Physiology of Ventilation

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Required Reading: Respiratory Physiology, A Clinical Approach, Schwartztein & Parker, Ch. 1; Ch. 2 (pp.9-17; Ch. 3

Objectives

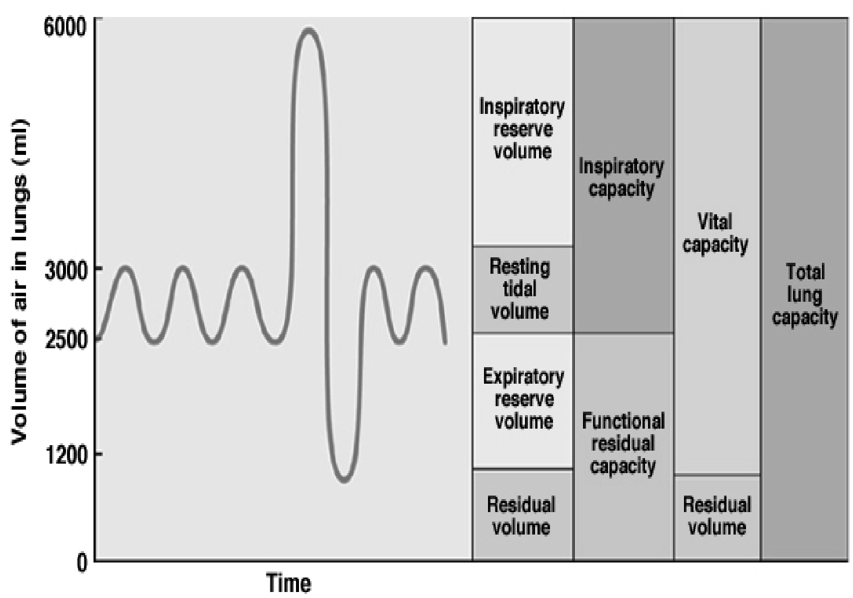
1. Diagram the relationship between tidal volume (V_T), residual volume (RV), inspiratory reserve volume (IRV), expiratory reserve volume (ERV), vital capacity (VC), total lung capacity (TLC) and functional residual capacity (FRC).
2. Describe the respiratory system as a two structure, three-compartment model, and describe the pressure in each compartment at rest.
3. Describe how the balance between the elastic recoil of the lungs & the chest wall determines FRC.
4. Describe how the relationship between alveolar (P_A), intrapleural (P_{pl}), atmospheric(P_{atm}) & transpulmonary pressure (P_L) determines airflow during a normal respiratory cycle.
5. Describe how lung volume, tissue elastance and alveolar surface tension affect the static compliance of the lungs.
6. Describe the static compliance of the normal lung with reference to the pressure-volume curve of the lung obtained during deflation from TLC to FRC. Contrast this relationship to the pressure-volume curves encountered in disease states that increase or decrease pulmonary compliance.

1. Lung Volumes & Capacities

Lung volume and its subdivisions can change under a variety of circumstances including disease.

Total lung capacity (TLC) is the maximum amount of air the lungs can hold. The total lung capacity is divided into four primary volumes: inspiratory reserve (IRV), tidal volume (V_T), expiratory reserve volume (ERV) and residual volume (RV).

It is useful to know that the "capacities" consist of the sums of two or more "volumes". For example, FRC=ERV+ RV.



2. The Two Structure, Three Compartment Model

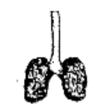
In order to understand how respiratory system works from a mechanical point of view, it is helpful to conceptualize it as two structures, the lungs and the chest wall, each with elastic properties. At FRC, the lungs have a tendency to recoil inwards; the chest wall a tendency to recoil outwards. If the lungs are removed from the thoracic cavity and no longer have the influences of the chest wall and pleural space acting on them, they would be almost completely air less, at a volume [minimal volume] substantially lower than they have *in situ*, within the thoracic cavity **(Fig.a)**.

Transmural pressure refers to the pressure inside relative to outside of a compartment. Under static conditions, the transmural pressure is equal to the elastic recoil pressure of the compartment. The **transmural pressure of the lungs** is also called **transpulmonary pressure .**

Since the lungs have a tendency to recoil inwards, inflating them requires an increase in transpulmonary pressure. Transpulmonary pressure can be increased by either 1) increasing the pressure inside relative to the pressure outside the lungs or 2) by decreasing the pressure outside relative to the pressure inside the lungs.

