severely impact breathing, because they reduce the surface area available for gas diffusion. As a result, the amount of oxygen in the blood decreases, whereas the carbon dioxide level increases. Dead space is created when no ventilation and/or perfusion takes place. **Anatomical dead space** or anatomical shunt, arises from an anatomical failure, while **physiological dead space** or physiological shunt, arises from a functional impairment of the lung or arteries.

An example of an anatomical shunt is the effect of gravity on the lungs. The lung is particularly susceptible to changes in the magnitude and direction of gravitational forces. When someone is standing or sitting upright, the pleural pressure gradient leads to increased ventilation further down in the lung. As a result, the intrapleural pressure is more negative at the base of the lung than at the top, and more air fills the bottom of the lung than the top. Likewise, it takes less energy to pump blood to the bottom of the lung than to the top when in a prone position. Perfusion of the lung is not uniform while standing or sitting. This is a result of hydrostatic forces combined with the effect of airway pressure. An anatomical shunt develops because the ventilation of the airways does not match the perfusion of the arteries surrounding those airways. As a result, the rate of gas exchange is reduced. Note that this does not occur when lying down, because in this position, gravity does not preferentially pull the bottom of the lung down.

A physiological shunt can develop if there is infection or edema in the lung that obstructs an area. This will decrease ventilation but not affect perfusion; therefore, the V/Q ratio changes and gas exchange is affected.

The lung can compensate for these mismatches in ventilation and perfusion. If ventilation is greater than perfusion, the arterioles dilate and the bronchioles constrict. This increases perfusion and reduces ventilation. Likewise, if ventilation is less than perfusion, the arterioles constrict and the bronchioles dilate to correct the imbalance.

LINK TO LEARNING

View the mechanics of breathing.

Click to view content (https://www.openstax.org/l/breathing)

39.4 Transport of Gases in Human Bodily Fluids

By the end of this section, you will be able to do the following:

- Describe how oxygen is bound to hemoglobin and transported to body tissues
- Explain how carbon dioxide is transported from body tissues to the lungs

Once the oxygen diffuses across the alveoli, it enters the bloodstream and is transported to the tissues where it is unloaded, and carbon dioxide diffuses out of the blood and into the alveoli to be expelled from the body. Although gas exchange is a continuous process, the oxygen and carbon dioxide are transported by different mechanisms.

Transport of Oxygen in the Blood

Although oxygen dissolves in blood, only a small amount of oxygen is transported this way. Only 1.5 percent of oxygen in the blood is dissolved directly into the blood itself. Most oxygen—98.5 percent—is bound to a protein called hemoglobin and carried to the tissues.

Hemoglobin

Hemoglobin, or Hb, is a protein molecule found in red blood cells (erythrocytes) made of four subunits: two alpha subunits and two beta subunits (Figure 39.19). Each subunit surrounds a central **heme group** that contains iron and binds one oxygen molecule, allowing each hemoglobin molecule to bind four oxygen molecules. Molecules with more oxygen bound to the heme groups are brighter red. As a result, oxygenated arterial blood where the Hb is carrying four oxygen molecules is bright red, while venous blood that is deoxygenated is darker red.

