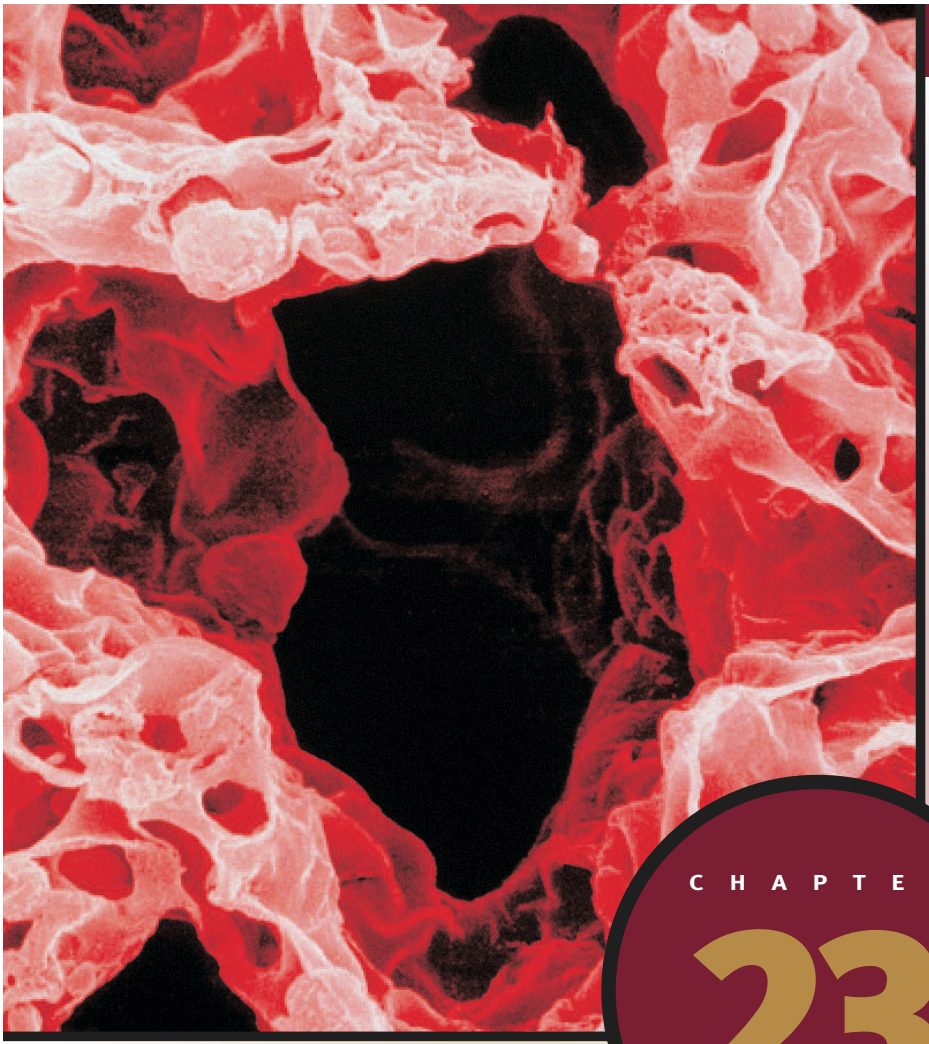


Colorized scanning electron micrograph (SEM) of the lung, showing alveoli, which are small chambers where gas exchange takes place between the air and the blood.

CHAPTER 23

Respiratory System

From our first breath at birth, the rate and depth of our respiration is unconsciously matched to our activities, whether studying, sleeping, talking, eating, or exercising. We can voluntarily stop breathing, but within a few seconds we must breathe again. Breathing is so characteristic of life that, along with the pulse, it's one of the first things we check for to determine if an unconscious person is alive.

Breathing is necessary because all living cells of the body require oxygen and produce carbon dioxide. The respiratory system allows exchange of these gases between the air and the blood, and the cardiovascular system transports them between the lungs and the cells of the body. The capacity to carry out normal activity is reduced without healthy respiratory and cardiovascular systems.

Respiration includes: (1) ventilation, the movement of air into and out of the lungs; (2) gas exchange between the air in the lungs and the blood, sometimes called external respiration; (3) transport of oxygen and carbon dioxide in the blood; and (4) gas exchange between the blood and the tissues, sometimes called internal respiration. The term *respiration* is also used in reference to cell metabolism, which is considered in chapter 25.

This chapter explains the *functions of the respiratory system* (814), the *anatomy and histology of the respiratory system* (814), *ventilation* (828), *measuring lung function* (833), *physical principles of gas exchange* (835), *oxygen and carbon dioxide transport in the blood* (838), *rhythmic ventilation* (843), *modification of ventilation* (845), and *respiratory adaptations to exercise* (849). We conclude the chapter by looking at the *effects of aging on the respiratory system* (850).

Functions of the Respiratory System

Objective

- ***Describe the functions of the respiratory system.***

Respiration is necessary because all living cells of the body require oxygen and produce carbon dioxide. The respiratory system assists in gas exchange and performs other functions as well.

1. *Gas exchange.* The respiratory system allows oxygen from the air to enter the blood and carbon dioxide to leave the blood and enter the air. The cardiovascular system transports oxygen from the lungs to the cells of the body and carbon dioxide from the cells of the body to the lungs. Thus, the respiratory and cardiovascular systems work together to supply oxygen to all cells and to remove carbon dioxide.
2. *Regulation of blood pH.* The respiratory system can alter blood pH by changing blood carbon dioxide levels.
3. *Voice production.* Air movement past the vocal folds makes sound and speech possible.
4. *Olfaction.* The sensation of smell occurs when airborne molecules are drawn into the nasal cavity.
5. *Protection.* The respiratory system provides protection against some microorganisms by preventing their entry into the body and by removing them from respiratory surfaces.

1. Explain the functions of the respiratory system.

Anatomy and Histology of the Respiratory System

Objectives

- ***Describe the structure and functions of the nasal cavity, pharynx, and larynx.***
- ***Describe the air passageways and the parts of the lungs, and how the muscles of respiration change thoracic volume.***
- ***Describe the pleural membranes, blood supply, and lymphatic supply of the lungs.***

The respiratory system consists of the nasal cavity, the pharynx, the larynx, the trachea, the bronchi, and the lungs (figure 23.1). The term **upper respiratory tract** refers to the nose, the pharynx, and associated structures; and the **lower respiratory tract** includes the larynx, trachea, bronchi, and lungs. The diaphragm and the muscles of the thoracic and abdominal walls are responsible for respiratory movements.

Nose

The **nasus** (nā′sŭs), or **nose,** consists of the external nose and the nasal cavity. The **external nose** is the visible structure that forms a prominent feature of the face. The largest part of the external nose is composed of cartilage plates (see figure 7.10*b*). The bridge of the nose consists of the nasal bones plus extensions of the frontal and maxillary bones.

The **nasal cavity** extends from the nares to the choanae (figure 23.2). The **nares** (nā′res; sing., nā′ris), or **nostrils,** are the external openings of the nasal cavity and the **choanae** (kō′an-ē) are the openings into the pharynx. The anterior part of the nasal cavity, just inside each naris, is the **vestibule** (ves′ti-bool; entry room). The vestibule is lined with stratified squamous epithelium that is continuous with the stratified squamous epithelium of the skin. The **hard palate** (pal′ăt) is a bony plate covered by a mucous membrane that forms the floor of the nasal cavity. It separates the nasal cavity from the oral cavity. The **nasal septum** is a partition dividing the nasal cavity into right and left parts (see figure 7.9*a*). The anterior part of the nasal septum is cartilage, and the posterior part consists of the vomer bone and the perpendicular plate of the ethmoid bone.

Three bony ridges called **conchae** (kon′kē; resembling a conch shell) modify the lateral walls of the nasal cavity. Beneath each concha is a passageway called a **meatus** (mē-ā′tŭs; a tunnel or passageway). Within the superior and middle meatus are openings from the various **paranasal sinuses** (see figure 7.10), and the opening of a **nasolacrimal** (nā-zō-lak′ri-măl) **duct** is within each inferior meatus (see figure 15.8).

The nasal cavity has several functions:

1. The nasal cavity is a passageway for air that's open even when the mouth is full of food.
2. The nasal cavity cleans the air. The vestibule is lined with hairs that trap some of the large particles of dust in the air. The nasal septum and nasal conchae increase the surface area of the nasal cavity and make airflow within the cavity

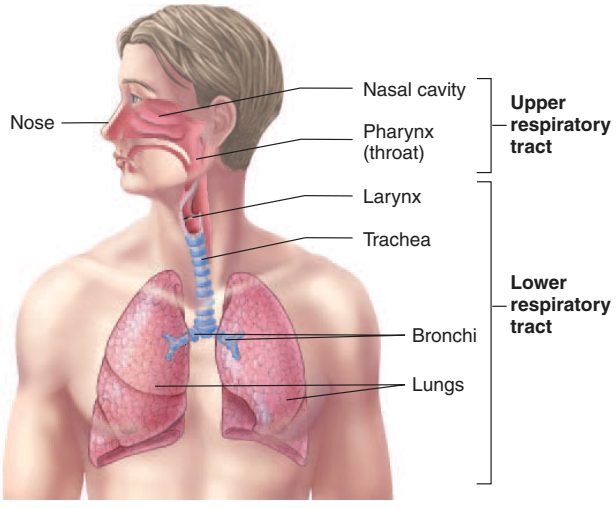


Figure 23.1 The Respiratory System

The upper respiratory tract consists of the nasal cavity and pharynx (throat). The lower respiratory tract consists of the larynx, trachea, bronchi, and lungs.