If the lungs were removed from the thoracic cavity, the chest wall would recoil or spring outward and expand to a larger size **(Fig.b)**. To increase or decrease the size (volume) of the chest wall from this resting position requires an alteration of the external or internal pressures acting on it. Contraction of inspiratory muscles expands the chest wall from its resting state and increased its transmural pressure. Contraction of the expiratory muscles compresses the chest wall and decreases its transmural pressure.

a



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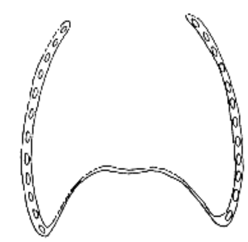

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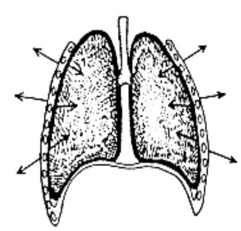


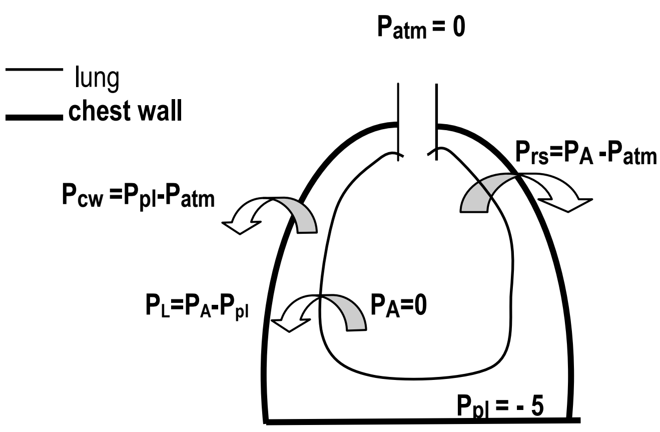


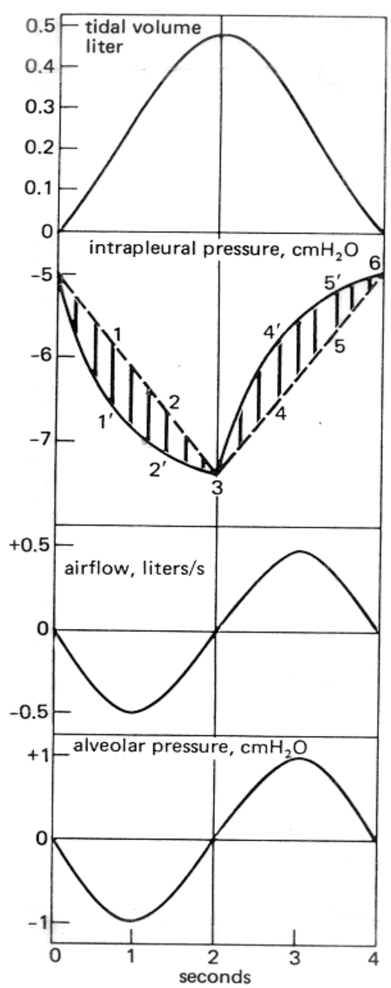
Figure c represents the lungs in situ at FRC. The figure on the left shows the pressures surrounding the lungs and chest wall at FRC. All pressures are measured in units of cmH_20 and considered in relative terms as compared to atmospheric pressure. Atmospheric pressure is conventionally considered to be zero. The transmural pressures of the lungs and chest wall are P_L and P_{cw} respectively. P_{atm}, P_A, and P_{pl} indicate atmosphereic, alveolar and intrapleural pressure respectively. FRC is the resting position of the respiratory system [P_{rs}=0]. At FRC, the respiratory muscles are relaxed and the elastic recoil of the lungs is equal in magnitude but opposite in direction to the elastic recoil of the chest wall and intrapleural pressure is subatmospheric, at about - 5 cmH_20. At the end of a normal breath, at FRC, there is no airflow in or out of the lungs and no pressure gradient between the atmosphere and alveoli to drive airflow the flow of air into the lungs. In order to draw air into the lungs, a difference in alveolar and atmospheric pressure must be created by the contraction of inspiratory muscles.

* <u>note:</u> intrapleural pressure at FRC is most textbooks is indicated as -5 cm H20. It is important to note that in the upright lung, intrapleural pressure at FRC varies depending on where it is measured; it is -3 at the base and -8 cm H20 at the apex of the lungs.

