RESPIRATORY SYSTEM

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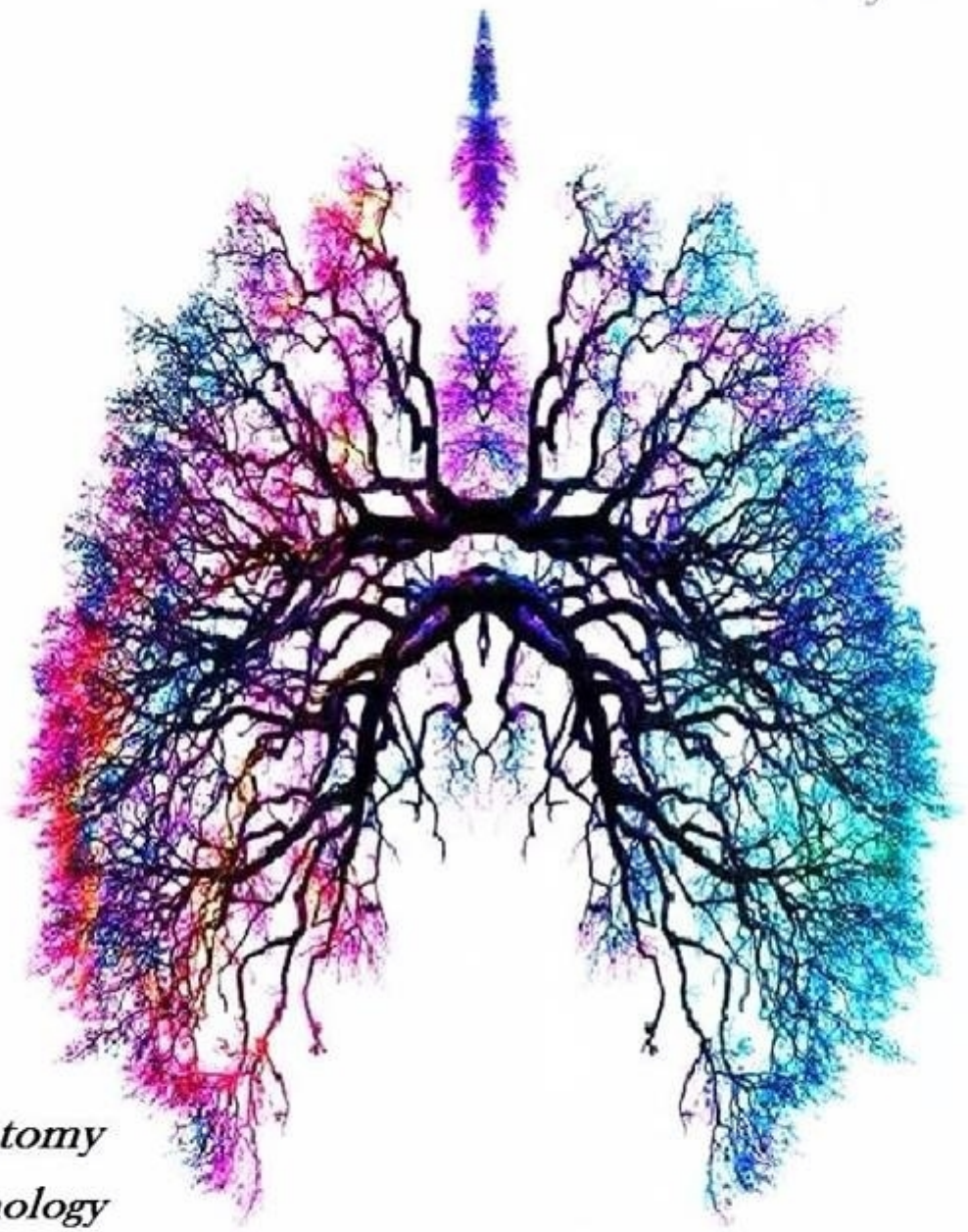

- ○ Anatomy
- ○ Pathology
- ● Physiology
- ○ Pharmacology
- ○ Microbiology
- ○ PBL

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Lecture # 4
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I. Obstructive vs. Restrictive Pulmonary Disease

-Obstructive Pulmonary Disease:

e.g.: **COPD** (which includes emphysema and chronic bronchitis), **Asthma**

In obstructive lung diseases inhalation is normal, but it's **difficult to exhale** all of the air out of the lungs. This means that at the end of exhalation, there would be an **abnormally** high amount of air left lingering in the lungs. **(The total lung capacity and volume are increased, increased compliance)**

-Restrictive Pulmonary Disease:

e.g.: **Pulmonary Fibrosis**

In restrictive lung diseases the lungs are **stiff and rigid**, making the lung **difficult to inflate**, therefore making it **difficult to inhale**. In other words, the lungs are restricted from fully expanding. **(The total lung capacity and volume are decreased, decreased compliance)**

The tests performed to diagnose these diseases are called Expiration Tests, since the disease is manifested during expiration.