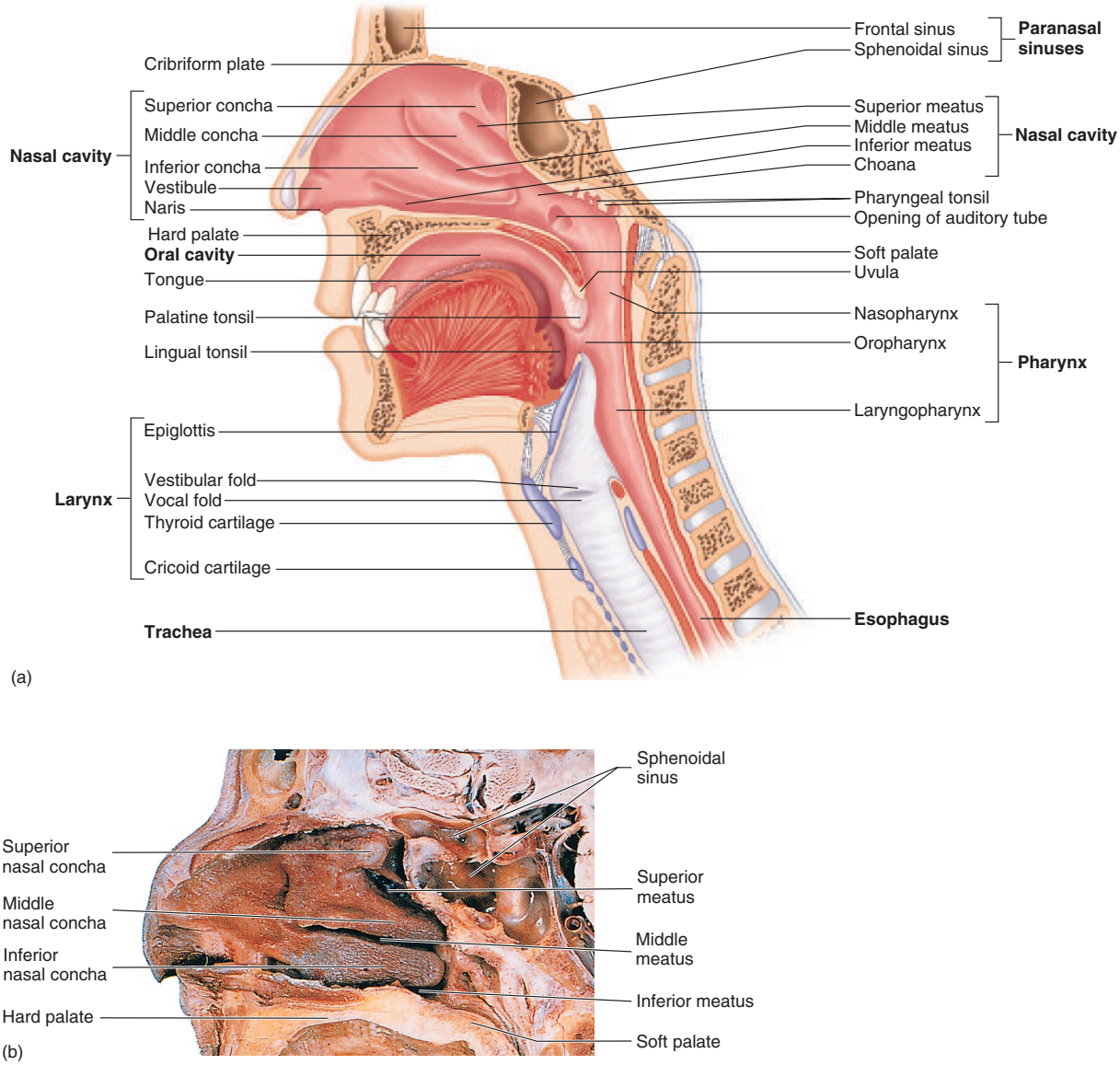


Figure 23.2 Nasal Cavity and Pharynx

(*a*) Sagittal section through the nasal cavity and pharynx viewed from the medial side. (*b*) Photograph of sagittal section of the head.

more turbulent, thereby increasing the likelihood that air comes into contact with the mucous membrane lining the nasal cavity. This mucous membrane consists of pseudostratified ciliated columnar epithelium with goblet cells, which secrete a layer of mucus. The mucus traps debris in the air, and the cilia on the surface of the mucous membrane sweep the mucus posteriorly to the pharynx, where it is swallowed and eliminated by the digestive system.

3. The nasal cavity humidifies and warms the air. Moisture from the mucous epithelium and from excess tears that drain into the nasal cavity through the nasolacrimal duct is added to the air as it passes through the nasal cavity. Warm blood flowing through the mucous membrane warms the air within the nasal cavity before it passes into the pharynx, thus preventing damage from cold air to the rest of the respiratory passages.

PREDICT 1

Explain what happens to your throat when you sleep with your mouth open, especially when your nasal passages are plugged as a result of having a cold. Explain what may happen to your lungs when you run a long way in very cold weather while breathing rapidly through your mouth.

4. The olfactory epithelium, the sensory organ for smell, is located in the most superior part of the nasal cavity (see figure 15.2).
5. The nasal cavity and paranasal sinuses are resonating chambers for speech.

Pharynx

The **pharynx** (far′ingks; throat) is the common opening of both the digestive and respiratory systems. It receives air from the nasal cavity and air, food, and drink from the oral cavity. Inferiorly, the pharynx is connected to the respiratory system at the larynx and to the digestive system at the esophagus. The pharynx is divided into three regions: the nasopharynx, the oropharynx, and the laryngopharynx (see figure 23.2).

The **nasopharynx** (nā′zō-far′ingks) is the superior part of the pharynx and extends from the choanae to the **soft palate,** which is an incomplete muscle and connective tissue partition separating the nasopharynx from the oropharynx. The **uvula** (ū′vū-lă; a grape) is the posterior extension of the soft palate. The soft palate prevents swallowed materials from entering the nasopharynx and nasal cavity. The nasopharynx is lined with a mucous membrane containing pseudostratified ciliated columnar epithelium with goblet cells. Debris-laden mucus from the nasal cavity is moved through the nasopharynx and swallowed. Two auditory tubes from the middle ears open into the nasopharynx (see figures 15.22 and 23.2*a*). Air passes through them to equalize air pressure between the atmosphere and the middle ears. The posterior surface of the nasopharynx contains the pharyngeal tonsil, or adenoid (ad′ĕ-noyd), which aids in defending the body against infection (see chapter 22). An enlarged pharyngeal tonsil can interfere with normal breathing and the passage of air through the auditory tubes.

The **oropharynx** (ōr′ō-far′ingks) extends from the uvula to the epiglottis. The oral cavity opens into the oropharynx through the **fauces** (faw′sēz). Thus, air, food, and drink all pass through the oropharynx. Moist stratified squamous epithelium lines the oropharynx and protects it against abrasion. Two sets of tonsils called the palatine tonsils and the lingual tonsils are located near the fauces.

The **laryngopharynx** (lă-ring′gō-far-ingks) extends from the tip of the epiglottis to the esophagus and passes posterior to the larynx. The laryngopharynx is lined with moist stratified squamous epithelium.

Larynx

The **larynx** (lar′ingks) consists of an outer casing of nine cartilages that are connected to one another by muscles and ligaments (figure 23.3). Six of the nine cartilages are paired, and three are unpaired. The largest of the cartilages is the unpaired **thyroid** (shield; refers to the shape of the cartilage) **cartilage,** or Adam's apple.

The most inferior cartilage of the larynx is the unpaired **cricoid** (krī′koyd; ring-shaped) **cartilage,** which forms the base of the larynx on which the other cartilages rest.

The third unpaired cartilage is the **epiglottis** (ep-i-glot′is; on the glottis). It's attached to the thyroid cartilage and projects as a free flap toward the tongue. The epiglottis differs from the other cartilages in that it consists of elastic rather than hyaline cartilage. During swallowing, the epiglottis covers the opening of the larynx and prevents materials from entering it.

