Measurement of Respiratory Rates and Volumes

The normal adult respiratory rate is about 12 to 18 breaths per minute. For children the rate is about 18-20 breaths per minute.

The volume of air moved into or out of the lungs in a resting inhalation or exhalation is known as tidal volume and is about 500 ml. If we multiply tidal volume by the number of breaths per minute we have the respiratory minute volume. For example in a resting adult:

\[ \text{RMV} = \text{Breaths/min} \times \text{Tidal volume} \]

If breaths/min = 15 and tidal volume = 500 ml

Respiratory minute volume (RMV) = 7500 ml or 7.5 Liters

The respiratory minute volume indicates how much air has entered the respiratory system.

Respiratory volumes can be measured with a device called a spirometer. Besides tidal volume other volumes can be measured including inspiratory reserve volume and expiratory reserve volume.

Inspiratory reserve volume (IRV) is the maximum amount of air that can be inhaled in addition to tidal volume. IRV is usually about 3300 ml in males and 1900 ml in females.

Expiratory reserve volume (ERV) is the maximum amount of air that can be exhaled in addition to tidal volume. ERV is about 1000 ml.

Residual volume (RV) is the amount of air remaining in the lungs after a maximal exhalation. RV is about 1200 ml in males and 1100 in females.

Combining respiratory volumes gives us respiratory capacities. These include vital capacity, inspiratory capacity, functional residual capacity and total lung capacity.

Vital capacity is the maximal amount of air that can move in and out of the lungs in a single breath. It is the sum of tidal volume, inspiratory reserve volume and expiratory reserve volume. It is about 4800 ml in males and 3400 ml in females.

Inspiratory capacity is the amount of air that can move into the lungs after resting inhalation and exhalation. Inspiratory capacity is the sum of tidal volume and inspiratory reserve volume.

Functional residual capacity is the air remaining in the lungs after a resting inhalation and exhalation. Functional residual capacity is the sum of expiratory reserve volume and residual volume.

Total lung capacity is the total volume of air in the lungs. It is the sum of vital capacity and residual volume. It is about 6000 ml in males and 4500 ml in females.
**Gas Laws**

Air moves into the lungs by means of changes in volume and pressure. Air is a combination of a number of gases. Air consists of nitrogen (78.6%), oxygen (20.9%), carbon dioxide (.04%) and a trace amount of other gases.

Air produces an atmospheric pressure of 760 mm Hg and this pressure is produced by a combination of gases. Each gas produces a pressure that is proportional to its amount in the whole. This is known as Dalton’s Law.

The pressure each gas produces in the mixture of gases is known as the partial pressure of gas. We can represent the partial and total pressure of a gas such as air as follows:

\[
P(\text{nitrogen}) + P(\text{oxygen}) + P(\text{water vapor}) + P(\text{carbon dioxide}) = P(\text{air}) = 760 \text{ mm Hg}
\]

For example if oxygen produces 20.9% of the total pressure of air then 20.9% of 760 mm Hg is about 159 mm Hg. So the partial pressure of oxygen is 159 mm Hg. We can denote partial pressure as PO2 or PCO2.

Partial pressure can be thought to be analogous to concentration. Henry’s Law states that at a given temperature the amount of gas in a solution is directly proportional to the partial pressure of the gas. Gas, like other substances, follows a concentration gradient. We can say that gas follows a partial pressure gradient. For example oxygen will move from a PO2 of 100 mm Hg to a PO2 of 80 mm Hg.

**Respiratory System Gas Exchange**

Air enters the respiratory tract and is warmed and humidified. It eventually reaches the alveoli and mixes with the air resident there. Thus alveolar air differs from atmospheric air. For example alveolar air contains more carbon dioxide than atmospheric air.

After reaching the alveoli gases diffuse across the respiratory membrane and into the surrounding capillaries. The PO2 of alveolar air is about 104 mm Hg and the PCO2 is about 40 mm Hg. The PO2 deoxygenated blood is about 40 mm Hg and the PCO2 is about 45 mm Hg. Oxygen and carbon dioxide both diffuse in opposite directions across the respiratory membrane. Oxygen diffuses from the alveolus to the blood (PO2 of 104 mm Hg to PO2 of 40 mm Hg) and carbon dioxide diffuses from the blood (PCO2 of 45 mm Hg) to the alveolus (PCO2 of 40 mm Hg) (figs. 21.1, 21.2).

Other factors affecting the diffusion of gases include the solubility, the size of the concentration gradient, and the surface area and thickness of the respiratory membrane.