REMINDER

A. Lung Volumes

1. Tidal Volume (Vt)
- is the volume inspired or expired with each normal breath.

2. Inspiratory Reserve Volume (IRV)
- is the volume that can be inspired over and above the tidal volume.
- is used during exercise.

3. Expiratory Reserve Volume (ERV)
- is the volume that can be expired after the expiration of a tidal volume.

4. Residual Volume (RV)
- is the volume that remains in the lungs after a maximal expiration.
- cannot be measured by spirometry.

5. Dead Space: a. Anatomic b. Physiologic

6. Ventilation Rate: a. Minute b. Alveolar

B. Lung Capacities

1. Inspiratory Capacity
- is the sum of Tidal Volume and IRV.

2. Functional Residual Capacity (FRC)
- is the sum of ERV and RV.
- is the volume remaining in the lungs after a tidal volume is expired.
- includes the RV, so it **cannot be measured by spirometry.**

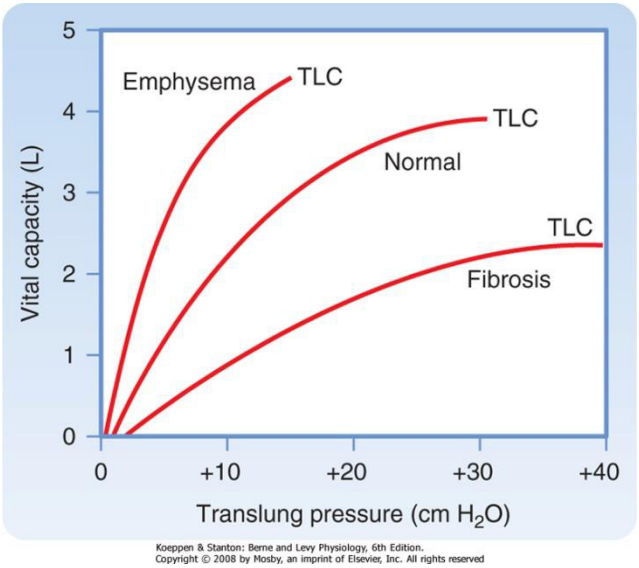
3. Vital Capacity (VC), or Forced Vital Capacity (FVC)
-is the sum of tidal volume, IRV, and ERV.
-is the volume of air that can be forcibly expired after a maximal inspiration.**4. Total Lung Capacity (TLC)**
- is the sum of all four lung volumes.
- is the volume in the lungs after a maximal inspiration.
- includes RV, so it **cannot be measured by spirometry.**

C. Forced Expiratory Volume in 1 second (FEV1)

- FEV1 is the volume of air that can be expired in the **first second** of a forced maximal expiration.
-FEV1 is **normally 80% of the forced Vital Capacity,** which is expressed as:
FEV1/ FVC= 0.8

	Obstructive (e.g. COPD/Asthma) (impaired expiration, too much air trapped)	**Restrictive (e.g. Pulmonary Fibrosis) (impaired inspiration, inability to inflate)**
Total Lung Capacity (TLC)	Increased	Decreased
Functional Residual Capacity (FRC= ERV + RV)	Increased	Decreased
Residual Volume (RV)	Increased	Decreased
FEV1/ FVC (Normal= 0.8)	Decreased (both FEV_1 and FVC are reduced, but FEV_1 is reduced more than FVC is: thus, **FEV_1/FVC is decreased**)	Normal or Increased (both FEV_1 and FVC are reduced, but FEV_1 is reduced less than FVC is: thus, **FEV_1/FVC is increased**)
Compliance	Increased	Decreased

II. Recognizing the Abnormalities in Graphs



A) *Notice the figure to the left:* ***volume vs. pressure***

-The slope of the curve is equal to: (ΔV/ΔP)