The paired **arytenoid** (ar-i-tē′noyd; ladle-shaped) **cartilages** articulate with the posterior, superior border of the cricoid cartilage, and the paired **corniculate** (kōr-nik′ū-lāt; horn-shaped) **cartilages** are attached to the superior tips of the arytenoid cartilages. The paired **cuneiform** (kū′nē-i-fōrm; wedge-shaped) **cartilages** are contained in a mucous membrane anterior to the corniculate cartilages (see figure 23.3*b*).

Two pairs of ligaments extend from the anterior surface of the arytenoid cartilages to the posterior surface of the thyroid cartilage. The superior ligaments are covered by a mucous membrane called the **vestibular folds,** or **false vocal cords** (see figures 23.3*c* and 23.4*a* and *b*). When the vestibular folds come together, they prevent food and liquids from entering the larynx during swallowing and prevent air from leaving the lungs, as when a person holds his or her breath.

The inferior ligaments are covered by a mucous membrane called the **vocal folds,** or **true vocal cords** (see figure 23.4). The vocal folds and the opening between them are called the **glottis** (glot′is). The vestibular folds and the vocal folds are lined with stratified squamous epithelium. The remainder of the larynx is lined with pseudostratified ciliated columnar epithelium. An inflammation of the mucosal epithelium of the vocal folds is called **laryngitis** (lar-in-jī′tis).

The larynx performs three important functions.

1. The thyroid and cricoid cartilages maintain an open passageway for air movement.
2. The epiglottis and vestibular folds prevent swallowed material from moving into the larynx.
3. The vocal folds are the primary source of sound production. Air moving past the vocal folds causes them to vibrate and produce sound. The greater the amplitude of the vibration, the louder is the sound. The force of air moving past the vocal folds determines the amplitude of vibration and the loudness of the sound. The frequency of vibrations determines pitch, with higher frequency vibrations producing higher pitched sounds and lower frequency fibrations producing lower pitched sounds. Variations in the length of the vibrating segments of the vocal folds affect the frequency of the vibrations. Higher-pitched tones are produced when only the anterior parts of the folds vibrate, and progressively lower tones result when longer sections of the folds vibrate. Because males

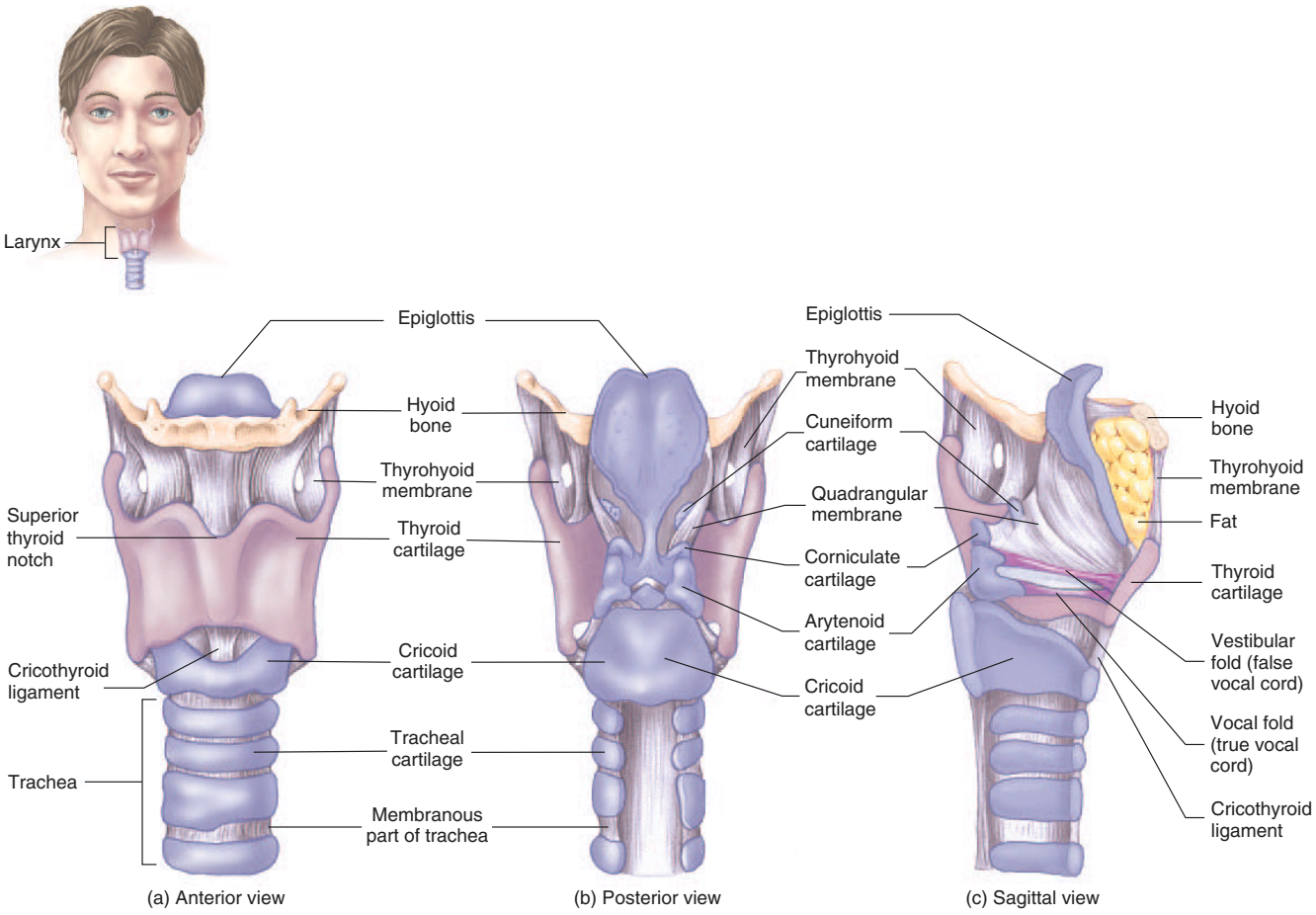


Figure 23.3 Anatomy of the Larynx

usually have longer vocal folds than females, they usually have lower-pitched voices. The sound produced by the vibrating vocal folds is modified by the tongue, lips, teeth, and other structures to form words. A person whose larynx has been removed because of carcinoma of the larynx can produce sound by swallowing air and causing the esophagus to vibrate.

Movement of the arytenoid and other cartilages is controlled by skeletal muscles, thereby changing the position and length of the vocal folds. When only breathing, lateral rotation of the arytenoid cartilages abducts the vocal folds, which allows greater movement of air (figure 23.4*c*). Medial rotation of the arytenoid cartilages adducts the vocal folds, places them in position for producing sounds, and changes the tension on them. (figure 23.4*d*). Anterior/posterior movement of the arytenoid cartilages also changes the length and tension of the vocal folds (figure 23.4*e*).

2. *Define upper and lower respiratory tract.*
3. *How are the structures of the nasal cavity responsible for its functions?*
4. *Name the three parts of the pharynx. With what structures does each part communicate?*
5. *Name and describe the three unpaired cartilages of the larynx. What are their functions?*
6. *Distinguish between the vestibular and vocal folds. How are sounds of different loudness and pitch produced by the vocal folds?*
7. *How does the position of the arytenoid cartilages change when just breathing versus making low-pitched and high-pitched sounds?*

Trachea

The **trachea** (trā′kē-ă), or windpipe, is a membranous tube that consists of dense regular connective tissue and smooth muscle reinforced with 15–20 C-shaped pieces of cartilage. The cartilages

