University of Anbar
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Lectures of human physiology

Lec. 7

Respiratory Physiology

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THE RESPIRATORY SYSTEM

The respiratory system is divided into a respiratory zone, which is the site of gas exchange between air and blood, and a conducting zone. The exchange of gases between air and blood occurs across the walls of respiratory alveoli, which permit rapid rates of gas diffusion.

The term *respiration* includes three separate but related functions: (1) **ventilation** (breathing); (2) **gas exchange,** which occurs between the air and blood in the lungs and between the blood and other tissues of the body; and (3) **oxygen utilization** by the tissues in the energy-liberating reactions of cell respiration. Ventilation and the exchange of gases (oxygen and carbon dioxide) between the air and blood are collectively called *external respiration.* Gas exchange between the blood and other tissues and oxygen utilization by the tissues are collectively known as *internal respiration.* Ventilation is the mechanical process that moves air into and out of the lungs. Because the oxygen concentration of air is higher in the lungs than in the blood, oxygen diffuses from air to blood. Carbon dioxide, conversely, moves from the blood to the air within the lungs by diffusing down its concentration gradient. As a result of this gas exchange, the inspired air contains more oxygen and less carbon dioxide than the expired air.

More importantly, blood leaving the lungs (in the pulmonary veins) has a higher oxygen and a lower carbon dioxide concentration than the blood delivered to the lungs in the pulmonary arteries. This is because the lungs function to bring the blood into gaseous equilibrium with the air. Gas exchange between the air and blood occurs entirely by diffusion through lung tissue. This diffusion occurs very rapidly because of the large surface area within the lungs and the very small diffusion distance between blood and air.

Structure of the Respiratory System

Gas exchange in the lungs occurs across an estimated 300 million tiny (about 100 µm in diameter) air sacs known as **alveoli.** Their enormous number provides a large surface area (60 to 80 square meters, or about 760 square feet) for diffusion of gases. The diffusion rate between the alveolar air and capillary blood also depends on the distance separating them. The thickness of the average alveolar cell and capillary endothelial cells is about 0.15 µm each, forming an extremely thin air-blood distance of only about 0.3 µm.

There are two types of alveolar cells, designated **type I alveolar cells** and **type II alveolar cells** (fig. 7.1). The type I alveolar cells comprise 95% to 97% of the total surface area of the lung; gas exchange with the blood thus occurs primarily through type I alveolar cells. These cells are accordingly very thin: where the basement membranes of the type I alveolar cells and capillary endothelial cells fuse, the diffusion distance between blood and air can be as little as 0.3 µm, which is about 1/100th the width of a human hair. The type II alveolar cells are the cells that secrete pulmonary surfactant and that reabsorb Na^{+1} and H_2O, thereby preventing fluid buildup within the alveoli.

Alveoli are polyhedral in shape and are usually clustered, like the units of a honeycomb (fig. 16.3). Air within one member of a cluster can enter other members through tiny pores. These clusters of alveoli usually occur at the ends of respiratory bronchioles, the very thin air tubes that end blindly in alveolar sacs. Individual alveoli also occur as separate outpouchings along the length of respiratory bronchioles. Although the distance between each respiratory bronchiole and its terminal alveoli is only about 0.5 mm, these units together constitute most of the mass of the lungs.