3. Normal Quiet Breathing

Air, like other fluids, moves from a region of higher pressure to a region of lower pressure. The flow of air into the lungs requires that **a pressure gradient between the atmosphere and the alveoli** be established. This driving pressure gradient is accomplished by the contraction of the inspiratory muscles. Contraction of the inspiratory muscles expands the chest wall, lowering the pressures in the thoracic cavity (both intrapleural and alveolar pressures decrease) - consider Boyle's law*. It is important to appreciate the **sequence of events:** muscle contraction results in **change in thoracic volume** leading to a **change in alveolar pressure** that in turn provides the driving pressure for **air flow** into the lungs **[i.e: muscle contraction → Δ V→ Δ P→ air flow].**

The following figure shows volume, pressure and airflow changes during a single idealized respiratory cycle.



inspiration expiration

- At the start of inspiration, the diaphragm contracts and descends, expanding the thoracic volume. The descent of the diaphragm compresses the abdominal contents and decompresses the contents of the thoracic cavity. With expansion of the thoracic cavity and its decompression, both intrapleural pressure and alveolar pressure decrease. Alveolar pressure decreases to a sub-atmospheric level and the pressure gradient for the flow of air into the lungs is established. Air flows into the lungs and lung volume increases until the alveolar pressure rises to the atmospheric level [0 cm H_2O] when the pressure gradient for flow of air into the lungs ceases to exist.

- At the end of quiet inspiration, intrapleural pressure reaches about - 8 cm H_20, and the transpulmonary pressure distending the lungs increases to 8 cm H_2O [$P_L = P_A - P_{pl} = 0 - (-8) = 8$ cm H_2O].

- During quiet expiration, the cycle is reversed, the inspiratory muscles relax and the inward elastic recoil of the lungs results in deflation of the lungs. During deflation, the lungs and chest wall move as one unit. Airflow out of the lungs ceases when alveolar pressure equals atmospheric pressure (0 cm H_2O).

***Consider Boyle's law:** In a closed system where the number of gas molecules is constant, at any constant temperature, the pressure exerted by a gas varies inversely with the volume of the gas. Therefore as the volume of gas increases, the pressure exerted by the gas decreases. Conversely, the pressure increases as the volume decreases.

Questions: 1) What is the driving pressure for air to flow into the lungs?
2) What created this driving pressure? 3) How come the alveolar pressure decrease swings but pleural pressure decrease is continuous throughout inspiration?

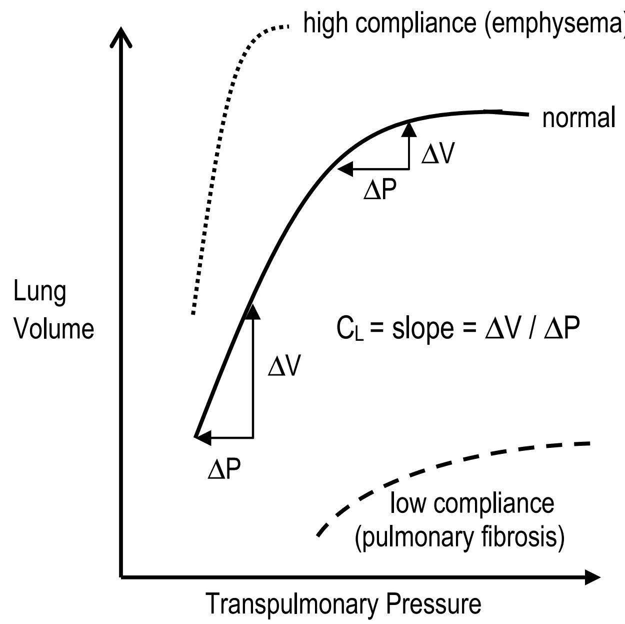
In order to expand the lungs, the inspiratory muscles must overcome two key factors: 1) **compliance of the lungs** and 2) **airways resistance** mainly in the form of frictional resistance to flow of air through the airways (see upcoming lecture on airway resistance). The force required to overcome the compliance of the lungs is indicated by the intrapleural pressure plot hatched line 1-5. The solid line 1'5', indicates the force required to overcome both the compliance of the lungs and airway resistance. The area between the two lines indicates the force required to overcome airway resistance.

4. Important Definitions: Compliance and Elastance

Compliance is the measure of **distensibility** of matter and specifies the ease with which matter can be stretched or distorted. Compliance is the inverse of elastance or elastic recoil, compliance=1/elastance. **Elastance** is property of matter that causes it to oppose stretch or distortion and the tendency of matter to return to its resting shape after deformation by an external force. The compliance of the lungs are often described by examining the pressure-volume characteristics of the lung under static conditions: when there is no flow of air and the respiratory muscles are relaxed. The transpulmonary pressure under these conditions reflects in magnitude the elastic recoil pressure of the lungs.