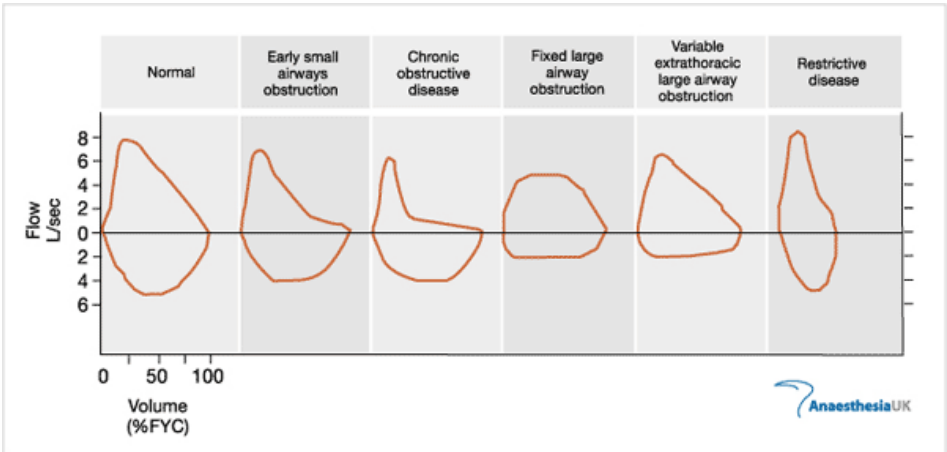
-In **Emphysema** (a type of **COPD**), the curve is shifted to the **left**. TLC is higher.

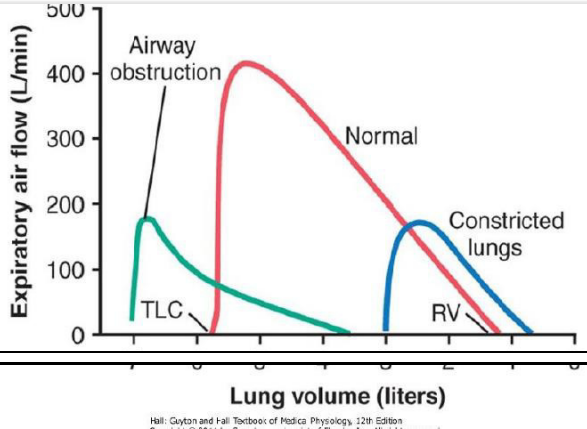
-In **Pulmonary Fibrosis**, the curve is shifted to the **right**. TLC is lower.

B) *Now look at the figures below:* ***flow vs.volume***

The Peak Expiratory Flow **(PEF)** is a person's maximum speed of expiration.

The **peak expiratory flow** in that of a **restrictive** pulmonary disease (e.g. pulmonary fibrosis) is near normal or lowers than that of a normal person.





Here is a more in-depth explanation from Guyton:

Abnormalities of the Maximum Expiratory Flow-Volume Curve

This figure shows the normal maximum expiratory flow-volume curve, along with two additional flow-volume curves recorded in two types of lung diseases constricted lungs and partial airway obstruction.

Note that the *constricted lungs* have both reduced total lung capacity (TLC) and reduced residual volume (RV). Furthermore, because the lung cannot expand to a normal maximum volume, even with the greatest possible expiratory effort, the maximal expiratory flow cannot rise to equal that of the normal curve. Constricted lung diseases include fibrotic diseases of the lung itself, and diseases that constrict the chest cage.

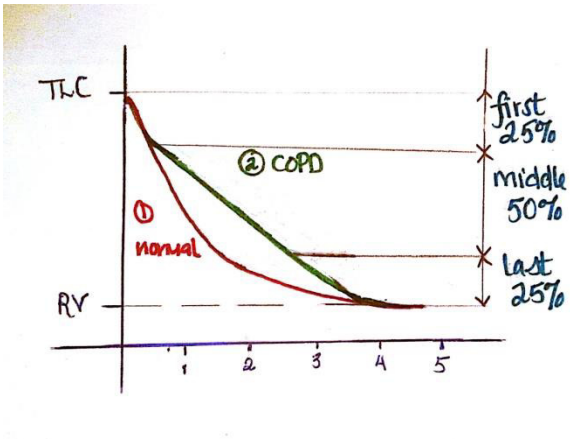
In diseases with *airway obstruction*, it is usually much more difficult to expire than to inspire because the closing tendency of the airways is greatly increased by the extra positive pressure required in the chest to cause expiration. By contrast, the extra negative pleural pressure that occurs during inspiration actually "pulls" the airways open at the same time that it expands the alveoli. Therefore, air tends to enter the lung easily but then becomes trapped in the lungs. Over a period of months or years, this effect increases both the TLC and the RV, as shown by the green curve in. Also, because of the obstruction of the airways and becausethey collapse more easily than normal airways, the maximum expiratory flow rate is greatly reduced. The classic disease that causes severe airway obstruction is *asthma*. Serious airway obstruction also occurs in some stages of *emphysema*.