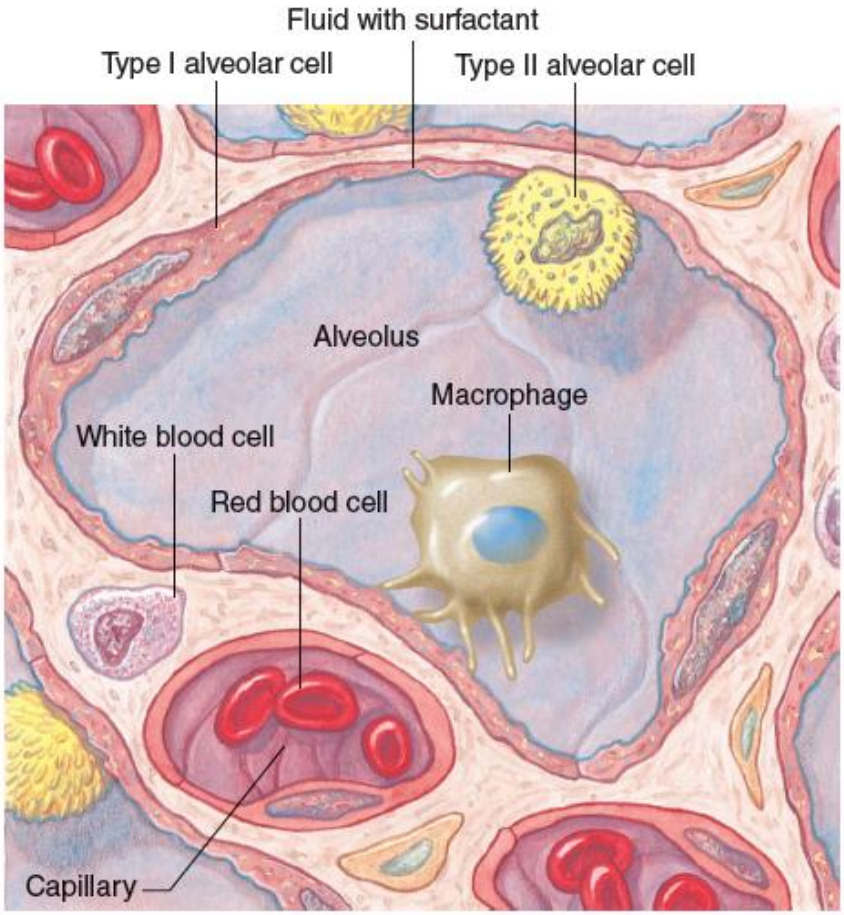


Figure 7.1 **The relationship between lung alveoli and pulmonary capillaries**

The air passages of the respiratory system are divided into two functional zones. The **respiratory zone** is the region where gas exchange occurs, and it therefore includes the respiratory bronchioles (because they contain separate outpouchings of alveoli) and the terminal alveolar sacs. The **conducting zone** includes all of the anatomical structures through which air passes before reaching the respiratory zone (fig. 7.2).

Air enters the respiratory bronchioles from *terminal bronchioles*, which are the narrowest of the airways that do not have alveoli and do not contribute to gas exchange. The terminal bronchioles receive air from larger airways, which are formed from successive branchings of the *right* and *left primary bronchi.* These two large air passages, in turn, are continuous with the *trachea*, or windpipe, which is located in the neck in front of the

esophagus (a muscular tube that carries food to the stomach). The trachea is a sturdy tube supported by rings of cartilage (fig. 7.3).