The Static Compliance of the Lungs (C_L)

The relationship between transpulmonary pressure and lung volume can be described for a range of transpulmonary pressures. This relationship is obtained under **static conditions** (no airflow) during **deflation of the lungs from TLC to FRC.** As transpulmonary pressure increases, lung volume naturally increase and this relationship is curvilinear. At relatively low lung volumes, the lungs are highly distensible and for a given change in transpulmonary pressure results in relatively large increases in lung volume. Whereas, at relatively high lung volumes, the lungs reach their limit of distensibility and for an equivalent change in transpulmonary pressure, there is little gain in lung volume. The measure of distensibility of the lung is called the **static compliance of the lung (C_L)** and is determined from the slope of the pressure-volume curve of the lungs ($C_L = \Delta V / \Delta P$; units = L/cm$H_2$0) near FRC.



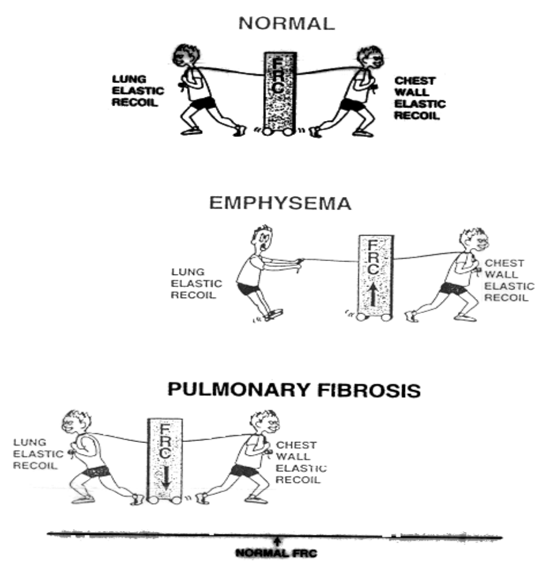
For comparison between lungs of different sizes, compliance is expressed per unit lung volume. This measurement is known as "specific compliance".

Representative Pressure-Volume Curves of the Lungs

The effect of changes in static compliance of the lungs on FRC are conceptualized in the cartoon on the right.

Compared to the normal, the P-V curve of the lungs in emphysema is shifted to the left, has a steep slope and TLC and FRC are elevated.

In contrast, in pulmonary fibrosis the curve is shifted to the right, has a shallow slope and TLC and FRC are decreased.



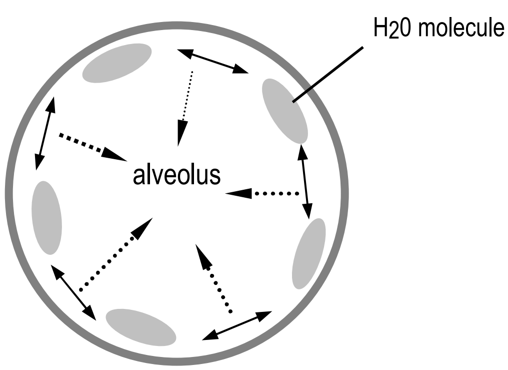
5. Key Factors that Affect Static Compliance of the Lungs

1. **Lung Volume** (see the slope of the normal P-V curve at low versus high lung volumes; consider the effect of surgical removal of lung tissue and hence a reduction in lung volume)

2. **Tissue Elastic Recoil** due to presence of elastin and collagen fibers in lung tissue. Consider:

   Aging Gradual loss of lung elastic tissue with advanced age increases compliance of the lungs.
   Disease Loss of elastin from lung tissue as in "emphysema" increases C_L. Increased collagen deposition in lung tissue in "pulmonary fibrosis" decreases lung compliance.

3. **Pulmonary Surfactant** produced by alveolar type II cells appears at about 25th week of gestation in the human fetus. It markedly reduces the surface tension at the alveolar-air interface and contributes to the distensibility of alveoli in the lungs. Lungs of prematurely born infants are deficient in pulmonary surfactant and prone to collapse. This deficiency results in the Neonatal Respiratory Distress Syndrome, NRDS, a condition that requires introduction of exogenous surfactant into the lungs to increase lung compliance and mechanical ventilation to prevent collapse of the lungs.



Alveolar surface tension
The attractive forces between the water (H_2O) molecules in the liquid film that lines the alveolus are responsible for surface tension.