C) FEF25-75% (Forced Midexpiratory Flow Rate): ***volume vs. time***

This is the average rate of airflow during the midportion of the forced vital capacity (FVC).

I.e.: It's the amount of time the patient needs to expire the middle 50% of the lung volume during expiration (L/s).

This is used in diagnosis to cancel the dilutional effects in the first 25% and the last 25% of expiration. This is because for **both** in normal and obstructed lungs, it is **easy** to empty the **first 25%** of the volume of the lung at the beginning of expiration, and **difficult** to empty the **last 25%** of the lung volume at the end of the forceful expiration.



This means that in those areas of the graph, there is no real difference between the normal person and the diseased patient. In order to differentiate between the two, we take the **mid 50% of the lung volume** and measure the expiratory rate, **which is <u>reduced</u> in both obstructive and restrictive disorders.**

III. Pathophysiology of Specific Pulmonary Abnormalities

Cigarette smoking doesn't cause isolated emphysema, it's overlapped with chronic bronchitis (both are COPDs). Sometimes the manifestation of one is predominant over the other.

A. Emphysema:

The diagnosis of emphysema is mainly based on pathological findings.

The term **pulmonary emphysema** literally means **excess air in the lungs**. However, this term is usually used to describe complex obstructive and destructive process of the lungs caused by many years of smoking. It results from the following major pathophysiologic changes in the lungs:

1. **Chronic infection, caused by inhaling smoke** or other substances that irritate the bronchi and bronchioles. The chronic infection seriously deranges the normal protective mechanisms of the airways, including **partial paralysis of the cilia of the respiratory epithelium**, an effect caused by nicotine. As a result, **mucus cannot be moved easily** out of the passageways. Also**, stimulation of excess mucus secretion** occurs, which further exacerbates the condition. Inhibition of the alveolar macrophages also occurs, so they become less effective in combating infection **(chronic bronchitis)**.

2. The infection, excess mucus, and inflammatory edema of the bronchiolar epithelium together cause **chronic obstruction** of many of the smaller airways.

3. The obstruction of the airways makes it especially difficult to expire, thus causing **entrapment of air in the alveoli and overstretching them**. This, combined with the lung infection, causes **marked destruction of as much as 50 to 80 percent of the alveolar walls.**

4. The elastic tissue of the alveolar walls are also destroyed by **Trypsin anti-proteases** (cigarette smoke inhibits anti-trypsin).

5. When the alveolar walls are destroyed- by the effect of proteases that are normally inhibited by anti-trypsin - **capillaries are destroyed** along with them, **thus increasing pulmonary vascular resistance and decrease the surface area of exchange**.*
This destruction of the alveoli and capillaries is irreversible.

**These equations clarify point number 5:*

↑Resistance (R) α 1/ ↓ (P^2) P: cross sectional area The resistance is inversely proportionate to the cross-sectional area squared	↑Pul. Arterial Pressure (P_a) = Q * ↑Pul. Resistance (R) Q: blood flow The pulmonary arterial pressure is directly proportionate to the pulmonary resistance

A decreased area of exchange results in **hypoxia**. This causes a **decrease in PO2,** which is a **pulmonary vasoconstrictor**, And this is another cause of increase pulmonary arterial pressure.

Local ↓PO2 causes vasodilatation everywhere in the body (systemic) except for the lungs.

Vasoconstriction will eventually lead to **pulmonary hypertension**, increasing the **afterload** of the right ventricle. The **right ventricle will dilate** (right ventricular failure) resulting in **heart disease** (congestive heart failure).

Another cause of pulmonary hypertension asides from smoking is living at high altitudes (e.g. The Andes)

The term for heart disease caused by lung disease is **CORPULMONALE.** Any lung disease resulting in hypoxia may cause Corpulmonale.