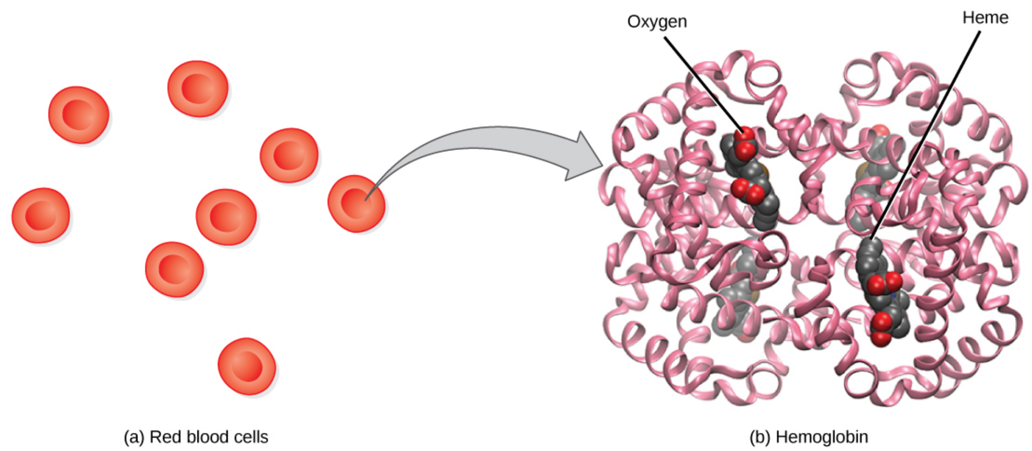

Figure 39.19 The protein inside (a) red blood cells that carries oxygen to cells and carbon dioxide to the lungs is (b) hemoglobin. Hemoglobin is made up of four symmetrical subunits and four heme groups. Iron associated with the heme binds oxygen. It is the iron in hemoglobin that gives blood its red color.

It is easier to bind a second and third oxygen molecule to Hb than the first molecule. This is because the hemoglobin molecule changes its shape, or conformation, as oxygen binds. The fourth oxygen is then more difficult to bind. The binding of oxygen to hemoglobin can be plotted as a function of the partial pressure of oxygen in the blood (x-axis) versus the relative Hb-oxygen saturation (y-axis). The resulting graph—an **oxygen dissociation curve**—is sigmoidal, or S-shaped (Figure 39.20). As the partial pressure of oxygen increases, the hemoglobin becomes increasingly saturated with oxygen.

VISUAL CONNECTION

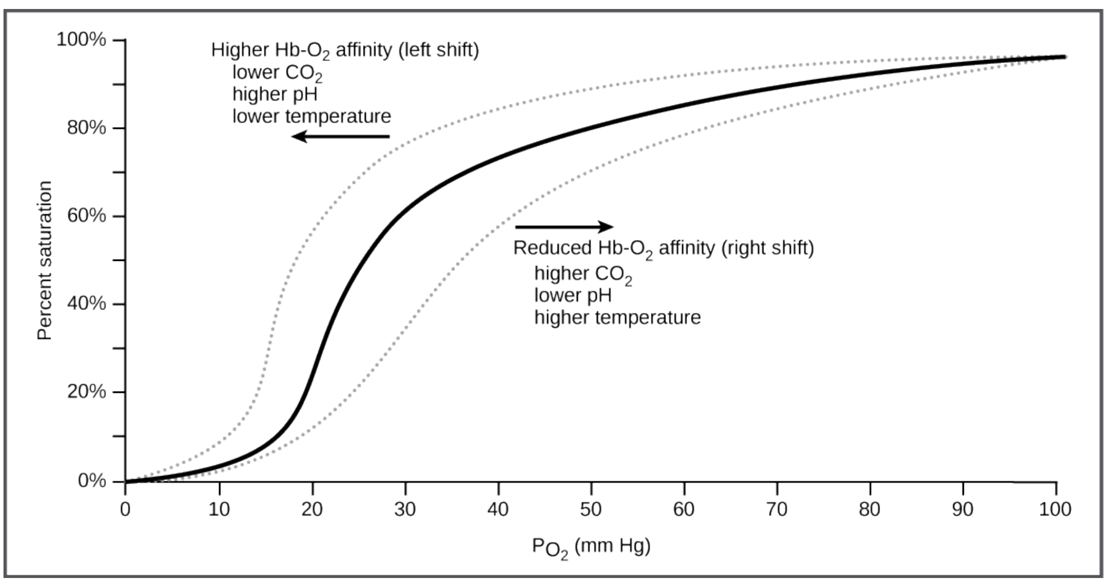

Figure 39.20 The oxygen dissociation curve demonstrates that, as the partial pressure of oxygen increases, more oxygen binds hemoglobin. However, the affinity of hemoglobin for oxygen may shift to the left or the right depending on environmental conditions.

