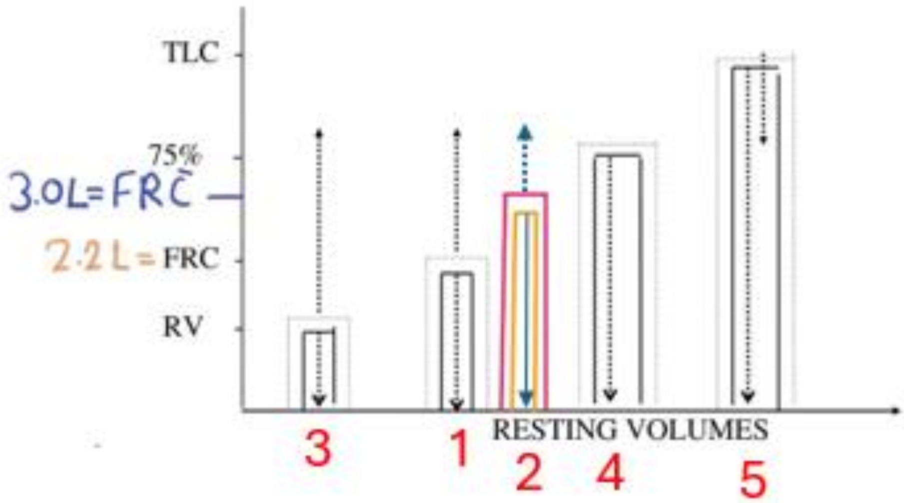
In reality, we are dealing with two "balloons": the lung (internal balloon) and the thorax (external balloon). Inflating one balloon inside another (2 balloons) is more challenging than inflating a single balloon.

This results in a reduced compliance (ΔV/ΔP). For example:

- Compliance of the lung = **200 mL/cmH$_2$O**
- Compliance of the thorax = **200 mL/cmH$_2$O**
- Compliance of the lung-thorax system (inside the body) = **100 mL/cmH$_2$O**

From the equation: 1/200 + 1/200 = 2/200 = 1/100 = 100

For a pressure change (ΔP) of 1 cmH$_2$O, the volume change (ΔV) is 200 mL.

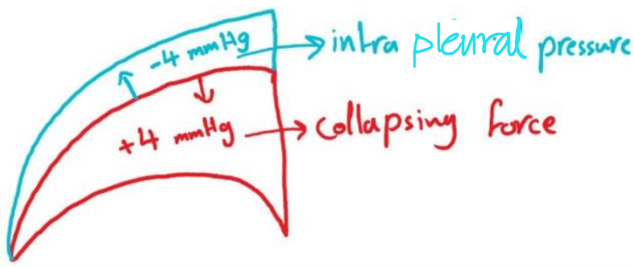


▪ Explanation of the Diagram

We will refer to each column by a number:

<u>In Column 1:</u>

- The lung still has a tendency to collapse (+4mmHg which has to be counteracted by the negative pressure of the thorax) until it reaches



minimal volume. Normally, we cannot reach minimal volume; we reach residual volume instead.

- The 4mmHg we discussed earlier equals the collapsing tendency of the lung or the expanding tendency of the thorax. For example, during open-heart surgery, the thorax expands, indicating that it is normally compressed leading to this value of a negative pressure (-4). The resting volume of the thorax equals 4.5 L (75% of TLC, which is 6 L). (The thorax has a tendency to expand and reach this resting volume)

At FRC (2.2L):

- The lung still has a tendency to collapse.
- The thorax has a tendency to expand.
- The lung-thorax system is at rest because these two forces are equal and opposite (+4 & -4). This makes FRC very important as it is the resting volume of the whole system.

<u>In Column 2:</u>

- In emphysema, destruction of elastic fibers increases the compliance, reducing the collapsing tendency (nothing brings the lung back when the elastic fibers are destroyed).
- In such a situation, collapsing and expanding tendencies of both the thorax and the lung, respectively, are unequal, with a greater expanding tendency of the thorax. To solve this, the lung collapsing tendency must increase and the expanding tendency of the thorax must decrease to balance both forces. This adjustment brings the system closer to the resting volume of the thorax, resulting in FRC' = 3.0 L. (FRC is the resting volume of the system regardless of its value, as it could differ in many cases, as is the case in emphysema)

<u>In Column 3:</u>

- In restrictive diseases, the collapsing tendency is substantial. Balancing requires reducing the collapsing tendency of the lung and increasing the expanding tendency of the thorax.
- The resting volume(FRC) is lower than the normal FRC.

Whether considering normal, obstructive, or restrictive conditions, FRC is the resting volume of the lung-thorax system.

- To move any elastic structure from its resting state, force must be applied (whether moving up or down in volume). For the elastic structure to return to its resting state, no force is needed; only the removal of the applied force is required. This principle makes expiration passive.

(Now consider some other cases with using the same figure above, but in normal individuals during respiration):

In Column 2: (after inhalation)

- Comparing tidal volume with FRC (2.2 L), the tendency of the lung to collapse increases, and the tendency of the thorax to expand decreases. The system tends to collapse.

  (Remember! After inhalation, the thorax is expanded as the diaphragm is constricted, and the lung is now inflated and filled with air and they both want to go back to their original state, both the lung and the thorax tend to collapse again).

In Column 3: (after forced expiration)

- Using expiratory muscles (exhalation of more air volume than the tidal volume) decreases the collapsing tendency of the lung (not to zero) and increases the expanding tendency of the thorax, enhancing the system's tendency to expand. Returning to FRC remains passive, making inspiration passive in this scenario.

In Column 4: (after forced inspiration)

- At 4.5 L, the lung's collapsing tendency is significant, while the thorax's expanding tendency equals zero. The system tends to collapse.

In Column 5: (after reaching the TLC)

- At TLC, the lung's collapsing tendency is substantial, and the thorax also tends to collapse. Both forces work in the same direction, creating a huge force/tendency of the whole system to collapse.

Version 2:

- **Amount/mass of He doesn't change instead of concentration**