B. Asthma:

Asthma is an **obstructive** disease in which expiration is impaired due to bronchospasm, characterized by decreased FVC, decreased FEV1, and **decreased FEV1/FVC.**

Air that should have been expired is not, leading to air trapping and **increased FRC.**

Main line of therapy: B2 agonists, inducing bronchodilation

If an increase in FEV1 by 12%, it may be reversible; otherwise it is an irreversible COPD. Glucocorticoids may have to be administered (e.g.: albutamol and salbutamol as inhalers)

<u>Pulmonary Function Tests (PFT) help diagnose these diseases.</u>

There is a mismatch in the V/Q Ratios of these diseases

Too much air and too little blood, the V/Q ratio is high, wasted ventilation (this will be further explained shortly).

IV. Ventilation (V), Perfusion (Q), and the (V/Q) Ratio

-The V/Q Ratio is the **ratio of alveolar ventilation (V) to pulmonary blood flow (Q).**

-Ventilation and perfusion (blood flow) matching is important to achieve the ideal exchange of O2 and CO2.
- Both ventilation and blood flow (perfusion) are **nonuniformly distributed** in the normal upright lung.

(V/Q) Ratios in Different Parts of the Lung:

1. Blood flow, or perfusion, is lowest at the apex and highest at the base because of **gravitational effects** on arterial pressure.

2. Ventilation is lower at the apex and higher at the base because of **gravitational effects in the upright lung**.
Importantly, however, the regional differences for ventilation are not as great as for perfusion.

Explanation of the previous point:
In order to inflate the lung, we make the pressure around it more negative.

There is a regional difference in the intrapleural pressure between the apex and base of the lung, i.e. the pressure around them is not the same.

The intrapleural pressure in the **apex** is equal to (-8), meaning the alveoli in the apex) are **totally** inflated (or already inflated) thus making it **difficult to further inflate them**.

The intrapleural pressure in the **base** is equal to (-2), meaning the alveoli in the base are **partially** inflated thus making it **easy to further inflate them.**

(This applies to the compliance curve of the lung which will be explained later in the sheet)

If we take a single breath of pure O2 (100% O2, 500 ml, 760 mmHg), then measure the tidal volume, **most of the air** will go to the **base**, since basal alveoli are easily inflated. Little air goes to apex, since apical alveoli are already inflated.

Conclusion:
Most of **ventilation** will go to the **basal alveoli,** meaning the **ventilation of the basal alveoli is more than the ventilation of the apical alveoli**.

3. Therefore, the V/Q ratio is higher at the apex (*3*) of the lung and lower at the base (less than 1) of the lung.

4. As a result of the regional differences in V/Q ratio, there are corresponding differences in the efficiency of gas exchange and in the resulting pulmonary capillary Po2 and Pco2.
Regional differences for Po2 are greater than those for Pco2.

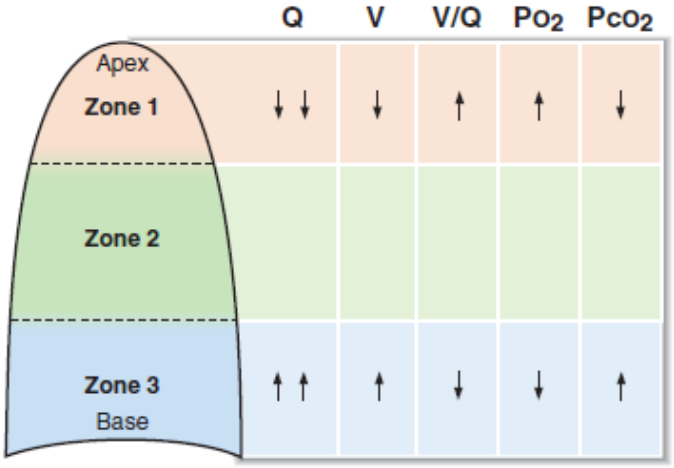
a. At the apex (higher V/Q), Po2 is highest and Pco2 is lowest (the entry of gases is higgher than the output as there's low perfusion) because gas exchange is less efficient.