The kidneys are responsible for removing excess H+ ions from the blood. If the kidneys fail, what would happen to blood pH and to hemoglobin affinity for oxygen?

Factors That Affect Oxygen Binding

The **oxygen-carrying capacity** of hemoglobin determines how much oxygen is carried in the blood. In addition to P_{O_2} , other environmental factors and diseases can affect oxygen carrying capacity and delivery.

Carbon dioxide levels, blood pH, and body temperature affect oxygen-carrying capacity (Figure 39.20). When carbon dioxide is in the blood, it reacts with water to form bicarbonate (HCO_3^-) and hydrogen ions (H^+). As the level of carbon dioxide in the blood increases, more H^+ is produced and the pH decreases. This increase in carbon dioxide and subsequent decrease in pH reduce the affinity of hemoglobin for oxygen. The oxygen dissociates from the Hb molecule, shifting the oxygen dissociation curve to the right. Therefore, more oxygen is needed to reach the same hemoglobin saturation level as when the pH was higher. A similar shift in the curve also results from an increase in body temperature. Increased temperature, such as from increased activity of skeletal muscle, causes the affinity of hemoglobin for oxygen to be reduced.

Diseases like sickle cell anemia and thalassemia decrease the blood's ability to deliver oxygen to tissues and its oxygen-carrying capacity. In **sickle cell anemia**, the shape of the red blood cell is crescent-shaped, elongated, and stiffened, reducing its ability to deliver oxygen (Figure 39.21). In this form, red blood cells cannot pass through the capillaries. This is painful when it occurs. **Thalassemia** is a rare genetic disease caused by a defect in either the alpha or the beta subunit of Hb. Patients with thalassemia produce a high number of red blood cells, but these cells have lower-than-normal levels of hemoglobin. Therefore, the oxygen-carrying capacity is diminished.

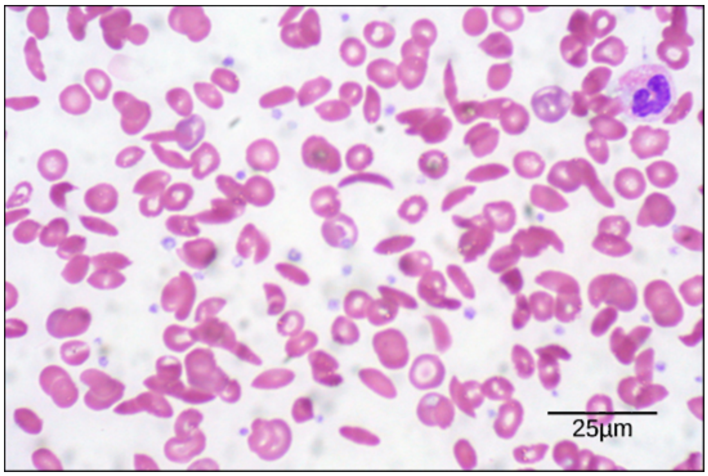

Figure 39.21 Individuals with sickle cell anemia have crescent-shaped red blood cells. (credit: modification of work by Ed Uthman; scale-bar data from Matt Russell)

Transport of Carbon Dioxide in the Blood

Carbon dioxide molecules are transported in the blood from body tissues to the lungs by one of three methods: dissolution directly into the blood, binding to hemoglobin, or carried as a bicarbonate ion. Several properties of carbon dioxide in the blood affect its transport. First, carbon dioxide is more soluble in blood than oxygen. About 5 to 7 percent of all carbon dioxide is dissolved in the plasma. Second, carbon dioxide can bind to plasma proteins or can enter red blood cells and bind to hemoglobin. This form transports about 10 percent of the carbon dioxide. When carbon dioxide binds to hemoglobin, a molecule called **carbaminohemoglobin** is formed. Binding of carbon dioxide to hemoglobin is reversible. Therefore, when it reaches the lungs, the carbon dioxide can freely dissociate from the hemoglobin and be expelled from the body.