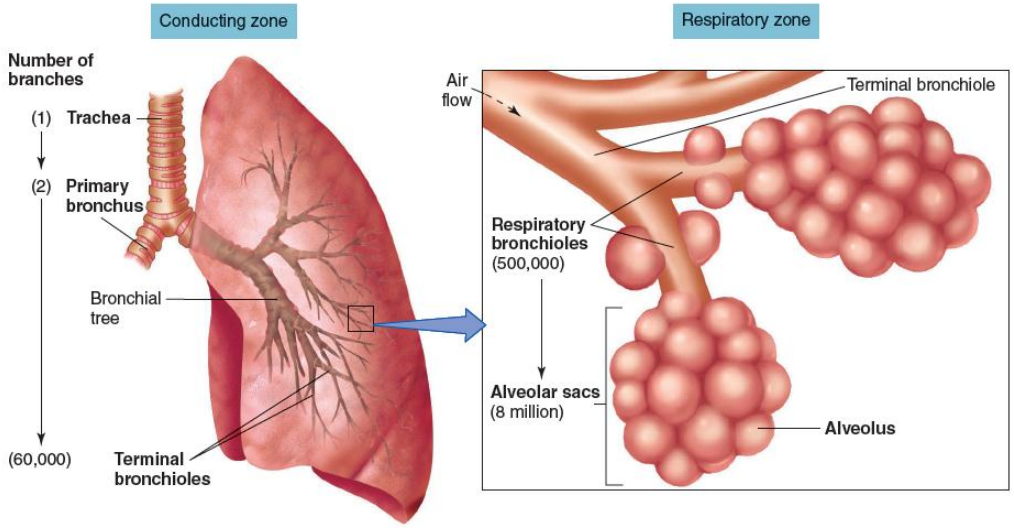


Figure 7.2 **The conducting and respiratory zones of the respiratory system**

Air enters the trachea from the pharynx, which is the cavity behind the palate that receives the contents of both the oral and nasal passages. In order for air to enter or leave the trachea and lungs, however, it must pass through a valve like opening called the glottis between the vocal folds. The ventricular and vocal folds are part of the larynx, or voice box, which guards the entrance to the trachea (fig.7.3). The projection at the front of the throat, commonly called the "Adam's apple," is formed by the largest cartilage of the larynx.

The conducting zone of the respiratory system, in summary, consists of the mouth, nose, pharynx, larynx, trachea, primary bronchi, and all successive branchings of the bronchioles up to and including the terminal bronchioles. In addition to conducting air into the respiratory zone, these structures serve additional functions: warming and humidification of the inspired air, and filtration and cleaning.

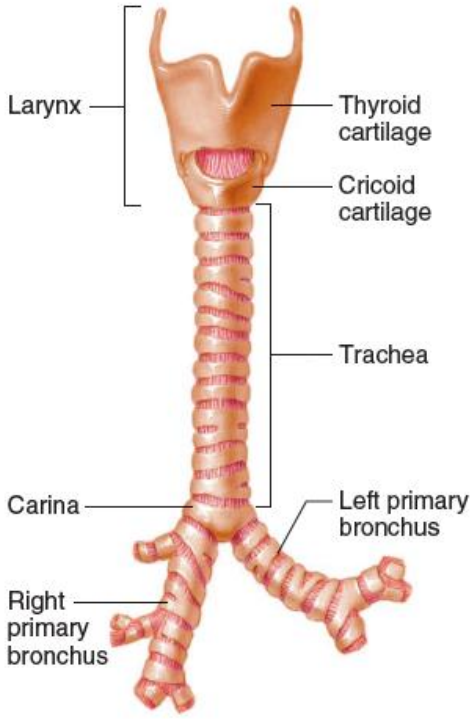


Figure 7.3 The conducting zone of the respiratory system

Mucus secreted by cells of the conducting zone structures serves to trap small particles in the inspired air and thereby performs a filtration function. This mucus is moved along at a rate of 1 to 2 cm per minute by cilia projecting from the tops of epithelial cells that line the conducting zone. There are about 300 cilia per cell that beat in a coordinated fashion to move mucus toward the pharynx, where it can either be swallowed or expectorated.

MECHANICS OF BREATHING

Normal, quiet inspiration results from muscle contraction, and normal expiration from muscle relaxation and elastic recoil. The amount of air inspired and expired can be measured in a number of ways to test pulmonary function.

The thorax must be sufficiently rigid to protect vital organs and provide attachments for a number of short, powerful muscles. However, breathing, or pulmonary ventilation, also requires a flexible thorax that can function as a bellows during the ventilation cycle. The structure of the rib cage and associated cartilages provides continuous elastic tension, so that when stretched by muscle contraction during inspiration, the rib cage can return passively to its resting dimensions when the muscles relax. This elastic recoil is greatly aided by the elasticity of the lungs. Pulmonary ventilation consists of two phases: inspiration and expiration. Inspiration (inhalation) and expiration (exhalation) are accomplished by alternately increasing and decreasing the volumes of the thorax and lungs.

Inspiration and Expiration

The diaphragm, innervated by two phrenic nerves composed of axons originating in C3 through C5 of the spinal cord, separates the thoracic and abdominal cavities and is the primary muscle of ventilation. Its function is aided by muscles that insert on the ribs. Between the bony portions of the rib cage are two layers of intercostal muscles: the external intercostal muscles and the internal intercostal muscles (fig.7.4). Between the costal cartilages, however, there is only one muscle layer, and its fibers are oriented similar to those of the internal intercostals. These muscles are therefore called the interchondral part of the internal intercostals. Another name for them is the parasternal intercostals.