The solubility of a gas in liquid is represented by the solubility coefficient. The solubility coefficient for oxygen is .024 and for carbon dioxide is .57. This means that carbon dioxide is much more soluble (or able to dissolve) in water than oxygen. Both oxygen and carbon dioxide are lipid soluble as well and can easily move across the respiratory membrane. Damage to the respiratory membrane tends to affect the diffusion of oxygen before affecting carbon dioxide due to the increased solubility of carbon dioxide. Internal oxygen levels can then decrease to dangerous levels. Giving supplemental oxygen helps to increase the concentration of oxygen and aid diffusion.

The respiratory membrane’s total area is about 70 square meters. Some diseases can adversely affect the respiratory membrane. These include emphysema and lung cancer. Emphysema creates large
chambers within the lung that decrease the surface area of the respiratory membrane. Lung cancer produces tumors that decrease surface area as well.

Partial pressure and the subsequent pressure gradient can change by increasing or decreasing alveolar ventilation. Breathing slowly and deeply lowers alveolar PCO2 as more CO2 exits the lungs with each breath.

Oxygenated blood leaves the pulmonary circulation and enters the systemic circulation for distribution to the tissues. The PO2 of oxygenated blood is 104 mm Hg and the PCO2 is 40 mm Hg in the pulmonary circulation. The oxygenated blood mixes with blood from the bronchial veins causing the PO2 to decrease to 95 mm Hg. Blood leaving the pulmonary circulation and entering the systemic circulation has a PO2 of 95 mm Hg.

Oxygenated blood eventually reaches the tissues. The intracellular PO2 is about 40 mm Hg and decreases to about 20 mm Hg in the cells. Oxygen then diffuses down its partial pressure gradient into the interstitium and cells. The blood is now deoxygenated with a PO2 of 40 mm Hg.

Carbon dioxide is produced in the cells as a byproduct of metabolism. Therefore the highest PCO2 in the system is at the cells. The PCO2 is about 46 mm Hg in the cells and about 45 mm Hg in the interstitium. The PCO2 of oxygenated blood is about 40 mm Hg. Carbon dioxide diffuses from the interstitium to the blood. The resulting PCO2 of deoxygenated blood leaving the tissues is then 45 mm Hg.

Deoxygenated blood returns to the lungs where the alveolar PCO2 is about 40 mm Hg. Carbon dioxide then diffuses to the alveoli and is expelled with each exhaled breath.
Figure 21.1. Respiratory gas exchange of oxygen. Oxygen diffuses from the alveolus (PO2 = 104 mm Hg) to deoxygenated blood (PO2 = 40 mm Hg). The PO2 of the capillary blood in the respiratory system increases to 104 mm Hg but then mixes with blood in the respiratory system which causes it to decrease to 95 mm Hg in the systemic circulation. Oxygen then travels to the tissues where it diffuses into the interstitium (PO2 = 40 mm Hg). The cycle then repeats.
Figure 21.2 Respiratory gas exchange for carbon dioxide. Carbon dioxide is generated in the tissues (PCO2 = 45 mm Hg). Carbon dioxide diffuses from oxygenated blood (PCO2 = 40 mm Hg) to the tissues. The resultant deoxygenated blood has a PCO2 of 45 mm Hg. The blood travels to the lungs where it encounters an alveolar PCO2 of 40 mm Hg. Carbon dioxide then diffuses into the alveoli and is expelled during exhalation.

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Carbon Dioxide Transport in the Blood

Carbon dioxide is transported in the blood by three mechanisms. These include carbon dioxide dissolved in plasma, carbon dioxide combining with hemoglobin and storage of carbon dioxide in the bicarbonate ion.

About 7% of the total carbon dioxide in blood is dissolved in plasma. Carbon dioxide also combines with hemoglobin to form a compound known as carbaminohemoglobin. About 23% of carbon dioxide is transported as carbaminohemoglobin. The majority of carbon dioxide (about 70%) is transported in the bicarbonate ion.

\[ \text{CO}_2 + \text{HbNH}_2 \leftrightarrow \text{HbNCOOH} \]

Carbon dioxide diffuses into red blood cells and encounters the enzyme carbonic anhydrase to form carbonic acid. Carbonic acid is an ionically bonded molecule that dissociates into bicarbonate and hydrogen ions. Bicarbonate ions diffuse out of the red blood cells into the plasma. In order to maintain ionic stability chloride ions move into the red blood cell in what is called the chloride shift (fig 21.3).

The reaction is reversible with either the storage or release of carbon dioxide depending on what is needed. For example in areas of low PCO2 such as in the alveoli the reaction will work in the direction to release CO2 for removal by the lungs. In areas of high PCO2 such as in the tissues the reaction will work in the direction to store CO2 in the bicarbonate ion (fig. 21.4).