Third, the majority of carbon dioxide molecules (85 percent) are carried as part of the **bicarbonate buffer system**. In this system, carbon dioxide diffuses into the red blood cells. **Carbonic anhydrase (CA)** within the red blood cells quickly converts the carbon dioxide into carbonic acid (H_2CO_3). Carbonic acid is an unstable intermediate molecule that immediately dissociates into **bicarbonate ions** (HCO_3^-) and hydrogen (H^+) ions. Since carbon dioxide is quickly converted into bicarbonate ions, this reaction allows for the continued uptake of carbon dioxide into the blood down its concentration gradient. It also results in the production of H^+ ions. If too much H^+ is produced, it can alter blood pH. However, hemoglobin binds to the free H^+ ions and thus limits shifts in pH. The newly synthesized bicarbonate ion is transported out of the red blood cell into the liquid component of the blood in exchange for a chloride ion (Cl^-); this is called the **chloride shift**. When the blood reaches the lungs, the bicarbonate ion is transported back into the red blood cell in exchange for the chloride ion. The H^+ ion dissociates from the hemoglobin and binds to the bicarbonate ion. This produces the carbonic acid intermediate, which is converted back into carbon dioxide through the enzymatic action of CA. The carbon dioxide produced is expelled through the lungs during exhalation.

$$CO_2 + H_2O \leftrightarrow \underset{\text{(carbonic acid)}}{H_2CO_3} \leftrightarrow \underset{\text{(bicarbonate)}}{HCO_3 + H^+}$$

The benefit of the bicarbonate buffer system is that carbon dioxide is "soaked up" into the blood with little change to the pH of the system. This is important because it takes only a small change in the overall pH of the body for severe injury or death to result. The presence of this bicarbonate buffer system also allows for people to travel and live at high altitudes: When the partial pressure of oxygen and carbon dioxide change at high altitudes, the bicarbonate buffer system adjusts to regulate carbon dioxide while maintaining the correct pH in the body.

Carbon Monoxide Poisoning

While carbon dioxide can readily associate and dissociate from hemoglobin, other molecules such as carbon monoxide (CO) cannot. Carbon monoxide has a greater affinity for hemoglobin than oxygen. Therefore, when carbon monoxide is present, it binds to hemoglobin preferentially over oxygen. As a result, oxygen cannot bind to hemoglobin, so very little oxygen is transported through the body (Figure 39.22). Carbon monoxide is a colorless, odorless gas and is therefore difficult to detect. It is produced by gas-powered vehicles and tools. Carbon monoxide can cause headaches, confusion, and nausea; long-term exposure can cause brain damage or death. Administering 100 percent (pure) oxygen is the usual treatment for carbon monoxide poisoning. Administration of pure oxygen speeds up the separation of carbon monoxide from hemoglobin.

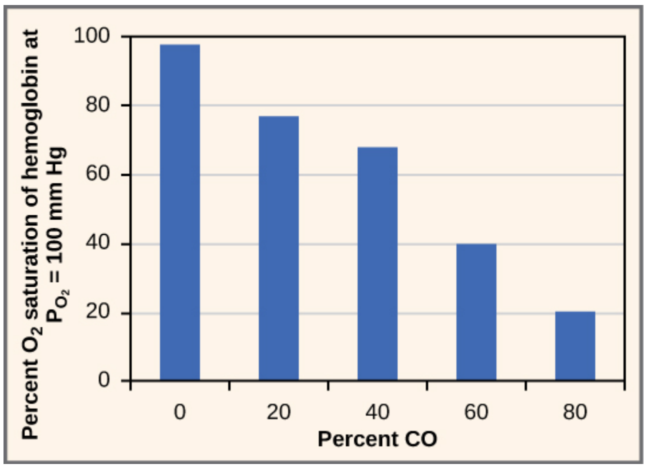

Figure 39.22 As percent CO increases, the oxygen saturation of hemoglobin decreases.