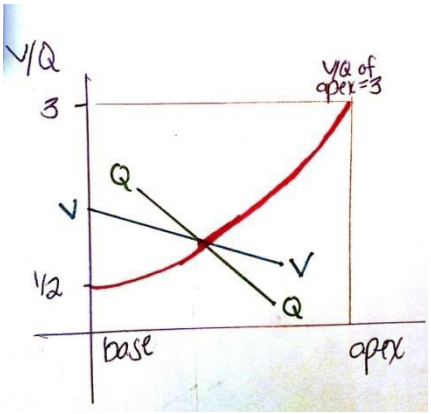
b. At the base (lower V/Q), Po2 is lowest and Pco2 is highest because gas exchange is more efficient.

table 4.6 V/Q Characteristics of Different Areas of the Lung

Area of Lung	Blood Flow	Ventilation	V/Q	Regional Arterial P_{O_2}	Regional Arterial P_{CO_2}
Apex	Lowest	Lower	Higher	Highest	Lower
Base	Highest	Higher	Lower	Lowest	Higher

V/Q = ventilation/perfusion ratio.





Mismatches in th V/Q Ratio:

A. V/Q ratio in pulmonary embolism (wasted ventilation, no perfusion)

If blood flow to a lung is completely blocked (e.g., by an embolism occluding a pulmonary artery), then blood flow to that lung is zero. If ventilation is normal, then **V/Q is infinite,** which is called **dead space.**

There is **no gas exchange** in a lung that is ventilated but not perfused.

The **Po2 and Pco2 of alveolar gas** will approach their values in **inspired air.** (*Guyton)*

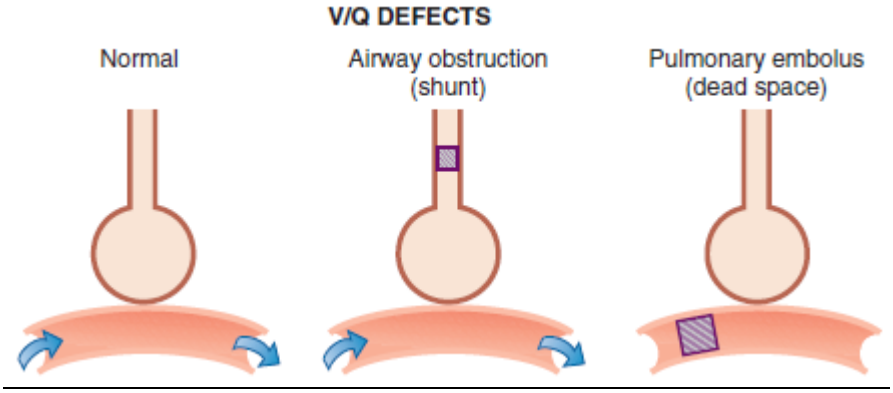
B. V/Q ratio in airway obstruction (wasted perfusion, no ventilation)

If the airways are completely obestructed then ventilation is zero. If blood flow is normal, then **V/Q is zero,** which is called a **shunt.** Mixing of blood occurs in the right atria or ventricle, but the hyperventilated region does not correct the hypoventilated region.

There is **no gas exchange** in a lung that is perfused but not ventilated.

Pulmonary vascular resistance occurs, leading to the increased afterload of the right ventricle, which is later proceeded by right ventricular hypertrophy and failure (Corpulmonale).

The **Po2 and Pco2 of pulmonary capillary blood** (and, therefore, of systemic arterial blood) **will approach their values in mixed venous blood.** *(Guyton)*



V. Compliance (C)=V/P

Compliance is the change in volume for a given change in pressure.
(How much change of volume you get per unit change in force;
force is directly proportional to negative pressure)

It describes the **distensibility** of the lungs and chest wall.

The pressure change is the force needed to inflate the lungs.

A simple way to understand compliance is how easily you can inflate or deflate a hollow struture.

