

**Objectives** 1-Define partial pressure of a gas, how is influenced by altitude.

- 2- Understand that the pressure exerted by each gas in a mixture of gases is independent of the pressure exerted by the other gases (Dalton's Law)
- 3- Understand that gases in a liquid diffuse from higher partial pressure to lower partial pressure (Henry's Law)
- 4- Describe the factors that determine the concentration of a gas in a liquid.
- 5- Describe the components of the alveolar-capillary membrane (i.e., what does a molecule of gas pass through).
- 6- Knew the various factors determining gas transfer: -

Surface area, thickness, partial pressure difference, and diffusion coefficient of gas

7- State the partial pressures of oxygen and carbon dioxide in the atmosphere, alveolar gas, at the end of the pulmonary capillary, in systemic capillaries, and at the beginning of a pulmonary capillary.



- After ventilation of the alveoli with fresh air the next step is the process called Diffusion of oxygen and carbon dioxide.
- The rate of diffusion of each of these gases is directly proportional to the pressure caused by this gas alone which is called the partial pressure of the gas
- Pressure is caused by the constant impact of kinetically moving molecules against a surface.



#### Quantifying the Net Rate of Diffusion in Fluids.

In addition to the pressure difference, several other factors affect the rate of gas diffusion in a fluid. They are (1) the solubility of the gas in the fluid, (2) the cross-sectional area of the fluid, (3) the distance through which the gas must diffuse, (4) the molecular weight of the gas, and (5) the temperature of the fluid. In the body, the last of these factors, the temperature, remains reasonably constant and usually need not be considered.

The greater the solubility of the gas, the greater the number of molecules available to diffuse for any given partial pressure difference. The greater the cross-sectional area of the diffusion pathway, the greater the total number of molecules that diffuse. Conversely, the greater the distance the molecules must diffuse, the longer it will take the molecules to diffuse the entire distance. Finally, the greater the velocity of kinetic movement of the molecules, which is inversely proportional to the square root of the molecular weight, the greater the rate of diffusion of the gas. All these factors can be expressed in a single formula, as follows:

in which D is the diffusion rate,  $\Delta P$  is the partial pressure difference between the two ends of the diffusion pathway, A is the cross-sectional area of the pathway, S is the solubility of the gas, d is the distance of diffusion, and MW is the molecular weight of the gas.

It is obvious from this formula that the characteristics of the gas itself determine two factors of the formula: solubility and molecular weight. Together, these two factors determine the *diffusion coefficient of the gas*, which is proportional to that is, the relative rates at which different gases at the same partial pressure levels will diffuse are proportional to their diffusion coefficients. Assuming that the diffusion coefficient for oxygen is 1,



# Factors That Determine the Partial Pressure of a Gas Dissolved in a Fluid.

The partial pressure of a gas in a solution is determined not only by its concentration but also by the *solubility coefficient* of the gas. That is, some types of molecules, <u>especially carbon dioxide</u>, <u>are physically or chemically attracted to water molecules</u>, whereas others are repelled. When molecules are attracted, far more of them can be dissolved without building up excess partial pressure within the solution. Conversely, in the case of those that are repelled, high partial pressure will develop with fewer dissolved molecules. These relations are expressed by the following formula, which is *Henry's law:* 

When partial pressure is expressed in atmospheres (1 atmosphere pressure equals 760 mm Hg) and concentration is expressed in volume of gas dissolved in each volume of water, the solubility coefficients for important respiratory gases at body temperature are the following:

From this table, one can see that carbon dioxide is more than 20 times as soluble as oxygen. Therefore, the partial pressure of carbon dioxide (for a given concentration) is less than one-twentieth that exerted by oxygen.





•In respiratory physiology, one deals with mixtures of gases, mainly of *oxygen, nitrogen*, and*carbon dioxide*. The rate of diffusion of each of these gases is directly proportional to the pressure caused by that gas alone, which is called the *partial pressure* of that gas. The concept of partial pressure can be explained as follows.