In the process of inspiration, as a result of the contraction of the muscles between the ribs, the ribs take a horizontal position after they were tilted slightly downward, and their end moves forward, and this leads to the expansion of the rib cage.

The diaphragm muscles contract and take a flat position after it was convex to the top, and the expansion of the rib cage leads to a decrease in pressure within the chest cavities and a decrease in pressure within the alveoli, so air enters the lungs.

In the process of expiration, it takes place as a result of the relaxation of the respiratory muscles and the return of the ribs and diaphragm to their position, as the size of the chest and lungs decreases, and thus the air exits from the lungs.

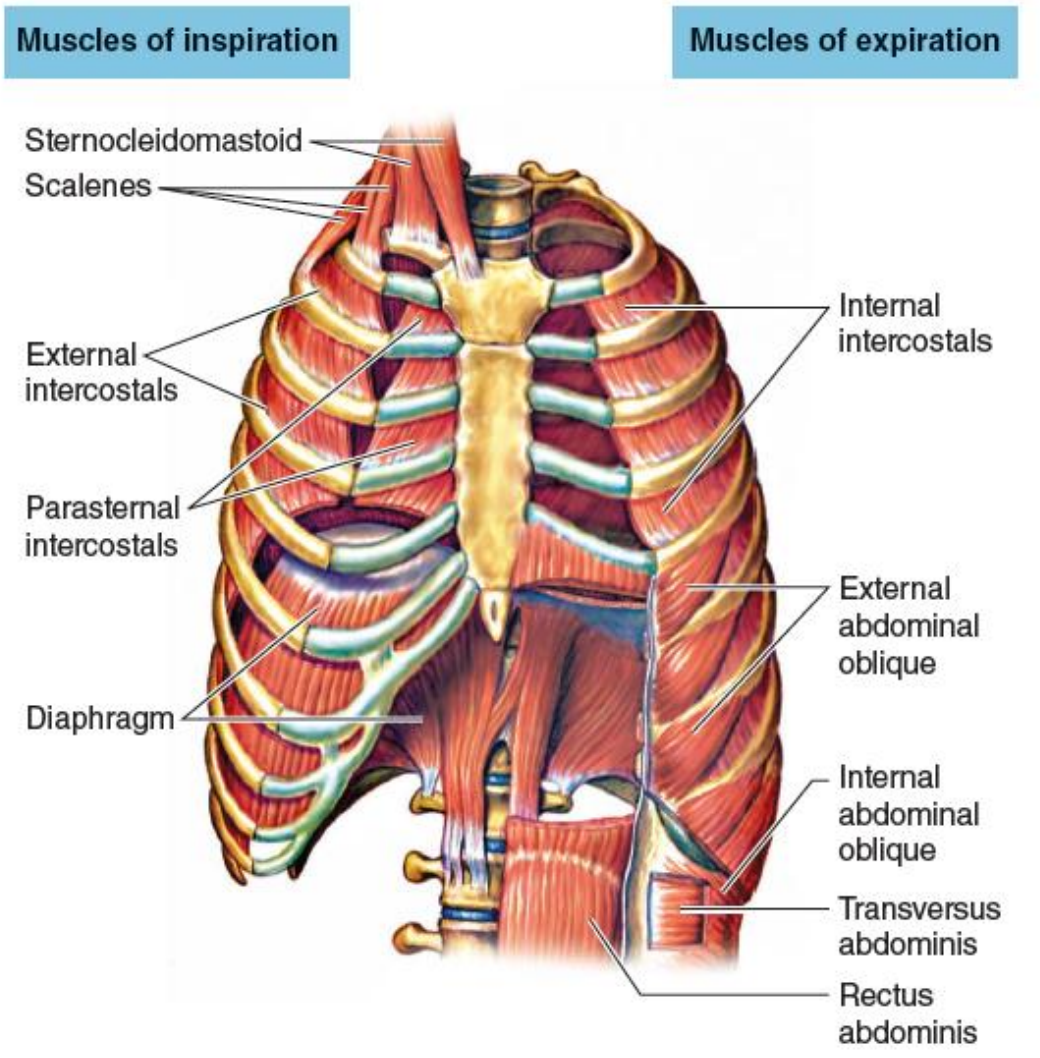


Figure 7.4 The muscles involved in breathing.