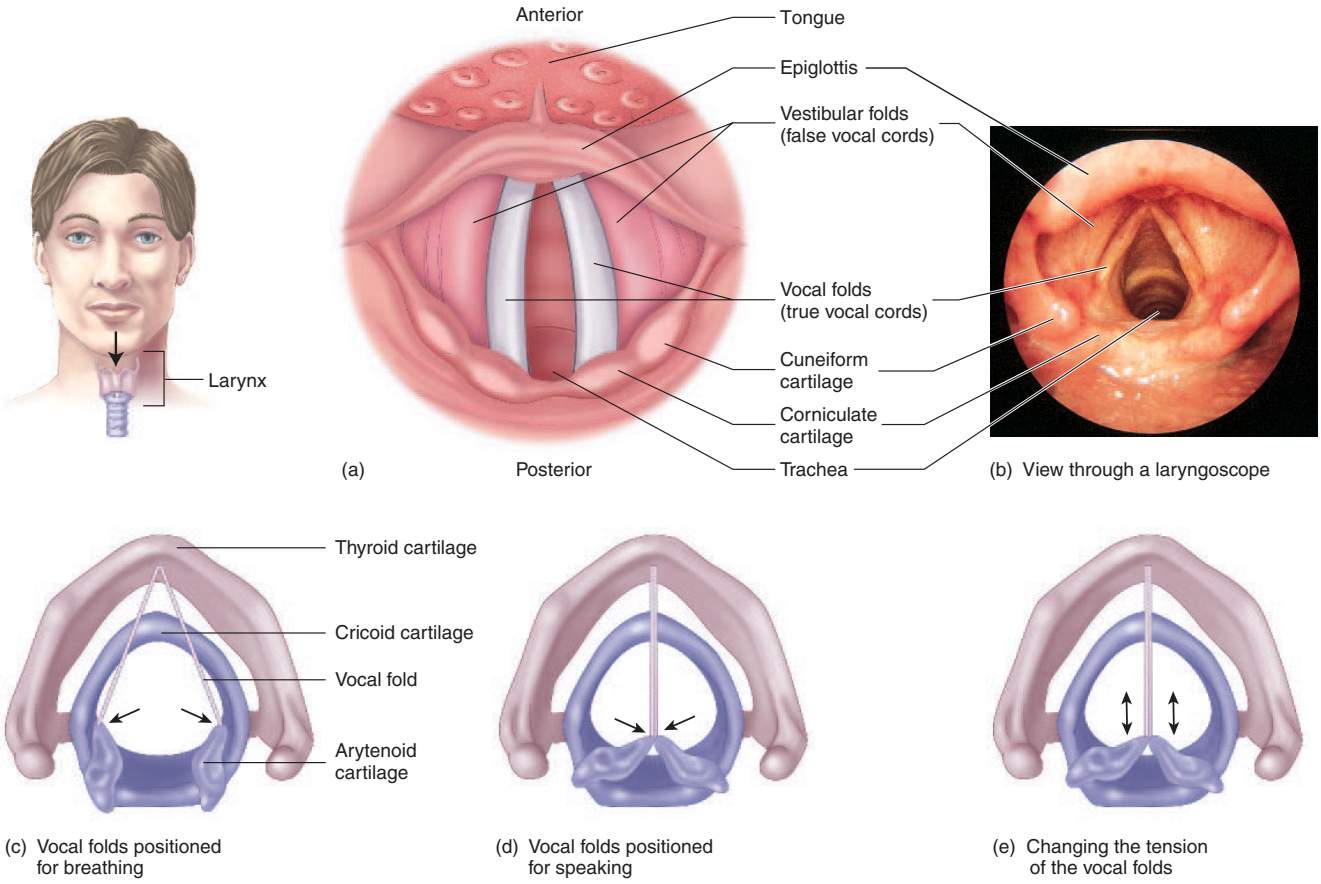


Figure 23.4 Vocal Folds

Arrow shows the direction of viewing the vocal folds. (*a*) The relationship of the vocal folds to the vestibular folds and the laryngeal cartilages. (*b*) Laryngoscopic view of the vocal folds. (*c*) Lateral rotation of the arytenoid cartilages positions the vocal folds for breathing. (*d*) Medial rotation of the arytenoid cartilages positions the vocal folds for speaking. (*e*) Anterior/posterior movement of the arytenoid cartilages changes the length and tension of the vocal folds.

support the anterior and lateral sides of the trachea (figure 23.5*a*). They protect the trachea and maintain an open passageway for air. The posterior wall of the trachea is devoid of cartilage and contains an elastic ligamentous membrane and bundles of smooth muscle called the **trachealis** (trā′kē-ā-lis) **muscle.** Contraction of the smooth muscle can narrow the diameter of the trachea. During coughing, this action causes air to move more rapidly through the trachea, which helps to expel mucus and foreign objects. The esophagus lies immediately posterior to the cartilage-free posterior wall of the trachea.

P R E D I C T 2

Explain what happens to the shape of the trachea when a person swallows a large mouthful of food. Why is this change of shape advantageous?

The mucous membrane lining the trachea consists of pseudostratified ciliated columnar epithelium with numerous goblet cells (figure 23.5*b*). The cilia propel mucus and foreign particles embedded in it toward the larynx, where the mucus enters the pharynx and is swallowed. Constant irritation to the trachea, such as occurs in smokers, can cause the tracheal epithelium to become moist stratified squamous epithelium that lacks cilia and goblet cells. Consequently, the normal function of the tracheal epithelium is lost.

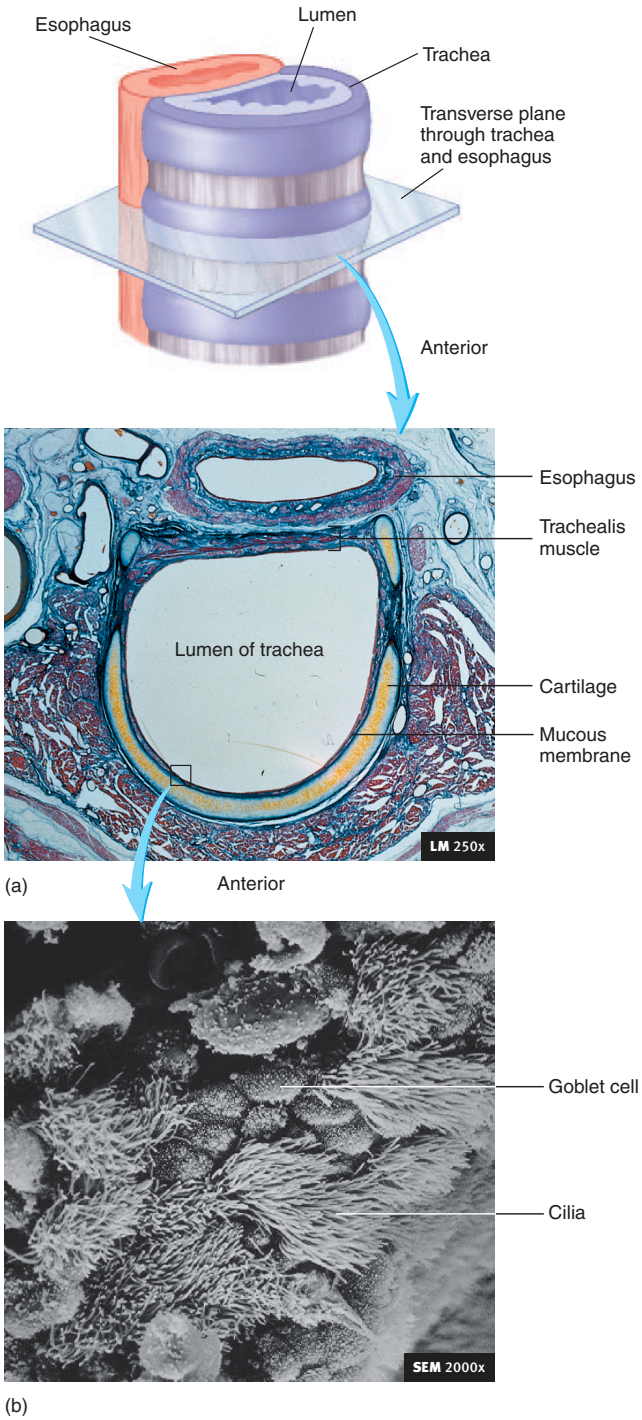


Figure 23.5 Trachea

(*a*) Photomicrograph of a transverse section of the trachea. The esophagus is next to the trachealis muscle, which connects the ends of the cartilage. (*b*) Scanning electron micrograph of the surface of the mucous membrane lining the trachea. Goblet cells with short microvilli are interspersed between ciliated cells.

Establishing Airflow

In cases of extreme emergency when the upper air passageway is blocked by a foreign object to the extent that the victim cannot breathe, quick reaction is required to save the person's life. The **Heimlich maneuver** is designed to force such an object out of the air passage by the sudden application of pressure to the abdomen. The person who performs the maneuver stands behind the victim with arms under the victim's arms and hands over the victim's abdomen between the navel and the rib cage. With one hand formed into a fist and the other hand over it, both hands are suddenly pulled toward the abdomen with an accompanying upward motion. This maneuver, if done properly, forces air up the trachea and dislodges most foreign objects.

In rare cases, when the obstruction cannot be removed using the Heimlich maneuver, it may be necessary to form an artificial opening in the victim's air passageway, followed with insertion of a tube to facilitate the passage of air. The preferred point of entry in emergency cases is through the membrane between the cricoid and thyroid cartilages, a procedure referred to as a **cricothyrotomy** (krī′kō-thī-rot′ō-mē). A **tracheotomy** (trā-kē-ot′ō-mē) makes an opening in the trachea, usually between the second and third cartilage rings. It is not advisable to enter the air passageway through the trachea in emergency cases because arteries, nerves, and the thyroid gland overlie the anterior surface of the trachea.