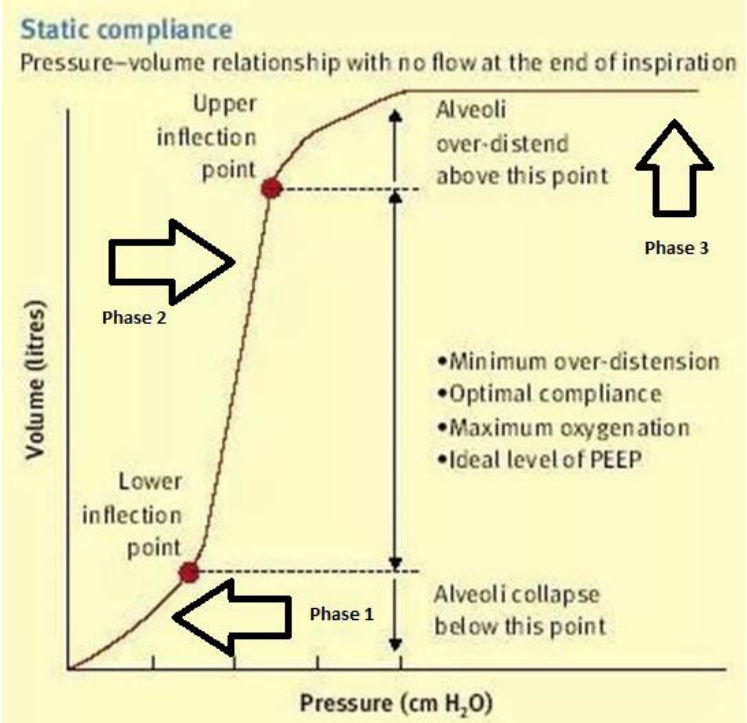
Let's picture blowing up a balloon.

-At first, you have to exert a lot of pressure, only to find a small increase in volume. (Not compliant, Phase 1)

-Afterwards, you can blow the ballon easily. Less applied pressure results in a large change in volume. (Maximal Compliance, Phase 2)

-The balloon eventually reaches its maximal volume, so even when pressure is applied, there is very little change in volume.
(The balloon is full, not compliant, Phase 3)

The same principle applies to the lungs



The slope of the curve (ΔV/ΔP) represents the compliance of the lung.

We start inflating the lung by making the pressure around it more negative, thus exerting force.

Phase 1:
The lung is incompliant or stiff, a lot of negative pressure must be exerted (excessive work, ATP, and oxygen consumption) to achieve a minimal increase in volume. This only occurs **abnormally** such as in respiratory distress syndrome.

Phase 2: Optimum Compliance
Any increase in pressure is followed by an increase in volume. A "pop" in pressure occurs **(critical opening pressure)**. Less pressure is needed to achieve larger changes in volume.
Here the slope of the volume-pressure curve becomes high.

Phase 3:
The lung has reached its **maximal volume**. Even when an adequate amount of pressure is applied, there is barely any increase in volume because the lung is already full.

Conclusion:
-It is difficult to inflate a completely collapsed lung because it isn't compliant.
-Inflating a lung that has reached its maximal volume is useless, since it isn't compliant.
-The "easiest way" to inflate a lung is when it's partially inflated (which is the case of normally functioning lungs).

VI. Closing Volume/ The Closing Test

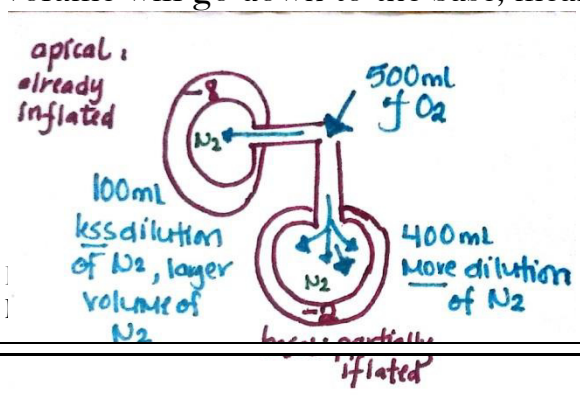
Closing volume (CV) is the volume of air that can be exhaled after the gravitationally dependent airways have closed.

The Closing Test is a very sensitive test which can detect any minute obstruction in the airways.

Remember how we said that ventilation of the basal alveoli is more than the ventilation of the apical alveoli? The more negative pressure around the apical alveoli make them totally inflated, decreasing their compliance making it more difficult to fill them with more air. On the other hand, the less negative pressure around the basal alveoli make them partially inflated, resulting in maximal compliance, making it easier for them to fill with air.

Inhalation:

Let's once again take a breath of pure O2 (500 ml), most of the tidal volume will go down to the base, meaning that the basal air would be more diluted than the apical air (higher dilution of N2).