Respiratory volumes and lung capacity

1- Tidal volume: The volume of air entering or leaving the lungs during normal breathing at rest (up to 500 cm^3)
2- Inspiration reserve volume: The volume of air that enters the lungs with the deepest possible inspiration after a normal inspiration (2500-3000 cm^3).
3- Expiration reserve volume: The volume of air leaving the lungs with the deepest expiration after a normal expiration (1500 cm^3).

Inspiration capacity I.C = T.V + I.R.V
Expiration capacity E.C = E.R.V + T.V

4- Vital capacity: The volume of air entering the lungs with the deepest inspiration and out with the deepest expiration.

Vital capacity = E.R.V +I.R.V + T.V

5- Residual volume: The amount of air remaining in the lungs even after the deepest exhalation (the lungs cannot completely empty the air) and is equal to 1500 cm^3 in a person.

From this we conclude that the total capacity of the lungs is the vital capacity + the residual volume.

Gas exchange

The current theory is the physical theory. This is according to the variation in the pressures of gases and it is also called the diffusion theory.

PO_2 = 40 mm/Hg
PCO_2 = 46mm/Hg
In blood passing to the lungs through the pulmonary vein.

There is an increase in the oxygen pressure from the air to the blood and an increase in the pressure of carbon dioxide from the blood to the air. Therefore, the oxygen is transferred from the alveoli to the blood, and the CO_2 is transferred from the blood to the alveoli by the process of simple diffusion

As for tissues, the opposite happens:

O_2 moves from the blood to the tissues (because it is higher in the blood)

CO_2 moves from tissues to blood (because it is higher in tissues).

HEMOGLOBIN AND OXYGEN TRANSPORT

Deoxyhemoglobin loads with oxygen to form oxyhemoglobin in the pulmonary capillaries, and a portion of the oxyhemoglobin unloads its oxygen in the capillaries of the systemic circulation. The bond strength between hemoglobin and oxygen, and thus the extent of unloading is changed under different conditions.

If the lungs are functioning properly, blood leaving in the pulmonary veins and traveling in the systemic arteries has a PO_2 of about 100 mmHg, indicating a plasma oxygen concentration of about 0.3 ml O_2 per 100 ml blood. The total oxygen content of the blood, however, cannot be derived if only the PO_2 of plasma is known. The total oxygen content depends not only on the PO_2 but also on the hemoglobin concentration. Arterial blood can carry 1.34 ml of oxygen per gram of hemoglobin. Therefore, if the PO_2 and hemoglobin concentration of the arterial blood are normal, this blood carries approximately 20 ml of O_2 per 100 ml of blood.

Hemoglobin

Most of the oxygen in the blood is contained within the red blood cells, where it is chemically bonded to **hemoglobin.** Each hemoglobin molecule consists of four polypeptide chains called *globins* and four iron-containing, disc-shaped organic pigment molecules called *hemes* (fig. 7.5). The protein part of hemoglobin is composed of two identical *alpha chains*, each 141 amino acids long, and two identical *beta chains*, each 146 amino acids long. Each of the four polypeptide chains is combined with one heme group. In the center of each heme group is one atom of iron, which can combine with one molecule of oxygen.