Surface Tension: When liquid molecules are completely surrounded by other molecules in liquid phase, they are mutually attracted and move freely in all directions. When there is a liquid-gas interface, the liquid molecules at the interface are strongly attracted to liquid molecules within the liquid mass. This cohesive force is called surface tension. It is this surface tension force that maintains the shape of a droplet and makes it possible or insects to walk on surface of a pond. The lungs contain a huge air-liquid interface, most of which consists of the lining of alveoli. However, the lung fluid lining also contains pulmonary surfactant that does two things: 1) lowers the surface tension of the lining fluid so we can breathe without too much effort, and 2) makes the alveoli stable against collapse. Pulmonary surfactant is produced by Type II alveolar cells and reduces alveolar surface tension by interspersing itself between the water molecules. This increases lung compliance and reduces the tendency of the lungs to recoil inward. **The presence of pulmonary surfactant causes the surface tension to decrease in proportion to the ratio of surfactant to alveolar surface area.** Although there lecture time is insufficient to explore why surfactant has this characteristic, this is a core issue that helps you have a deeper understanding of this area and worthwhile to pursue (see pages 51- 53 in the Schwartztein textbook).

Appendix

Common symbols used in respiratory physiology

Primary Symbols denoting physical quantities

P pressure, tension or partial pressure of a gas
V volume of a gas
F fractional concentration of a gas
Q volume of blood

Secondary Symbols denoting the location of the gas

I inspired gas	a arterial blood
E expired gas	v venous blood
A alveolar gas	c capillary blood

Tertiary Symbols indicating particular gases

O_2=oxygen
CO_2 =carbon dioxide
N_2=nitrogen

In addition

• denotes time derivative of a physical quantity (i.e. the given quantity per unit time).
_ denotes average (mean)
′ denotes end capillary

Examples Of Respiratory Symbols

V_E minute ventilation

V_{O2} oxygen consumption

V_{CO2} carbon dioxide production

F_{EN2} fraction of expired nitrogen

v mixed venous

B_f breathing frequency

V_T tidal volume

V_D volume of dead space

P_{AO2} partial pressure of oxygen in the alveoli

P_{aCO2} partial pressure of carbon dioxide in the arterial blood

Concepts you should be familiar with from high school or first year science. Please review The Laws Governing Behaviour of Gases

Avogadro's Hypothesis Equal volume of different gases at equal temperature contain the same number of molecules. Similarly, equal numbers of molecules in identical volumes and at the same temperature will exert the same pressure. One mole of any gas will contain 6.02X 10^{23} molecules and will occupy a volume of 22.4 liters at a temperature of O °C and a pressure of 760 mmHg.

Ideal Gas Law **$PV = nRT$** where

R = universal gas constant =62.3656 L.mmHg/mole degree
n= number of moles of gas present
T is temperature in degrees Kelvin

The ideal gas law is the based on the following other laws that specify the relationship between the 3 factors affect the volume of a gas: pressure, temperature and amount.

- At a constant temperature the same amount of gas will decrease in volume with an increase in pressure **(Boyle's Law)**
- At constant pressure, the same amount of gas will increase in volume with an increase in temperature **(Charles' Law** or Gay Lussac's Law).

Hence at a constant temperature and pressure, the same amount of gas will remain at constant volume; the only factor that would change the volume would be an increase in the number of moles of gas present.

Dalton's Law of Partial Pressures In a gas mixture the pressure exerted by each individual gas in a space is independent of the pressure of other gases in the same mixture.
e.g. Total pressure of dry air = $P_{O2} + P_{CO2} + P_{N2}$
e.g. Alveolar gas mixture): $P_A = PA_{H2O} + PA_{O2} + PA_{CO2} + PA_{N2}$

Partial Pressure of a Gas in a Liquid Gases such as CO_2, O_2 and N_2 that are in physical solution in a liquid such as plasma, continually escape from the liquid into the gas phase and may also return to the liquid. When the rate of a gas coming out of solution is equal to the rate at which it enters the solution, the system is in equilibrium for that gas and liquid. At equilibrium, the partial pressure of a gas in gas phase is equal to the partial pressure (or tension) of the gas in liquid.

Partial Pressure of Water Vapour: Water molecules tend to either leave (forming water vapour) or enter their aqueous media (liquid water) and equilibrium occurs when the partial pressure of the water vapour above the liquid is equal to the vapour pressure of the liquid water. Water vapour does not obey the gas laws: As the pressure on any gas mixture increases, water molecules enter the liquid phase and the partial pressure of the water vapour remains constant.

Henry's Law: The amount of a gas that dissolves in a specific volume of liquid with which it does not combine chemically is almost directly proportional to the partial pressure of that gas in gas phase and its solubility (Bunsen) coefficient. Note that solubility coefficients differ for different gases and are temperature dependant.