The hydrogen ions will bind to hemoglobin or move into the blood plasma. Most of the hydrogen ions bind to hemoglobin which acts as a buffer to help to maintain a narrow range of blood pH. Some hydrogen ions move into plasma directly affecting the blood pH.

Respiratory Acidosis/Alkalosis

Because most of the carbon dioxide is transported by the bicarbonate ion with subsequent release of hydrogen ions, a buildup of carbon dioxide in the blood will produce a lower pH. This is known as respiratory acidosis and can result from the inability of the lungs to get rid of excess carbon dioxide such as in diseases like emphysema or chronic bronchitis. You can generate a mild case of respiratory acidosis by simple holding your breath. The cells continue to produce carbon dioxide but the lungs are not removing it through exhalation. Carbon dioxide builds up in the lungs producing the hydrogen ion byproduct and the blood begins to become acidic.

Likewise you can produce a mild state of respiratory alkalosis by hyperventilating. In this case too much carbon dioxide is removed by the lungs and the hydrogen ion concentration subsequently decreases.
Figure 21.3. Storage of carbon dioxide in bicarbonate ions. Carbon dioxide combines with water and carbonic anhydrase to form carbonic acid that dissociates into bicarbonate and hydrogen ions. Both move out of the red blood cell with chloride ions moving in to maintain ionic stability. Carbon dioxide also enters the red blood cell and combines with hemoglobin. This process occurs in areas of high PCO2 where carbon dioxide needs to be transported.
Figure 21.4. In areas of low PCO2 the process reverses. Bicarbonate and hydrogen ions enter the red blood cell and are converted to carbonic acid which converts to water and carbon dioxide. Hemoglobin also releases carbon dioxide. Both mechanisms work to release carbon dioxide for diffusion into the lungs so that it can be expelled by exhalation.

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**Oxygen Transport**

Most of the oxygen transported in blood is bound to hemoglobin to form oxyhemoglobin. A small amount of oxygen is dissolved in plasma. Each hemoglobin molecule can bind with four oxygen molecules. Hemoglobin can also release oxygen to form deoxyhemoglobin. There are almost 300 million hemoglobin molecules in one red blood cell. The functional characteristics of hemoglobin are also variable and respond to changes in PO2, pH, and temperature.

The degree of oxygen binding to hemoglobin can be represented by what is known as an oxygen–hemoglobin saturation curve (fig. 21.25). If all of the hemoglobin is fully bound with oxygen molecules then the saturation is 100%.

By examining the saturation curve we can see that in areas of lower PO2 hemoglobin tends to release oxygen. In other words we can say that hemoglobin decreases its affinity for oxygen binding. This makes sense because low areas of PO2 such as in the tissues require free oxygen to diffuse into the interstitium and supply the cells. For example tissue PO2 is about 40 mm Hg. At this PO2 hemoglobin is about 75% saturated which means that about 23% of the oxygen bound to hemoglobin was released. The remaining 75% of oxygen acts like a reserve in case PO2 goes even lower. In the tissues small changes in PO2 can have a large effect on the release of oxygen. This helps to ensure that the tissues receive enough oxygen so they can function properly.

Likewise in areas of higher PO2 we see that hemoglobin is almost completely saturated (about 98%). This means that hemoglobin would bind with oxygen in areas such as the alveolar capillaries so that oxygen can be carried to the tissues. For example alveolar PO2 is about 104 mm Hg. By examining the curve we can see that hemoglobin is 98% saturated. Even if PO2 drops to 80 mm Hg we see that hemoglobin is still 95.8% saturated.

The functional characteristics of hemoglobin can change. Hemoglobin saturation is affected by changes in pH, temperature and PCO2.

As pH decreases more free hydrogen ions are bound to hemoglobin changing its function and causing it to release oxygen more readily. In other words we can say that in areas of lower pH hemoglobin decreases its affinity for oxygen binding. Likewise in areas of increased pH will increase hemoglobin’s affinity for oxygen binding. This change in binding affinity for oxygen is known as the Bohr effect (Christian Bohr).

Hemoglobin also changes with respect to carbon dioxide binding at the same time it changes for oxygen binding. As pH decreases hemoglobin increases its affinity for carbon dioxide binding. Likewise in areas of increased pH hemoglobin will decrease its affinity for carbon dioxide binding. These changes in hemoglobin function for carbon dioxide are known as the Haldane effect.

An increase in PCO2 has the same effect as a decrease in pH. Hemoglobin again decreases its affinity for oxygen binding. Release of hydrogen ions and bound carbon dioxide work to produce this effect.