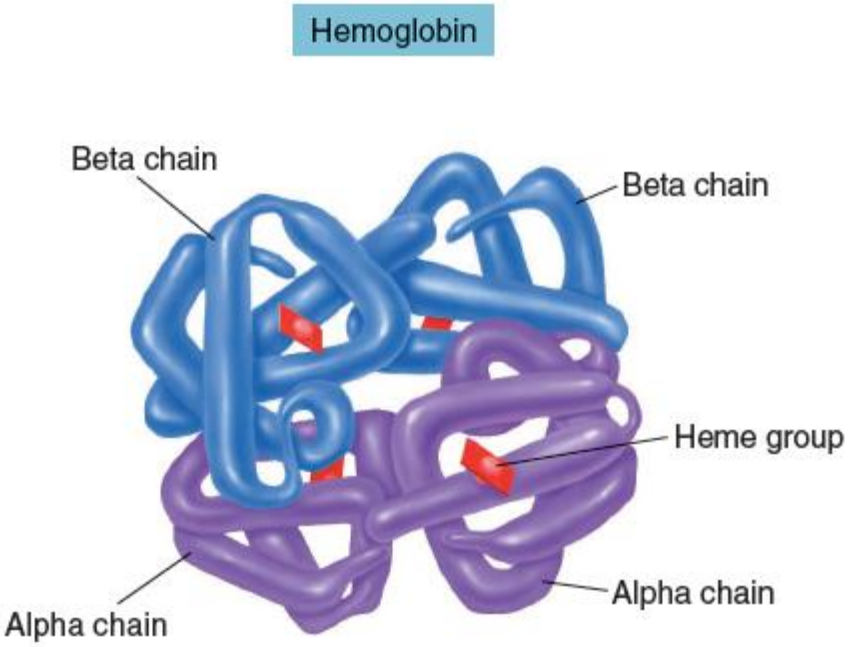
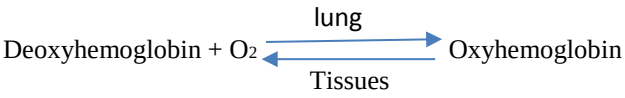


Figure 7.5 The structure of hemoglobin

The Loading and Unloading Reactions

Deoxyhemoglobin and oxygen combine to form oxyhemoglobin; this is called the **loading reaction.** Oxyhemoglobin, in turn, dissociates to yield deoxyhemoglobin and free oxygen molecules; this is the **unloading reaction.** The loading reaction occurs in the lungs and the unloading reaction occurs in the systemic

capillaries. Loading and unloading can thus be shown as a reversible reaction:



The extent to which the reaction will go in each direction depends on two factors: (1) the PO_2 of the environment and (2) the *affinity*, or bond strength, between hemoglobin and oxygen. High PO_2 drives the equation to the right (favors the loading reaction); at the high PO_2 of the pulmonary capillaries, almost all the deoxyhemoglobin molecules combine with oxygen. Low PO_2 in the systemic capillaries drives the reaction in the opposite direction to promote unloading. The extent of this unloading depends on how low the PO_2 values are.

CARBON DIOXIDE TRANSPORT

Carbon dioxide is carried by the blood in three forms: (1) as *dissolved* CO_2 in the plasma—carbon dioxide is about 21 times more soluble than oxygen in water, and about one-tenth of the total blood CO_2 is dissolved in plasma; (2) as *carbaminohemoglobin* —about one-fifth of the total blood CO_2 is carried attached to an amino acid in hemoglobin (carbaminohemoglobin should not be confused with carboxyhemoglobin, formed when carbon monoxide binds to the heme groups of hemoglobin); and (3) as *bicarbonate ion*, which accounts for most of the CO_2 carried by the blood (fig. 7.6).