Consider air, which has an approximate composition of 79 percent nitrogen and 21 percent oxygen. The total pressure of this mixture at sea level averages 760 mm Hg. It is clear from the preceding description of the molecular basis of pressure that each gas contributes to the total pressure in direct proportion to its concentration. Therefore, 79 percent of the 760 mm Hg is caused by nitrogen (600 mm Hg) and 21 percent by oxygen (160 mm Hg). Thus, the "partial pressure" of nitrogen in the mixture is 600 mm Hg, and the "partial pressure" of oxygen is 160 mm Hg; the total pressure is 760 mm Hg, the sum of the individual partial pressures. The partial pressures of individual gases in a mixture are designated by the symbols PO<sub>2</sub>, PCO<sub>2</sub>, PN<sub>2</sub>, PHe, and so forth.





#### **Diffusion of Gases Through Tissues**

The gases that are of respiratory importance are all highly soluble in lipids and, consequently, are highly soluble in cell membranes. Because of this, the major limitation to the movement of gases in tissues is the rate at which the gases can diffuse through the tissue water instead of through the cell membranes. Therefore, diffusion of gases through the tissues, including through the respiratory membrane, is almost equal to the diffusion of gases in water,



#### Expired Air Is a Combination of Dead Space Air and Alveolar Air

**Figure 39-6** Oxygen and carbon dioxide partial pressures in the various portions of normal expired air. The overall composition of expired air is determined by (1) the amount of the expired air that is dead space air and (2) the amount that is alveolar air. Figure 39-6 shows the progressive changes in oxygen and carbon dioxide partial pressures in the expired air during the course of expiration. The first portion of this air, the dead space air from the respiratory passageways, is typical humidified air, as shown in <u>Table 39-1</u>. Then, progressively more and more alveolar air becomes mixed with the dead space air until all the dead space air has finally been washed out and nothing but alveolar air is expired at the end of expiration. Therefore, the method of collecting alveolar air for study is simply to collect a sample of the last portion of the expired air after forceful expiration has removed all the dead space air.

Normal expired air, containing both dead space air and alveolar air, has gas concentrations and partial pressures approximately as shown in <u>Table 39-1</u> (i.e., concentrations between those of alveolar air and humidified atmospheric air).



- At resting condition 250 ml of oxygen enter the pulmonary capillaries/min at ventilatory rate of 4.2 L/min.
- During exercise 1000 ml of oxygen is absorbed by the pulmonary capillaries per minute, the rate of alveolar ventilation must increase 4 times to maintain the alveolar PO2 at the normal value of 104 mmHg.
- Normal rate of CO2 excretion is 200 ml/min, at normal rate of alveolar ventilation of 4.2 L/min.

#### Oxygen Concentration and Partial Pressure in the Alveoli

Oxygen is continually being absorbed from the alveoli into the blood of the lungs, and new oxygen is continually being breathed into the alveoli from the atmosphere. The more rapidly oxygen is absorbed, the lower its concentration in the alveoli becomes; conversely, the more rapidly new oxygen is breathed into the alveoli from the atmosphere, the higher its concentration becomes. Therefore, oxygen concentration in the alveoli, as well as its partial pressure, is controlled by (1) the rate of absorption of oxygen into the blood and (2) the rate of entry of new oxygen into the lungs by the ventilatory process.

**Figure 39-4** Effect of alveolar ventilation on the alveolar  $PO_2$  at two rates of oxygen absorption from the...<u>Figure 39-4</u> shows the effect of both alveolar ventilation and rate of oxygen absorption into the blood on the alveolar partial pressure of oxygen (PO<sub>2</sub>). One curve represents oxygen absorption at a rate of 250 ml/min, and the other curve represents a rate of 1000 ml/min. At a normal ventilatory rate of 4.2 L/min and an oxygen consumption of 250 ml/min, the normal operating point in <u>Figure 39-4</u> is point A. The figure also shows that when 1000 milliliters of oxygen is being absorbed each minute, as occurs during moderate exercise, the rate of alveolar ventilation must increase fourfold to maintain the alveolar  $PO_2$  at the normal value of 104 mm Hg.