Exhalation:

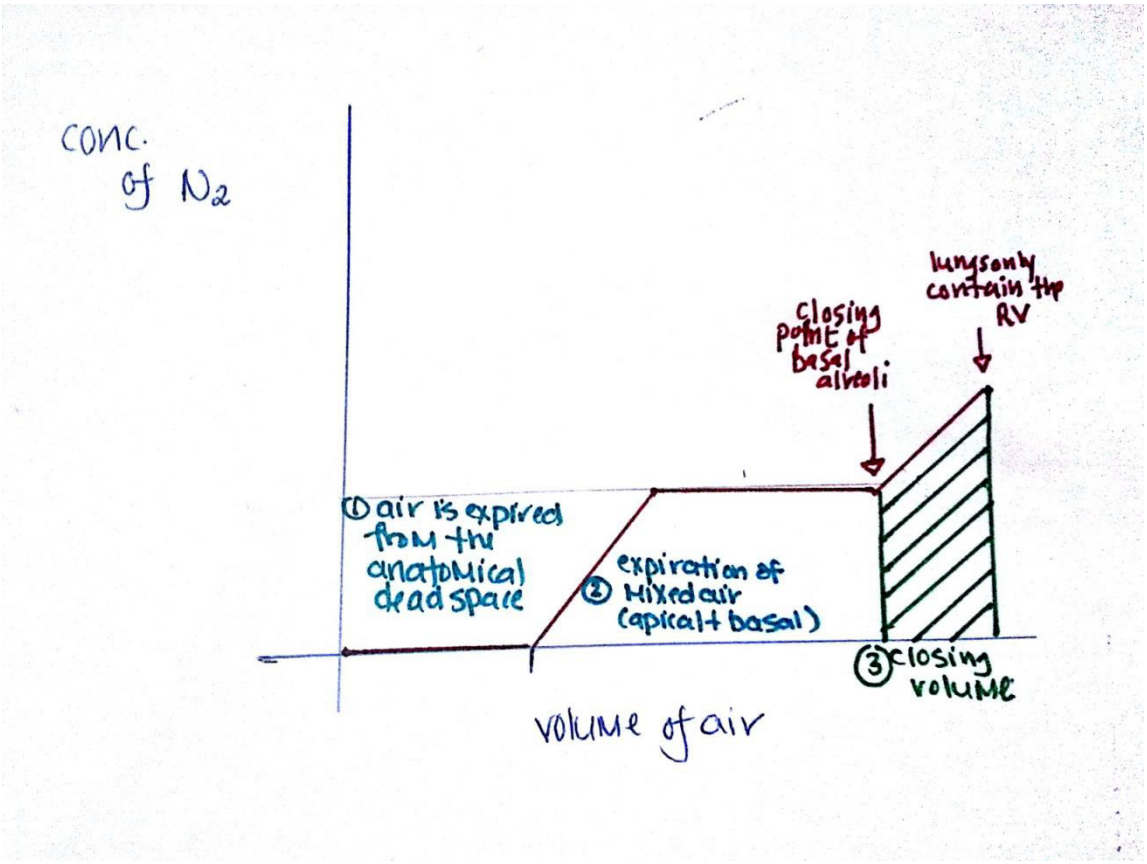
1) The air within the **Anatomical Dead Space** is expired. (The ADS can be calculated with this test).

2) **Mixed air** is expired from both the apical and basal alveoli.

3) If there happens to be **slight narrowing/obstruction** of the apical or basal airways, the **basal alveoli have a tendency to close first** at the end of expiration, since they are surrounded by less negative pressure. **A marked increase in the volume of N2 is then observed. (Closing Point)**

The air exhaled afterwards accounts for the **Closing Volume**.

4) In this case the last portion of air will be expired from the apical alveoli (where the N2 was less diluted, because they hadn't been ventilated), resulting in markedly increase in N2 volume.



This test is used in the early diagnosis of obstructive diseases.

-Normal people reach the closing point (closing of basal alveoli) near the residual volume, meaning the exhaled air comes from both the apical and basal alveoli (the basal alveoli are still patent).

-In the case of obstruction, the closing volume keeps rising and may reach the Funtional Residual Capacity (FRC).

-Some normal lung obstruction may occur with aging. The closing volume (10% of TLC) is usually less than the residual volume (15% of TLC).

Normally, the closing volume isn't reached. At the end of expiration, the Residual Volume is immediately achieved.

Sources: Lecture Recording, Guyton and Hall Textbook of Medical Physiology 12th edition, BRS Physiology 6th edition

When life gives you lemons, squeeze them in peoples' eyes

Dedications to: Ula Isleem & Muhannad Haddadin