KEY TERMS

alveolar P_{O_2} partial pressure of oxygen in the alveoli (usually around 100 mmHg)

alveolar duct duct that extends from the terminal bronchiole to the alveolar sac

alveolar sac structure consisting of two or more alveoli that share a common opening

alveolar ventilation how much air is in the alveoli

alveolus (plural: alveoli) (also, air sac) terminal region of the lung where gas exchange occurs

anatomical dead space (also, anatomical shunt) region of the lung that lacks proper ventilation/perfusion due to an anatomical block

bicarbonate (HCO_3^-) ion ion created when carbonic acid dissociates into H^+ and (HCO_3^-)

bicarbonate buffer system system in the blood that absorbs carbon dioxide and regulates pH levels

bronchiole airway that extends from the main tertiary bronchi to the alveolar sac

bronchus (plural: bronchi) smaller branch of cartilaginous tissue that stems off of the trachea; air is funneled through the bronchi to the region where gas exchange occurs in alveoli

carbaminohemoglobin molecule that forms when carbon dioxide binds to hemoglobin

carbonic anhydrase (CA) enzyme that catalyzes carbon dioxide and water into carbonic acid

chloride shift exchange of chloride for bicarbonate into or out of the red blood cell

compliance measurement of the elasticity of the lung

dead space area in the lung that lacks proper ventilation or perfusion

diaphragm domed-shaped skeletal muscle located under lungs that separates the thoracic cavity from the abdominal cavity

elastic recoil property of the lung that drives the lung tissue inward

elastic work work conducted by the intercostal muscles, chest wall, and diaphragm

expiratory reserve volume (ERV) amount of additional air that can be exhaled after a normal exhalation

FEV1/FVC ratio ratio of how much air can be forced out of the lung in one second to the total amount that is forced out of the lung; a measurement of lung function that can be used to detect disease states

flow-resistive work of breathing performed by the alveoli and tissues in the lung

forced expiratory volume (FEV) (also, forced vital capacity) measure of how much air can be forced out of the lung from maximal inspiration over a specific amount of time

functional residual capacity (FRC) expiratory reserve volume plus residual volume

functional vital capacity (FVC) amount of air that can be forcibly exhaled after taking the deepest breath possible

heme group centralized iron-containing group that is surrounded by the alpha and beta subunits of hemoglobin

hemoglobin molecule in red blood cells that can bind oxygen, carbon dioxide, and carbon monoxide

inspiratory capacity (IC) tidal volume plus inspiratory reserve volume

inspiratory reserve volume (IRV) amount of additional air that can be inspired after a normal inhalation

intercostal muscle muscle connected to the rib cage that contracts upon inspiration

intrapleural space space between the layers of pleura

larynx voice box, a short passageway connecting the pharynx and the trachea

lung capacity measurement of two or more lung volumes (how much air can be inhaled from the end of an expiration to maximal capacity)

lung volume measurement of air for one lung function (normal inhalation or exhalation)

mucin complex glycoprotein found in mucus

mucus sticky protein-containing fluid secretion in the lung that traps particulate matter to be expelled from the body

nasal cavity opening of the respiratory system to the outside environment

obstructive disease disease (such as emphysema and asthma) that arises from obstruction of the airways; compliance increases in these diseases

oxygen dissociation curve curve depicting the affinity of oxygen for hemoglobin

oxygen-carrying capacity amount of oxygen that can be transported in the blood

partial pressure amount of pressure exerted by one gas within a mixture of gases

particulate matter small particle such as dust, dirt, viral particles, and bacteria that are in the air