Another effect shown in Figure 39-4 is that an extremely marked increase in alveolar ventilation can never increase the alveolar  $PO_2$  above 149 mm Hg as long as the person is breathing normal atmospheric air at sea level pressure, because this is the maximum  $PO_2$  in humidified air at this pressure. If the person breathes gases that contain partial pressures of oxygen higher than 149 mm Hg, the alveolar  $PO_2$  can approach these higher pressures at high rates of ventilation.

#### CO<sub>2</sub> Concentration and Partial Pressure in the Alveoli

**Figure 39-5** Effect of alveolar ventilation on the alveolar  $PCO_2$  at two rates of carbon dioxide excretion from...Carbon dioxide is continually being formed in the body and then carried in the blood to the alveoli; it is continually being removed from the alveoli by ventilation. Figure 39-5 shows the effects on the alveolar partial pressure of carbon dioxide ( $PCO_2$ ) of both alveolar ventilation and two rates of carbon dioxide excretion, 200 and 800 ml/min. One curve represents a normal rate of carbon dioxide excretion of 200 ml/min. At the normal rate of alveolar ventilation of 4.2 L/min, the operating point for alveolar PCO<sub>2</sub> is at point A in Figure 39-5 (i.e., 40 mm Hg).

Two other facts are also evident from Figure 39-5 : First, the alveolar  $PCO_2$  increases directly in proportion to the rate of carbon dioxide excretion, as represented by the fourfold elevation of the curve (when 800 milliliters of  $CO_2$  are excreted per minute). Second, the alveolar  $PCO_2$  decreases in inverse proportion to alveolar ventilation. Therefore, the concentrations and partial pressures of both oxygen and carbon dioxide in the alveoli are determined by the rates of absorption or excretion of the two gases and by the amount of alveolar ventilation.









### Terminology

O<sub>2</sub> content: amount of O<sub>2</sub> in blood (mL O<sub>2</sub>/100 mL blood)

 $O_2$ -binding capacity: maximum amount of  $O_2$  bound to hemoglobin (mL  $O_2$ /100 mL blood) measured at 100% saturation.

Percent saturation: % of heme groups bound to O<sub>2</sub>

% saturation of Hb = <u>oxygen content</u> x 100 oxygen capacity

Dissolved  $O_2$ : Unbound  $O_2$  in blood (mL  $O_2/100$  mL blood).



#### **Reversible Combination of Oxygen with Hemoglobin**

The chemistry of hemoglobin is presented in <u>Chapter 32</u>, where it was pointed out that the oxygen molecule combines loosely and reversibly with the hemo portion of hemoglobin. When PO<sub>2</sub> is high, as in the pulmonary capillaries, oxygen binds with the hemoglobin, but when PO<sub>2</sub> is low, as in the tissue capillaries, oxygen is released from the hemoglobin. This is the basis for almost all oxygen transport from the lungs to the tissues.

#### Maximum Amount of Oxygen That Can Combine with the Hemoglobin of the Blood.

The blood of a normal person contains about 15 grams of hemoglobin in each 100 milliliters of blood, and each gram of hemoglobin can bind with a maximum of 1.34 milliliters of oxygen (1.39 milliliters when the hemoglobin is chemically pure, but impurities such as methemoglobin reduce this). Therefore, 15 times 1.34 equals 20.1, which means that, on average, the 15 grams of hemoglobin in 100 milliliter of blood can combine with a total of about 20 milliliters of oxygen if the hemoglobin is 100 percent saturated. This is usually expressed as 20 volumes percent. The oxygen-hemoglobin dissociation curve for the normal person can also be expressed in terms of volume percent of oxygen, as shown by the far right scale in Figure 40-8, instead of percent saturation of hemoglobin.