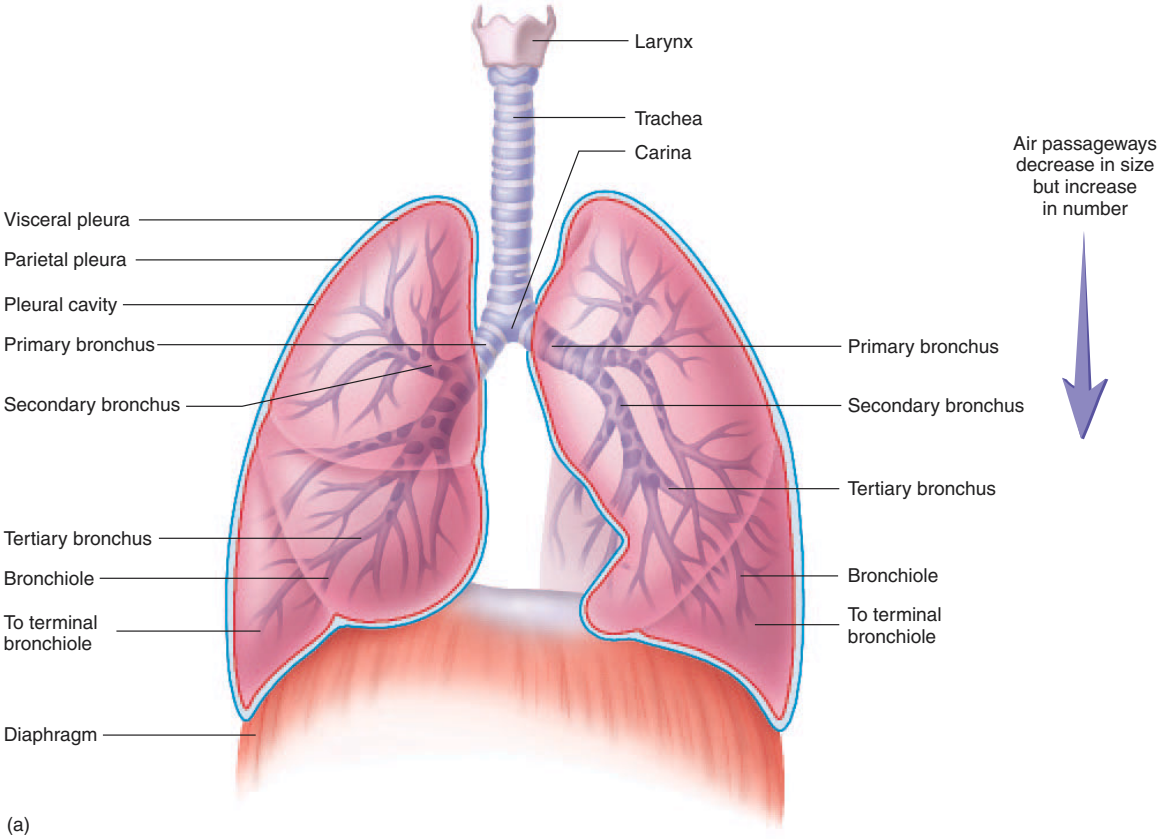
The trachea has an inside diameter of 12 mm and a length of 10–12 cm, descending from the larynx to the level of the fifth thoracic vertebra (figure 23.6). The trachea divides to form two smaller tubes called **primary bronchi** (brong′kī; sing., bronchus, brong′kŭs; windpipe). The most inferior tracheal cartilage forms a ridge called the **carina** (kă-rī′nă), which separates the openings into the primary bronchi. The carina is an important radiologic landmark. In addition, the mucous membrane of the carina is very sensitive to mechanical stimulation, and foreign objects reaching the carina stimulate a powerful cough reflex. Once a foreign object passes the carina, coughing usually stops.

Tracheobronchial Tree

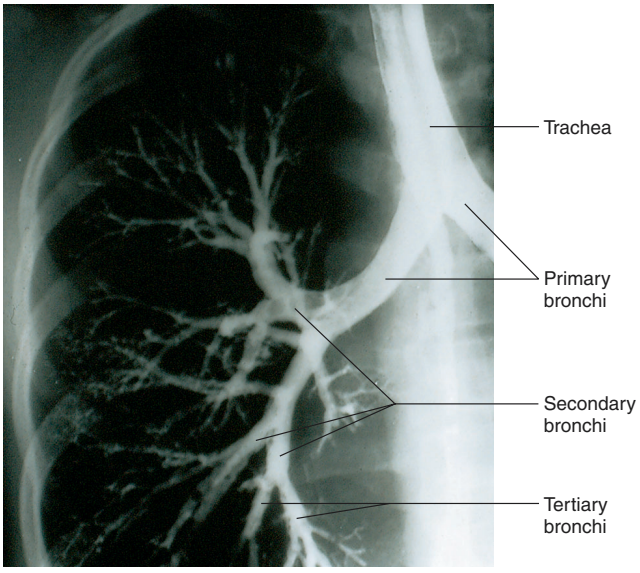
The trachea divides to form primary bronchi, which, in turn, divide to form smaller and smaller bronchi, until, eventually, many microscopically small tubes and sacs are formed. Beginning with the trachea, all the respiratory passageways are called the **tracheobronchial** (trā′kē-ō-brong′kē-ăl) **tree** (see figure 23.6). Based on function, the tracheobronchial tree can be subdivided into the conducting zone and the respiratory zone.

Conducting Zone

The **conducting zone** extends from the trachea to small tubes called terminal bronchioles (see figure 23.6). Approximately 16 generations of branching occur from the trachea to the terminal bronchioles. The conducting zone functions as a passageway for air movement and contains epithelial tissue that helps to remove debris from the air and move it out of the tracheobronchial tree.



(a)



(b)

Figure 23.6 Tracheobronchial Tree

(*a*) The conducting zone of the tracheobronchial tree begins at the trachea and ends at the terminal bronchioles. (*b*) A bronchogram is a radiograph of the tracheobronchial tree. A contrast medium, which makes the passageways visible, is injected through a catheter after a topical anesthetic is applied to the mucous membranes of the nose, pharynx, larynx, and trachea.

The trachea divides into the left and right primary bronchi, which extend to the lungs (see figure 23.6). The right primary bronchus is shorter, has a wider diameter, and is more vertical than the left primary bronchus.

PREDICT 3

Into which lung would a foreign object that's small enough to pass into a primary bronchus most likely become lodged and block air movement?

The primary bronchi divide into **secondary (lobar) bronchi** within each lung. Two secondary bronchi exist in the left lung, and three exist in the right lung. The secondary bronchi, in turn, give rise to **tertiary (segmental) bronchi.** The bronchi continue to branch, finally giving rise to **bronchioles** (brong′kē-ōlz), which are less than 1 mm in diameter. The bronchioles also subdivide several times to become even smaller **terminal bronchioles.**

As the air passageways of the lungs become smaller, the structure of their walls changes. Like the trachea, the primary bronchi are supported by C-shaped cartilage connected by smooth muscle. In the secondary bronchi, the C-shaped cartilages are replaced with cartilage plates, and smooth muscle forms a layer between the cartilage and the mucous membrane. As the bronchi become smaller, the cartilage becomes more sparse and smooth muscle becomes more abundant. The terminal bronchioles have no cartilage, and the smooth muscle layer is prominent. Relaxation and contraction of the smooth muscle within the bronchi and bronchioles can change the diameter of the air passageways and thereby change the volume of air moving through them. For example, during exercise, the diameter can increase, which reduces the resistance to airflow and thereby increases the volume of air moved. During an **asthma attack,** however, contraction of the smooth muscle in the terminal bronchioles, which have no cartilage in their walls, can result in decreased diameter, increased resistance to airflow, and greatly reduced airflow. In severe cases, air movement can be so restricted that death results.

The bronchi are lined with a pseudostratified ciliated columnar epithelium. The larger bronchioles are lined with ciliated simple columnar epithelium, which changes to ciliated simple cuboidal epithelium in the terminal bronchioles. The epithelium in the conducting part of the air passageways functions as a mucus–cilia escalator, which traps debris in the air and removes it from the respiratory system.

Respiratory Zone

The **respiratory zone** extends from the terminal bronchioles to small air-filled chambers called **alveoli** (al-vē′ō-lī; hollow cavity), which are the sites of gas exchange between the air and blood. Approximately seven generations of branching are present in the respiratory zone. The terminal bronchioles divide to form **respiratory bronchioles** (figure 23.7), which have a limited ability for gas exchange because of a few attached alveoli. As the respiratory bronchioles divide to form smaller respiratory bronchioles, the number of attached alveoli increases. The respiratory bronchioles give rise to **alveolar** (al-vē′ō-lăr) **ducts,** which are like long branching hallways with many open doorways. The doorways open into alveoli, which become so numerous that the alveolar duct wall is little more than a succession of alveoli. The alveolar ducts end as two or three **alveolar sacs,** which are chambers connected to two or more alveoli.

The tissue surrounding the alveoli contains elastic fibers that allow the alveoli to expand during inspiration and recoil during expiration. The lungs are very elastic, and when inflated, they are capable of expelling the air and returning to their original, uninflated state. Even when not inflated, however, the lungs retain some air, which gives them a spongy quality.

The walls of respiratory bronchioles consists of collagenous and elastic connective tissue with bundles of smooth muscle. The epithelium in the respiratory bronchioles is a simple cuboidal epithelium. The alveolar ducts and alveoli consist of simple squamous epithelium. Although the epithelium of the respiratory zone is not ciliated, debris from the air can be removed by macrophages that move over the surfaces of the cells. The macrophages don't accumulate in the respiratory zone because they either move into nearby lymphatic vessels or enter terminal bronchioles, thereby becoming entrapped in mucus that is swept to the pharynx.