Increased temperatures also decrease hemoglobin’s affinity for oxygen binding. Again hemoglobin works to release oxygen into the tissues during times of increased metabolism such as with exercise or fever.
The changes in hemoglobin’s function with decreases in pH, increases in PCO2 and temperature can be represented by a right shift in the saturation curve. Likewise in areas of higher pH, lower PCO2 and decreased temperature hemoglobin resumes its normal function. We can say the saturation curve shifts to the left.

For example exercise will cause an increased metabolic demand in the tissues and subsequent need for oxygen supply and removal of carbon dioxide. PCO2 increases in skeletal muscle tissue with a subsequent increase in hydrogen ion concentration resulting in a lower pH. Byproducts of anaerobic metabolism such as lactic acid also work to decrease pH.

The decrease in pH causes a right shift in the hemoglobin saturation curve. In other words hemoglobin works to release oxygen in the tissues and pick up carbon dioxide more readily. At the lungs however pH is in the normal range. Hemoglobin then works to release carbon dioxide and bind with oxygen for transport to the tissues. The saturation curve then shifts to the right in skeletal muscle and then back to the left in the lungs.

![Oxygen-hemoglobin saturation curve](http://commons.wikimedia.org/wiki/File:Hb_saturation_curve.png)
Neural Control of Respiration

Neural control of respiration begins in the brainstem at the medulla oblongata and the pons. The medulla contains the medullary respiratory center. The medullary respiratory center consists of two groups of neurons called the dorsal and ventral respiratory groups.

The dorsal respiratory group consists of two groups of neurons located in the posterior area of the medulla oblongata. This group is primarily responsible for contraction of the diaphragm for regulation of breathing rate. The neurons receive input from other parts of the brain and receptors that sense changes in concentrations of gases and pH.

The ventral respiratory group stimulates the external and internal intercostals and abdominal muscles. This group works to regulate breathing rhythm.

The pons contains the pneumotaxic center (now called the pontine respiratory group). This center works with the centers in the medulla and helps to fine tune breathing rate and rhythm. The pneumotaxic center also receives input from other centers in the brain.

The apneustic center also resides in the pons. The pneumotaxic center inhibits the apneustic center to help control exhalation. However if damage to the brainstem occurs the person can exhibit what is known as apneustic breathing. This consists of a very slow respiration rate with a deep inhalation held for ten to twenty seconds followed by shallow and brief exhalations that provide little pulmonary ventilation.

All of the above respiratory centers innervate the phrenic and intercostals nerves.

Neural Events of Breathing

For normal resting breathing the following neural events occur. The dorsal respiratory group becomes active causing contraction of the diaphragm and external intercostal muscles. Air moves into the lungs. The dorsal respiratory group is now inhibited causing relaxation of the respiratory muscles and passive exhalation.

For forceful breathing both the dorsal and ventral respiratory groups are active causing the respiratory muscles and accessory muscles to contract. Part of the ventral respiratory group that innervates the muscles of expiration is inhibited. Air moves into the lungs. The dorsal respiratory group is now inhibited while the ventral respiratory group is activated. The muscles of inspiration relax while the muscles of expiration contract. Air is expelled from the lungs.

Other Neural Centers

Breathing is not entirely unconscious. We can decide to take in a deep breath or hold our breath. The cerebral cortex provides connections to the brainstem centers for breathing. The limbic system also affects breathing. For example strong emotions elicited in the limbic system can speed up breathing.

Sensory Feedback for Breathing

Chemoreceptors that sense changes in concentration of PO2 and pH are involved in controlling respiration. These receptors are located in the medulla oblongata as well as the carotid and aortic bodies. The carotid bodies connect to the medulla via the glossopharyngeal nerve (CN IX). The aortic body connects to the medulla via the vagus nerve (CN X).
The medulla oblongata senses changes in pH by way of carbon dioxide diffusion. Increased blood levels of carbon dioxide result in an increased rate and depth of breathing. The respiratory centers are very sensitive to changes in PCO2. Small increases in PCO2 can cause large increases in respiratory rate. A greater than normal PCO2 is called hypercapnia while a lower than normal PCO2 is called hypocapnia.

Neural respiratory centers are also sensitive to changes in PO2 but changes in PCO2 account for the majority of respiratory regulation. If PO2 levels decrease while PCO2 levels remain normal there will be a subsequent increase in respiration rate. A lower than normal PO2 is called hypoxia. Small changes in PO2 do not cause an appreciable stimulation of the respiratory centers.

Hering-Breuer Reflex

Another neural control mechanism is the Hering-Breuer reflex. This reflex is a protective mechanism and prevents overinflation of the lungs. Stretch receptors on the walls of the bronchi and bronchioles send impulses to the vagus nerve to the medulla oblongata. The impulses inhibit the respiratory centers and produce exhalation.