Figure 40-9 Effect of blood PO<sub>2</sub> on the quantity of oxygen bound with hemoglobin in each 100 milliliters of...Amount of Oxygen Released from the Hemoglobin When Systemic Arterial Blood Flows Through the Tissues.

The total quantity of oxygen *bound with hemoglobin* in normal systemic arterial blood, which is 97 percent saturated, is about 19.4 milliliters per 100 milliliters of blood. This is shown in <u>Figure 40-9</u>. On passing through the tissue capillaries, this amount is reduced, on average, to 14.4 milliliters ( $PO_2$  of 40 mm Hg, 75 percent saturated hemoglobin). Thus, *under normal conditions, about 5 milliliters of oxygen are transported from the lungs to the tissues by each 100 milliliters of blood flow*.

Transport of Oxygen During Strenuous Exercise.

During heavy exercise, the muscle cells use oxygen at a rapid rate, which, in extreme cases, can cause the muscle interstitial fluid PO<sub>2</sub> to fall from the normal 40 mm Hg to as low as 15 mm Hg. At this low pressure, only 4.4 milliliters of oxygen remain bound with the hemoglobin in each 100 milliliters of blood, as shown in <u>Figure 40-9</u>. Thus, 19.4 – 4.4, or 15 milliliters, is the quantity of oxygen actually delivered to the tissues by each 100 milliliters of blood flow. Thus, three times as much oxygen as normal is delivered in each volume of blood that passes through the tissues.



#### Role of Hemoglobin in Oxygen Transport

<u>Normally, about 97 percent of the oxygen transported from the lungs to the</u> <u>tissues is carried in chemical combination with hemoglobin</u> in the red blood cells. <u>The remaining 3 percent is transported in the dissolved state in the water</u> <u>of the plasma and blood cells</u>. Thus, *under normal conditions*, oxygen is carried to the tissues almost entirely by hemoglobin.

# Figure 40-8 Oxygen-hemoglobin dissociation curve.Oxygen-Hemoglobin Dissociation Curve.

Figure 40-8 shows the oxygen-hemoglobin dissociation curve, which demonstrates a progressive increase in the percentage of hemoglobin bound with oxygen as blood  $PO_2$  increases, which is called the *percent saturation of hemoglobin*. Because the blood leaving the lungs and entering the systemic arteries usually has a  $PO_2$  of about 95 mm Hg, one can see from the dissociation curve that the *usual oxygen saturation of systemic arterial blood averages 97 percent*. Conversely, in normal venous blood returning from the peripheral tissues, the  $PO_2$  is about 40 mm Hg, and *the saturation of hemoglobin averages 75 percent*.







# Factors That Shift the Oxygen-Hemoglobin Dissociation Curve—Their Importance for Oxygen Transport

**Figure 40-10** Shift of the oxygen-hemoglobin dissociation curve to the right caused by an increase in...The oxygen-hemoglobin dissociation curves of Figures 40-8 and Figure 40-9 are for normal, average blood. However, a number of factors can displace the dissociation curve in one direction or the other in the manner shown in Figure 40-10. This figure shows that when the blood becomes slightly acidic, with the pH decreasing from the normal value of 7.4 to 7.2, the oxygen-hemoglobin dissociation curve shifts, on average, about 15 percent to the right. Conversely, an increase in pH from the normal 7.4 to 7.6 shifts the curve a similar amount to the left.

In addition to pH changes, several other factors are known to shift the curve. Three of these, all of which shift the curve to the *right*, are (1) increased carbon dioxide concentration, (2) increased blood temperature, and (3) increased 2,3-biphosphoglycerate (BPG), a metabolically important phosphate compound present in the blood in different concentrations under different metabolic conditions

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What is P50? The partial pressure of oxygen needed to maintain a SaO2 of 50

#### Increased Delivery of Oxygen to the Tissues When Carbon Dioxide and Hydrogen Ions Shift the Oxygen-Hemoglobin Dissociation Curve—The Bohr Effect.