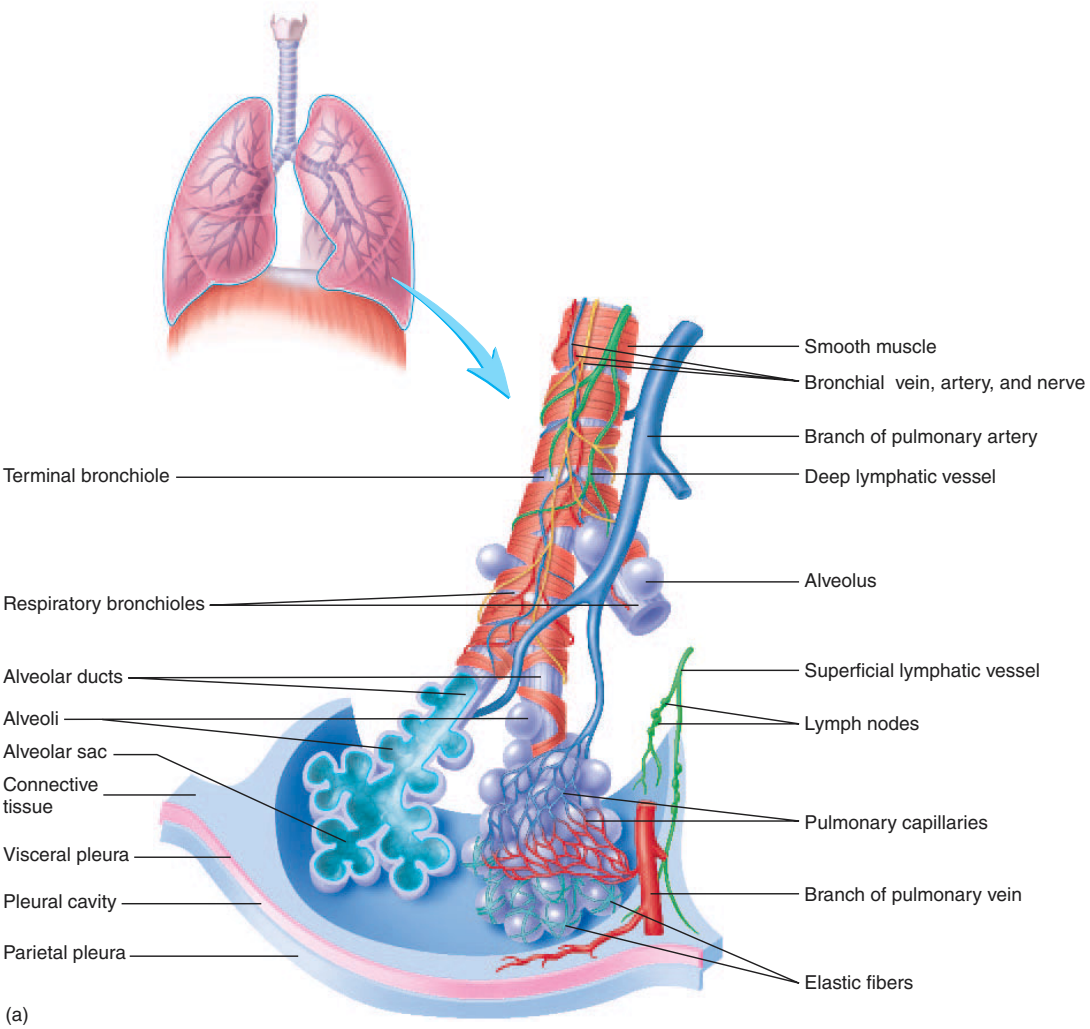
Approximately 300 million alveoli are in the two lungs. The average diameter of the alveoli is approximately 250 μm, and their walls are extremely thin. Two types of cells form the alveolar wall (figure 23.8*a*). **Type I pneumocytes** are thin, squamous epithelial cells that form 90% of the alveolar surface. Most gas exchange between alveolar air and the blood takes place through these cells. **Type II pneumocytes** are round or cube-shaped secretory cells that produce surfactant, which makes it easier for the alveoli to expand during inspiration (see "Lung Recoil" on p. 829).

The **respiratory membrane** of the lungs is where gas exchange between the air and blood takes place. It is mainly formed by the alveolar walls and surrounding pulmonary capillaries (figure 23.8*b*), but there's some contribution by the respiratory bronchioles and alveolar ducts. The respiratory membrane is very thin to facilitate the diffusion of gases. It consists of

1. a thin layer of fluid lining the alveolus;
2. the alveolar epithelium composed of simple squamous epithelium;
3. the basement membrane of the alveolar epithelium;
4. a thin interstitial space;
5. the basement membrane of the capillary endothelium;
6. the capillary endothelium composed of simple squamous epithelium.

Lungs

The **lungs** are the principal organs of respiration, and on a volume basis they are among the largest organs of the body. Each lung is conical in shape, with its base resting on the diaphragm and its apex extending superiorly to a point approximately 2.5 cm



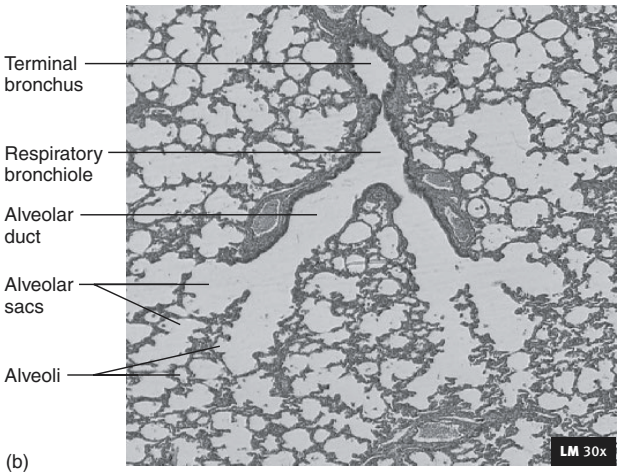


Figure 23.7 Bronchioles and Alveoli

(*a*) Alveoli, the sites of gas exchange between air and blood, are connected to respiratory bronchioles and alveolar ducts and are surrounded by capillaries. (*b*) Photomicrograph of lung tissue.