pharynx throat; a tube that starts in the internal nares and runs partway down the neck, where it opens into the esophagus and the larynx

physiological dead space (also, physiological shunt) region of the lung that lacks proper ventilation/perfusion due to a physiological change in the lung (like inflammation or edema)

pleura tissue layer that surrounds the lungs and lines the interior of the thoracic cavity

pleurisy painful inflammation of the pleural tissue layers

primary bronchus (also, main bronchus) region of the airway within the lung that attaches to the trachea and bifurcates to each lung where it branches into secondary bronchi

recruitment process of opening airways that normally remain closed when the cardiac output increases

residual volume (RV) amount of air remaining in the lung after a maximal expiration

resistance measurement of lung obstruction

respiratory bronchiole terminal portion of the bronchiole tree that is attached to the terminal bronchioles and alveoli ducts, alveolar sacs, and alveoli

respiratory distress syndrome disease that arises from a deficient amount of surfactant

respiratory quotient (RQ) ratio of carbon dioxide production to each oxygen molecule consumed

respiratory rate number of breaths per minute

restrictive disease disease that results from a restriction and decreased compliance of the alveoli; respiratory distress syndrome and pulmonary fibrosis are examples

sickle cell anemia genetic disorder that affects the shape of red blood cells, and their ability to transport oxygen and move through capillaries

spirometry method to measure lung volumes and to diagnose lung diseases

surfactant detergent-like liquid in the airways that lowers the surface tension of the alveoli to allow for expansion

terminal bronchiole region of bronchiole that attaches to the respiratory bronchioles

thalassemia rare genetic disorder that results in mutation of the alpha or beta subunits of hemoglobin, creating smaller red blood cells with less hemoglobin

tidal volume (TV) amount of air that is inspired and expired during normal breathing

total lung capacity (TLC) sum of the residual volume, expiratory reserve volume, tidal volume, and inspiratory reserve volume

trachea cartilaginous tube that transports air from the larynx to the primary bronchi

venous P_{CO_2} partial pressure of carbon dioxide in the veins (40 mm Hg in the pulmonary veins)

venous P_{O_2} partial pressure of oxygen in the veins (100 mm Hg in the pulmonary veins)

ventilation/perfusion (V/Q) mismatch region of the lung that lacks proper alveolar ventilation (V) and/or arterial perfusion (Q)

vital capacity (VC) sum of the expiratory reserve volume, tidal volume, and inspiratory reserve volume

CHAPTER SUMMARY

39.1 Systems of Gas Exchange

Animal respiratory systems are designed to facilitate gas exchange. In mammals, air is warmed and humidified in the nasal cavity. Air then travels down the pharynx, through the trachea, and into the lungs. In the lungs, air passes through the branching bronchi, reaching the respiratory bronchioles, which house the first site of gas exchange. The respiratory bronchioles open into the alveolar ducts, alveolar sacs, and alveoli. Because there are so many alveoli and alveolar sacs in the lung, the surface area for gas exchange is very large. Several protective mechanisms are in place to prevent damage or infection. These include the hair and mucus in the nasal cavity that trap dust, dirt, and other particulate matter before they can enter the system. In the lungs, particles are trapped in a mucus layer and transported via cilia up to the esophageal opening at the top of the trachea to be swallowed.

39.2 Gas Exchange across Respiratory Surfaces

The lungs can hold a large volume of air, but they are not usually filled to maximal capacity. Lung volume measurements include tidal volume, expiratory reserve volume, inspiratory reserve volume, and residual volume. The sum of these equals the total lung capacity. Gas movement into or out of the lungs is dependent on the pressure of the gas. Air is a mixture of gases; therefore, the partial pressure of each gas can be calculated to determine how the gas will flow in the lung. The difference between the partial pressure of the gas in the air drives oxygen into the tissues and carbon dioxide out of the body.