A shift of the oxygen-hemoglobin dissociation curve <u>to the right in</u> response to increases in blood carbon dioxide and hydrogen ions has a significant effect by enhancing the release of oxygen from the blood in the tissues and enhancing oxygenation of the blood in the lungs. This is called the *Bohr effect*,which can be explained as follows: As the blood passes through the tissues, carbon dioxide diffuses from the tissue cells into the blood. This increases the blood PCO<sub>2</sub>, which in turn raises the blood H<sub>2</sub>CO<sub>3</sub>(carbonic acid) and the hydrogen ion concentration. These effects shift the oxygenhemoglobin dissociation curve to the right and downward, as shown in <u>Figure</u> <u>40-10</u>, forcing oxygen away from the hemoglobin and therefore delivering increased amounts of oxygen to the tissues.

Exactly the opposite effects occur in the lungs, where carbon dioxide diffuses from the blood into the alveoli. This reduces the blood  $PCO_2$  and decreases

the hydrogen ion concentration, shifting the oxygen-hemoglobin dissociation <u>curve to the left</u> and upward. Therefore, the quantity of oxygen that binds with the hemoglobin at any given alveolar  $PO_2$  becomes considerably increased, thus allowing greater oxygen transport to the tissues.

Effect of BPG to Cause Rightward Shift of the Oxygen-Hemoglobin Dissociation Curve.

The normal BPG in the blood keeps the oxygen-hemoglobin dissociation curve shifted slightly to the right all the time. In hypoxic conditions that last longer than a few hours, the quantity of BPG in the blood increases considerably, thus shifting the oxygen-hemoglobin dissociation curve even farther to the right. This causes oxygen to be released to the tissues at as much as 10 mm Hg higher tissue oxygen pressure than would be the case without this increased BPG. Therefore, under some conditions, the BPG mechanism can be important for adaptation to hypoxia, especially to hypoxia caused by poor tissue blood flow



The Rt and Lt shifts:

 Rt shift means the oxygen is unloaded to the tissues from Hb, while <u>Lt shift means</u> loading or attachment of oxygen to Hb.

Increased 2,3DPG, H+, Temperature, PCO2 shift the curve to right.

- 2,3DPG is synthesized in RBCs from the glycolytic pathway, it binds tightly to reduced Hb. increased 2,3 DPG facilitate the oxygen release and shifts the dissociation curve to Rt.
- ▶ 2,3 DPG increases in the RBCs in anemia and hypoxemia, and thus serves as an important adaptive response in maintaining tissue oxygenation
- ▶ Fetal Hb: has a P50 of 20 mmHg in comparison to 27 mmHg of adult Hb.



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# Rightward Shift of the Oxygen-Hemoglobin Dissociation Curve During Exercise.

During exercise, several factors shift the dissociation curve considerably to the right, thus delivering extra amounts of oxygen to the active, exercising muscle fibers. The exercising muscles, in turn, release large quantities of carbon dioxide; this and several other acids released by the muscles increase the hydrogen ion concentration in the muscle capillary blood. In addition, the temperature of the muscle often rises  $2^{\circ}$  to  $3^{\circ}$ C, which can increase oxygen delivery to the muscle fibers even more. All these factors act together to shift the oxygen-hemoglobin dissociation curve of the muscle capillary blood considerably to the right. This rightward shift of the curve forces oxygen to be released from the blood hemoglobin to the muscle at PO<sub>2</sub> levels as great as 40 mm Hg, even when 70 percent of the oxygen has already been removed from the hemoglobin. Then, in the lungs, the shift occurs in the opposite direction, allowing the pickup of extra amounts of oxygen from the alveoli.