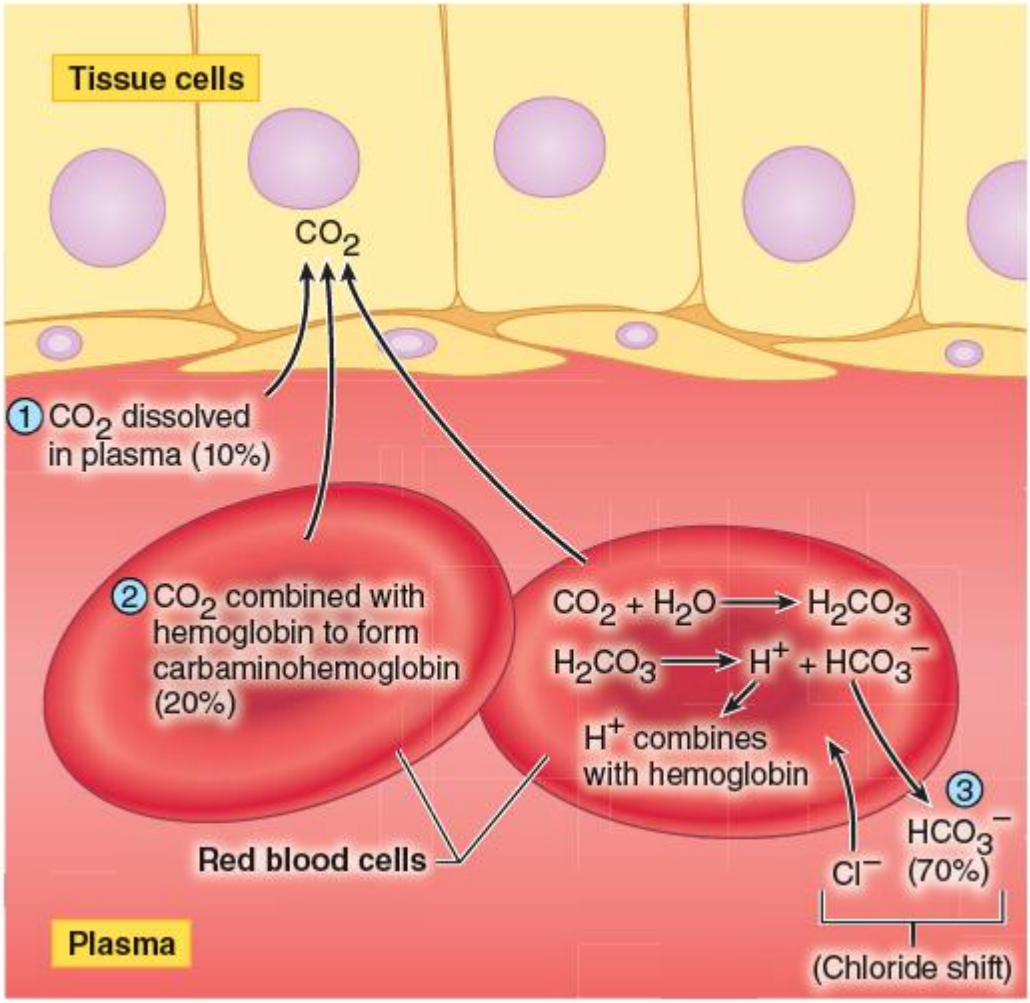


Figure 7.6 **Carbon dioxide transport and the chloride shift.**

Carbon dioxide is able to combine with water to form carbonic acid. This reaction occurs spontaneously in the plasma at a slow rate, but it occurs much more rapidly within the red blood cells because of the catalytic action of the enzyme **carbonic anhydrase.** Since this enzyme is confined to the red blood cells, most of the carbonic acid is produced there rather than in the plasma. The formation of carbonic acid from CO_2 and water is favored by the high P_{CO2} found in the capillaries of the systemic circulation.

$$CO_2 + H_2O \xrightarrow[high\ pco2]{carbonic\ anhydrase} H_2CO_3$$

The Chloride Shift

As a result of catalysis by carbonic anhydrase within the red blood cells, large amounts of carbonic acid are produced as blood passes through the systemic capillaries. The buildup of carbonic acid concentrations within the red blood cells favors the dissociation of these molecules into hydrogen ions (protons, which contribute to the acidity of a solution) and HCO_3^- (bicarbonate), as shown by this equation

$$H_2CO_3 \longrightarrow H^+ + HCO_3^-$$

The hydrogen ions (H^+) released by the dissociation of carbonic acid are largely buffered by their combination with deoxyhemoglobin within the red blood cells. Although the unbuffered hydrogen ions are free to diffuse out of the red blood cells, more bicarbonate diffuses outward into the plasma than does H^+. As a result of the "trapping" of hydrogen ions within the red blood cells by their attachment to hemoglobin and the outward diffusion of bicarbonate, the inside of the red blood cell gains a net positive charge. This attracts chloride ions (Cl^-), which move into the red blood cells as HCO_3^- moves out. This exchange of anions as blood travels through the tissue capillaries is called the chloride shift.