39.3 Breathing

The structure of the lungs and thoracic cavity control the mechanics of breathing. Upon inspiration, the diaphragm contracts and lowers. The intercostal muscles contract and expand the chest wall outward. The intrapleural pressure drops, the lungs expand, and air is drawn into the airways. When exhaling, the intercostal muscles and diaphragm relax, returning the intrapleural pressure back to the resting state. The lungs recoil and airways close. The air passively exits the lung. There is high surface tension at the air-airway interface in the lung. Surfactant, a mixture of phospholipids and lipoproteins, acts like a detergent in the airways to reduce surface tension and allow for opening of the alveoli.

Breathing and gas exchange are both altered by changes in the compliance and resistance of the lung. If the compliance of the lung decreases, as occurs in restrictive diseases like fibrosis, the airways stiffen and collapse upon exhalation. Air becomes trapped in the lungs, making breathing more difficult. If resistance increases, as happens with asthma or emphysema, the airways become obstructed, trapping air in the lungs and causing breathing to become difficult. Alterations in the ventilation of the airways or perfusion of the arteries can affect gas exchange. These changes in ventilation and perfusion, called V/Q mismatch, can arise from anatomical or physiological changes.

39.4 Transport of Gases in Human Bodily Fluids

Hemoglobin is a protein found in red blood cells that is comprised of two alpha and two beta subunits that surround an iron-containing heme group. Oxygen readily binds this heme group. The ability of oxygen to bind increases as more oxygen molecules are bound to heme. Disease states and altered conditions in the body can affect the binding ability of oxygen, and increase or decrease its ability to dissociate from hemoglobin.

Carbon dioxide can be transported through the blood via three methods. It is dissolved directly in the blood, bound to plasma proteins or hemoglobin, or converted into bicarbonate. The majority of carbon dioxide is transported as part of the bicarbonate system. Carbon dioxide diffuses into red blood cells. Inside, carbonic anhydrase converts carbon dioxide into carbonic acid (H_2CO_3), which is subsequently hydrolyzed into bicarbonate (HCO_3^-) and H^+. The H^+ ion binds to hemoglobin in red blood cells, and bicarbonate is transported out of the red blood cells in exchange for a chloride ion. This is called the chloride shift. Bicarbonate leaves the red blood cells and enters the blood plasma. In the lungs, bicarbonate is transported back into the red blood cells in exchange for chloride. The H^+ dissociates from hemoglobin and combines with bicarbonate to form carbonic acid with the help of carbonic anhydrase, which further catalyzes the reaction to convert carbonic acid back into carbon dioxide and water. The carbon dioxide is then expelled from the lungs.

VISUAL CONNECTION QUESTIONS

1. Figure 39.7 Which of the following statements about the mammalian respiratory system is false?
   a. When we breathe in, air travels from the pharynx to the trachea.
   b. The bronchioles branch into bronchi.
   c. Alveolar ducts connect to alveolar sacs.
   d. Gas exchange between the lung and blood takes place in the alveolus.

2. Figure 39.13 Which of the following statements is false?
   a. In the tissues, P_{O_2} drops as blood passes from the arteries to the veins, while P_{CO_2} increases.
   b. Blood travels from the lungs to the heart to body tissues, then back to the heart, then the lungs.
   c. Blood travels from the lungs to the heart to body tissues, then back to the lungs, then the heart.
   d. P_{O_2} is higher in air than in the lungs.

3. Figure 39.20 The kidneys are responsible for removing excess H+ ions from the blood. If the kidneys fail, what would happen to blood pH and to hemoglobin affinity for oxygen?