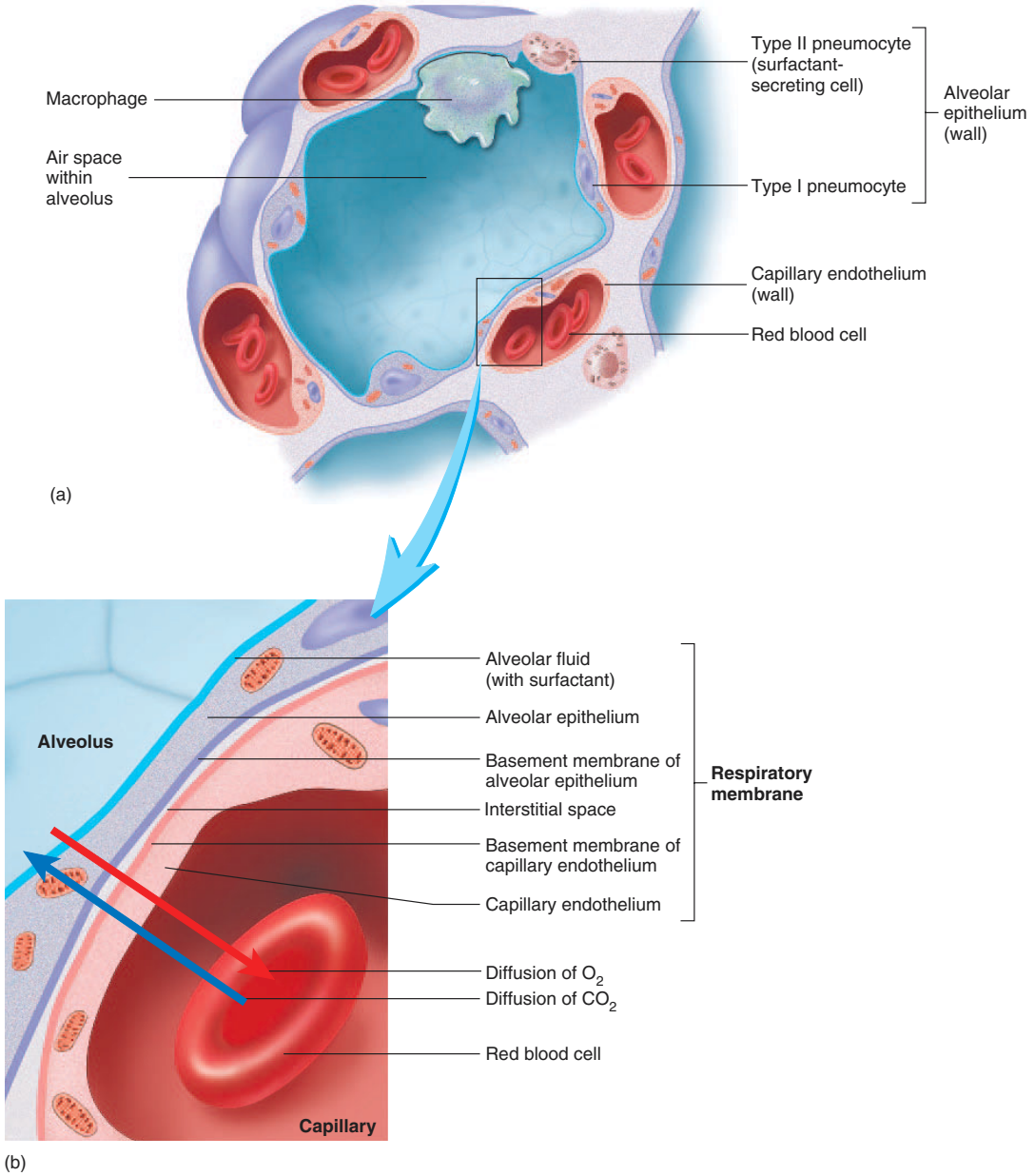


Figure 23.8 Alveolus and the Respiratory Membrane

(*a*) Section of an alveolus showing the air-filled interior and thin walls composed of simple squamous epithelium. The alveolus is surrounded by elastic connective tissue and blood capillaries. (*b*) Diffusion of oxygen and carbon dioxide across the six thin layers of the respiratory membrane.

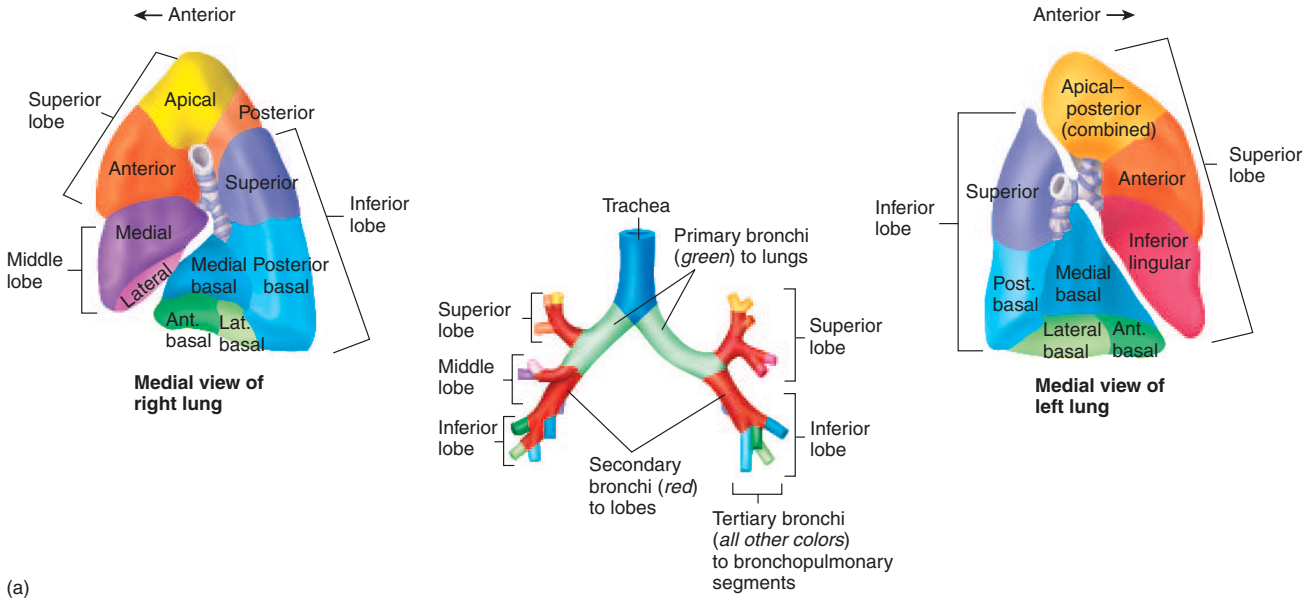
superior to the clavicle. The right lung is larger than the left and weighs an average of 620 g, whereas the left lung weighs an average of 560 g.

The **hilum** (hī′lŭm) is a region on the medial surface of the lung where structures, such as the primary bronchus, blood vessels, nerves, and lymphatic vessels, enter or exit the lung. All the structures passing through the hilum are referred to as the **root of the lung.**

The right lung has three **lobes,** and the left lung has two (figure 23.9). The lobes are separated by deep, prominent **fissures** on the surface of the lung, and each lobe is supplied by a secondary bronchus. The lobes are subdivided into **bronchopulmonary segments,** which are supplied by the tertiary bronchi. Nine bronchopulmonary segments are present in the left lung, and 10 are present in the right lung. The bronchopulmonary segments are

separated from each other by connective tissue partitions, which are not visible as surface fissures. Individual diseased bronchopulmonary segments can be surgically removed, leaving the rest of the lung relatively intact, because major blood vessels and bronchi don't cross the connective tissue partitions. The bronchopulmonary segments are subdivided into **lobules** by incomplete connective tissue walls. The lobules are supplied by the bronchioles.

8. What are the parts of the conducting and respiratory zones of the tracheobronchial tree?



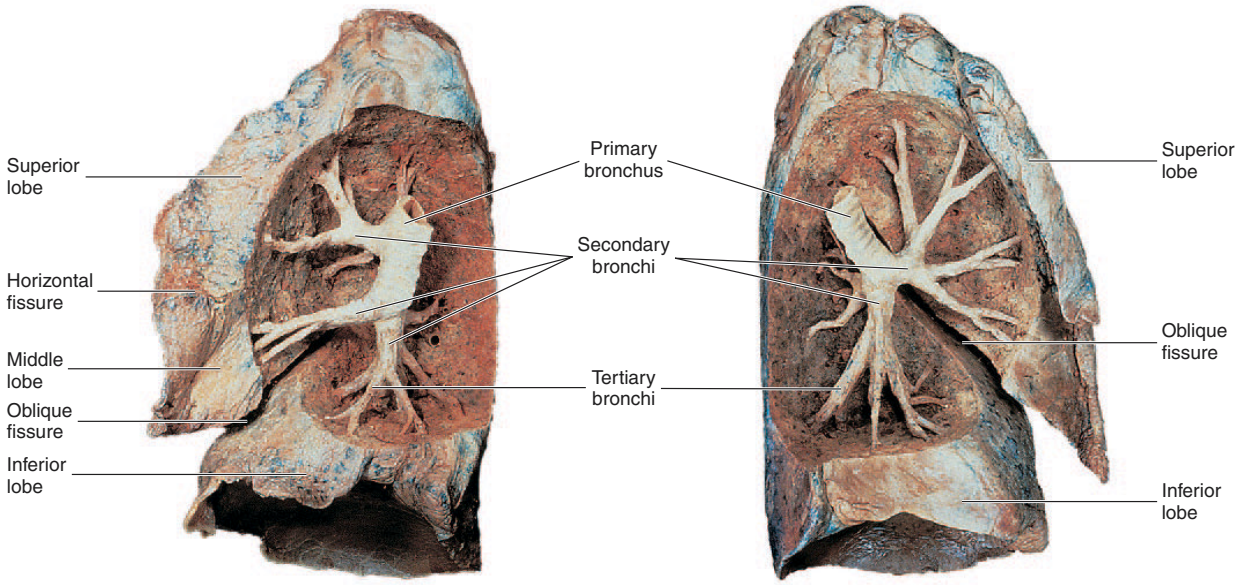


Figure 23.9 Lobes and Bronchopulmonary Segments of the Lungs

(*a*) The trachea (*blue*), primary bronchi (*green*), secondary bronchi (*red*), and tertiary bronchi (*all other colors*) are in the center of the figure, surrounded by two views of each lung, showing the bronchopulmonary segments. In general, each bronchopulmonary segment is supplied by a tertiary bronchus (*color-coded to match the bronchopulmonary segment it supplies*). (*b*) Photograph of the lungs showing the bronchi supplying the lung lobes.

9. *Describe the arrangement of cartilage, smooth muscle, and epithelium in the tracheobronchial tree. Explain why breathing becomes more difficult during an asthma attack.*
10. *How is debris removed from the conducting and respiratory zones?*
11. *Name the two types of cells in the alveolar wall, and state their functions.*
12. *List the parts of the respiratory membrane.*
13. *Distinguish among a lung, a lung lobe, a bronchopulmonary segment, and a lobule. How are they related to the tracheobronchial tree?*

Thoracic Wall and Muscles of Respiration

The **thoracic wall** consists of the thoracic vertebrae, ribs, costal cartilages, the sternum, and associated muscles (see chapters 7 and 10). The **thoracic cavity** is the space enclosed by the thoracic wall and the **diaphragm** (di′ă-fram, meaning partition), which separates the thoracic cavity from the abdominal cavity. The diaphragm and other skeletal muscles associated with the thoracic wall are responsible for respiration (figure 23.10). The **muscles of inspiration** include the diaphragm, external intercostals, pectoralis minor, and scalenes. Contraction of the diaphragm is responsible for approximately two-thirds of the increase in thoracic volume during inspiration. The external intercostals, pectoralis minor and scalene muscles also increase thoracic volume by elevating the ribs. The **muscles of expiration** consist of muscles that depress the ribs and sternum, such as the abdominal muscles and the internal intercostals. Although the internal intercostals are most active during expiration, and the external intercostals are most active during inspiration, the primary function of these muscles is to stiffen the thoracic wall by contracting at the same time. By so doing, they prevent inward collapse of the thoracic cage during inspiration.