The unloading of oxygen is increased by the bonding of H^+ (released from carbonic acid) to oxyhemoglobin. This is the Bohr effect, and results in increased conversion of oxyhemoglobin to deoxyhemoglobin. Now, deoxyhemoglobin bonds H^+ more strongly than does oxyhemoglobin, so the act of unloading its oxygen improves the ability of hemoglobin to buffer the H^+ released by carbonic acid. Removal of H^+ from solution by its bonding to hemoglobin then acts through the action to favor the continued production of carbonic acid, which increases the ability

of the blood to transport carbon dioxide. In this way, carbon dioxide transport enhances oxygen unloading and oxygen unloading improves carbon dioxide transport.

The Reverse Chloride Shift

When blood reaches the pulmonary capillaries (fig. 7.8), deoxyhemoglobin is converted to oxyhemoglobin. Because oxyhemoglobin has a weaker affinity for H^+ than does deoxyhemoglobin, hydrogen ions are released within the red blood cells. This attracts HCO_3^- from the plasma, which combines with H^+ to form carbonic acid:

$$H^+ + HCO_3^- \rightarrow H_2CO_3$$

Under conditions of lower $P_{CO2,}$ as occurs in the pulmonary capillaries, carbonic anhydrase catalyzes the conversion of carbonic acid to carbon dioxide and water:

$$H_2CO_3 \xrightarrow[Low\ po2]{carbonic\ anhydrase} CO_2 + H_2O$$

In review, as blood goes through the systemic capillaries the carbonic anhydrase within the red blood cells converts carbon dioxide into carbonic acid. Dissociation of the carbonic acid into bicarbonate and H 1 results in the diffusion of bicarbonate out of the red blood cells into the plasma in exchange for chloride. This part of the carbon dioxide transport story is described as the chloride shift.

ACID-BASE BALANCE OF THE BLOOD

The pH of blood plasma is maintained within a narrow range of values through the functions of the lungs and kidneys. The lungs regulate the carbon dioxide concentration of the blood, and the kidneys regulate the bicarbonate concentration.

The blood plasma within arteries normally has a pH between 7.35 and 7.45, with an average of 7.40. Some of these hydrogen ions are derived from the ionization of carbonic acid formed from carbon dioxide and water as indicated in these equations

$$CO_2 + H\,2\,O \rightleftharpoons H_2CO_3$$
$$H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

As previously described, carbon dioxide produced by tissue cells through aerobic respiration is transported mostly as bicarbonate in the blood plasma. During the reverse chloride shift that occurs in pulmonary capillaries, bicarbonate is converted into carbonic acid and then changed into carbon dioxide. Because CO_2 is a volatile gas released in the expired breath, carbonic acid is referred to as a volatile acid. This is significant because its blood concentration is uniquely regulated by breathing. All other acids in the blood — including lactic acid, fatty acids, ketone bodies, and so on—are nonvolatile acids that cannot be eliminated through ventilation.

A fall in blood pH below 7.35 is called **acidosis** because the pH is to the acid side of normal. Acidosis does not mean acidic (pH less than 7); a blood pH of 7.2, for example, represents serious acidosis. Similarly, a rise in blood pH above 7.45 is called alkalosis. Both of these conditions are categorized into respiratory and metabolic components of acid-base balance.

Respiratory acidosis is caused by inadequate ventilation (hypoventilation), which results in a rise in the plasma concentration of carbon dioxide, and thus carbonic acid. Respiratory **alkalosis**, by contrast, is caused by excessive ventilation (hyperventilation).

Respiratory acidosis or alkalosis occurs when the carbon dioxide concentrations are abnormal.

-Reference

Fox, S. I. (2014). Fox Human Physiology.