REVIEW QUESTIONS

4. The respiratory system ________.
   a. provides body tissues with oxygen
   b. provides body tissues with oxygen and carbon dioxide
   c. establishes how many breaths are taken per minute
   d. provides the body with carbon dioxide

5. Air is warmed and humidified in the nasal passages. This helps to ________.
   a. ward off infection
   b. decrease sensitivity during breathing
   c. prevent damage to the lungs
   d. all of the above

6. Which is the order of airflow during inhalation?
   a. nasal cavity, trachea, larynx, bronchi, bronchioles, alveoli
   b. nasal cavity, larynx, trachea, bronchi, bronchioles, alveoli
   c. nasal cavity, larynx, trachea, bronchioles, bronchi, alveoli
   d. nasal cavity, trachea, larynx, bronchioles, bronchi, alveoli

7. The inspiratory reserve volume measures the ________.
   a. amount of air remaining in the lung after a maximal exhalation
   b. amount of air that the lung holds
   c. amount of air that can be further exhaled after a normal breath
   d. amount of air that can be further inhaled after a normal breath

8. Of the following, which does not explain why the partial pressure of oxygen is lower in the lung than in the external air?
   a. Air in the lung is humidified; therefore, water vapor pressure alters the pressure.
   b. Carbon dioxide mixes with oxygen.
   c. Oxygen is moved into the blood and is headed to the tissues.
   d. Lungs exert a pressure on the air to reduce the oxygen pressure.

9. The total lung capacity is calculated using which of the following formulas?
   a. residual volume + tidal volume + inspiratory reserve volume
   b. residual volume + expiratory reserve volume + inspiratory reserve volume
   c. expiratory reserve volume + tidal volume + inspiratory reserve volume
   d. residual volume + expiratory reserve volume + tidal volume + inspiratory reserve volume

10. How would paralysis of the diaphragm alter inspiration?
   a. It would prevent contraction of the intercostal muscles.
   b. It would prevent inhalation because the intrapleural pressure would not change.
   c. It would decrease the intrapleural pressure and allow more air to enter the lungs.
   d. It would slow expiration because the lung would not relax.

11. Restrictive airway diseases ________.
   a. increase the compliance of the lung
   b. decrease the compliance of the lung
   c. increase the lung volume
   d. decrease the work of breathing

12. Alveolar ventilation remains constant when ________.
   a. the respiratory rate is increased while the volume of air per breath is decreased
   b. the respiratory rate and the volume of air per breath are increased
   c. the respiratory rate is decreased while increasing the volume per breath
   d. both a and c

13. Which of the following will NOT facilitate the transfer of oxygen to tissues?
   a. decreased body temperature
   b. decreased pH of the blood
   c. increased carbon dioxide
   d. increased exercise

14. The majority of carbon dioxide in the blood is transported by ________.
   a. binding to hemoglobin
   b. dissolution in the blood
   c. conversion to bicarbonate
   d. binding to plasma proteins

15. The majority of oxygen in the blood is transported by ________.
   a. dissolution in the blood
   b. being carried as bicarbonate ions
   c. binding to blood plasma
   d. binding to hemoglobin

CRITICAL THINKING QUESTIONS

16. Describe the function of these terms and describe where they are located: main bronchus, trachea, alveoli, and acinus.
17. How does the structure of alveoli maximize gas exchange?
18. What does FEV1/FVC measure? What factors may affect FEV1/FVC?
19. What is the reason for having residual volume in the lung?
20. How can a decrease in the percent of oxygen in the air affect the movement of oxygen in the body?
21. If a patient has increased resistance in his or her lungs, how can this be detected by a doctor? What does this mean?
22. How would increased airway resistance affect intrapleural pressure during inhalation?
23. Explain how a puncture to the thoracic cavity (from a knife wound, for instance) could alter the ability to inhale.
24. When someone is standing, gravity stretches the bottom of the lung down toward the floor to a greater extent than the top of the lung. What implication could this have on the flow of air in the lungs? Where does gas exchange occur in the lungs?
25. What would happen if no carbonic anhydrase were present in red blood cells?
26. How does the administration of 100 percent oxygen save a patient from carbon monoxide poisoning? Why wouldn't giving carbon dioxide work?