#### Transport of Oxygen in the Dissolved State

At the normal arterial  $PO_2$  of 95 mm Hg, about 0.29 milliliter of oxygen is dissolved in every 100 milliliters of water in the blood, and when the  $PO_2$  of the blood falls to the normal 40 mm Hg in the tissue capillaries, only 0.12 milliliters of oxygen remains dissolved. In other words, 0.17 milliliters of oxygen is normally transported in the dissolved state to the tissues by each 100 milliliters of arterial blood flow. This compares with almost 5 milliliters of oxygen transported by the red cell hemoglobin. Therefore, the amount of oxygen transported to the tissues in the dissolved state is normally slight, only about 3 percent of the total, as compared with 97 percent transported by the hemoglobin.



# Combination of Hemoglobin with Carbon Monoxide—Displacement of Oxygen

Figure 40-12 Carbon monoxide-hemoglobin dissociation curve. Note the extremely low carbon monoxide...Carbon monoxide combines with hemoglobin at the same point on the hemoglobin molecule as does oxygen; it can therefore displace oxygen from the hemoglobin, thereby decreasing the oxygen-carrying capacity of blood. Further, it binds with about 250 times as much tenacity as oxygen, which is demonstrated by the carbon monoxidehemoglobin dissociation curve in Figure 40-12. This curve is almost identical to the oxygen-hemoglobin dissociation curve, except that the carbon monoxide partial pressures, shown on the abscissa, are at a level 1/250of those for the oxygenhemoglobin dissociation curve of Figure 40-8. Therefore, a carbon monoxide partial pressure of only 0.4 mm Hg in the alveoli, 1/250 that of normal alveolar oxygen (100 mm Hg PO<sub>2</sub>), allows the carbon monoxide to compete equally with the oxygen for combination with the hemoglobin and causes half the hemoglobin in the blood to become bound with carbon monoxide instead of with oxygen. Therefore, a carbon monoxide pressure of only 0.6 mm Hg (a volume concentration of less than one part per thousand in air) can be lethal.

### Transport of carbon dioxide in the blood

Carbon dioxide is transported in three forms.

- Dissolved CO2 7%
- bicarbonate ions 70 %
- Carbaminohemoglobin (with Hb) 23%.
  Each 100 ml of blood carry 4 ml of CO2 from the tissues/min.



### The Haldane effect

- When oxygen binds with hemoglobin, carbon dioxide is released- to increase CO2 transport
- Binding of Hb with O2 at the lung causes the Hb to become a stronger acid and , this in turn displaces CO2 from the blood and into the alveoli
- Change in blood acidity during CO2 transport.

Arterial blood has a PH of 7.41 that of venous blood with higher PCO2 falls to 7.37 ( i.e change of 0.04 unit takes place)



#### **Respiratory Exchange Ratio**

The discerning student will have noted that normal transport of oxygen from the lungs to the tissues by each 100 milliliters of blood is about 5 milliliters, whereas normal transport of carbon dioxide from the tissues to the lungs is about 4 milliliters. Thus, under normal resting conditions, only about 82 percent as much carbon dioxide is expired from the lungs as oxygen is taken up by the lungs. The ratio of carbon dioxide output to oxygen uptake is called the *respiratory exchange ratio* (R). That is,

The value for R changes under different metabolic conditions. When a person is using exclusively carbohydrates for body metabolism, R rises to 1.00. Conversely, when a person is using exclusively fats for metabolic energy, the R level falls to as low as 0.7. The reason for this difference is that when oxygen is metabolized with carbohydrates, one molecule of carbon dioxide is formed for each molecule of oxygen consumed; when oxygen reacts with fats, a large share of the oxygen combines with hydrogen atoms from the fats to form water instead of carbon dioxide. In other words, when fats are metabolized, the *respiratory quotient of the chemical reactions* in the tissues is about 0.70 instead of 1.00. (The tissue respiratory quotient is discussed in <u>Chapter 71</u>.) For a person on a normal diet consuming average amounts of carbohydrates, fats, and proteins, the average value for R is considered to be 0.825.