The diaphragm is dome-shaped, and the base of the dome attaches to the inner circumference of the inferior thoracic cage (see figure 10.15). The top of the dome is a flat sheet of connective tissue called the **central tendon.** In normal, quiet inspiration, contraction of the diaphragm results in inferior movement of the central tendon with very little change in the overall shape of the dome. Inferior movement of the central tendon can occur because of relaxation of the abdominal muscles, which allows the abdominal organs to move out of the way of the diaphragm. As the depth of inspiration increases, inferior movement of the central tendon is prevented by the abdominal organs. Continued contraction of the diaphragm causes it to flatten as the lower ribs are elevated. In addition, other muscles of inspiration can elevate the ribs. As the ribs are elevated, the costal cartilages allow lateral rib movement and lateral expansion of the thoracic cavity (figure 23.11). The ribs slope inferiorly from the vertebrae to the sternum, and elevation of the ribs also increases the anterior–posterior dimension of the thoracic cavity.

Expiration during quiet breathing occurs when the diaphragm and external intercostals relax and the elastic properties of the thorax and lungs cause a passive decrease in thoracic volume. In

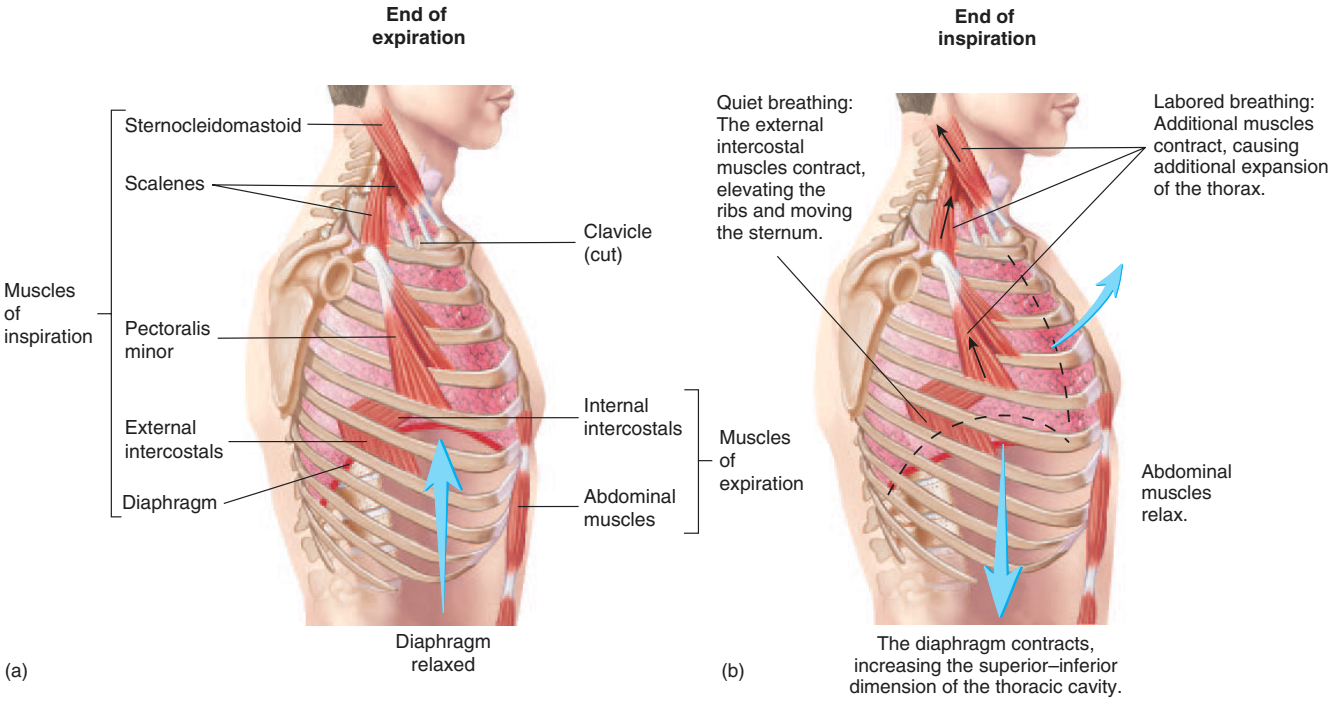


Figure 23.10 Effect of the Muscles of Respiration on Thoracic Volume

(*a*) Muscles of respiration at the end of expiration. (*b*) Muscles of respiration at the end of inspiration.

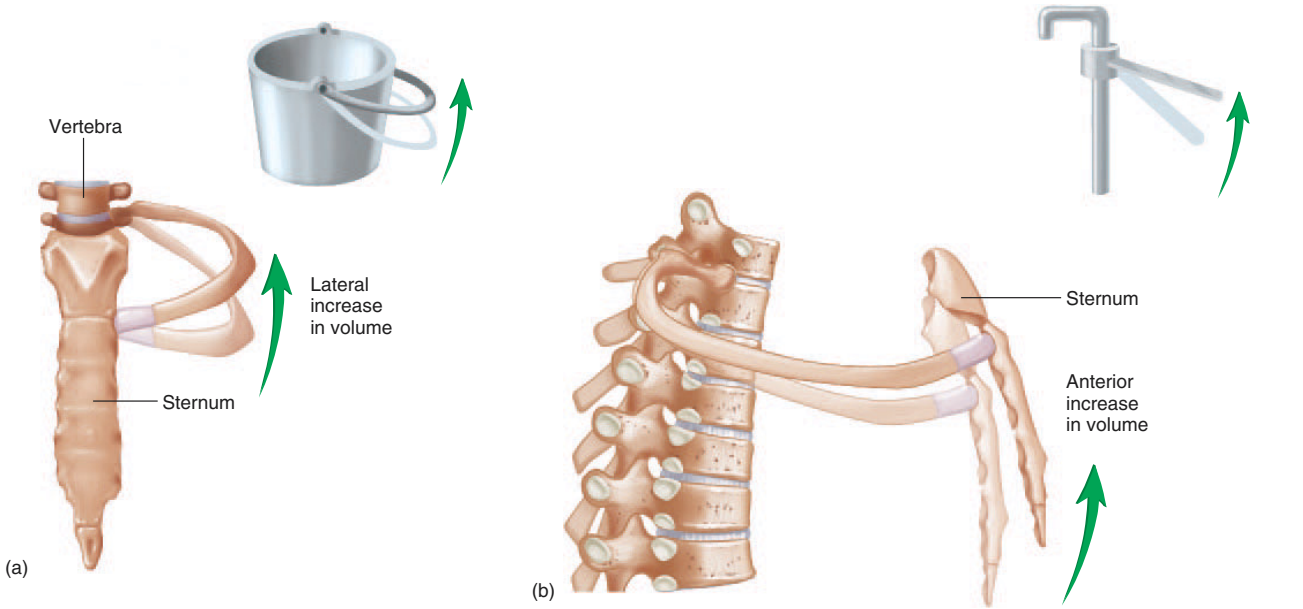


Figure 23.11 Effect of Rib and Sternum Movement on Thoracic Volume

(*a*) Elevation of the rib in the "bucket-handle" movement laterally increases thoracic volume. (*b*) As the rib is elevated, rotation of the rib in the "pump-handle" movement increases thoracic volume anteriorly.

addition, contraction of the abdominal muscles helps to push abdominal organs and the diaphragm in a superior direction.

The Role of Abdominal Muscles in Breathing

The importance of the abdominal muscles in breathing can be observed in a person with a spinal cord injury that causes flaccid paralysis of the abdominal muscles. In the upright position, the abdominal organs and diaphragm are not pushed superiorly and passive recoil of the thorax and lungs is inadequate for normal expiration. An elastic binder around the abdomen can help such patients. When lying down, the weight of the abdominal organs can assist in expiration.

Several differences can be recognized between normal, quiet breathing and labored breathing. During labored breathing, all of the inspiratory muscles are active, and they contract more forcefully than during quiet breathing, causing a greater increase in thoracic volume (see figure 23.10*b*). During labored breathing, forceful contraction of the internal intercostals and the abdominal muscles produces a more rapid and greater decrease in thoracic volume than would be produced by the passive recoil of the thorax and lungs.

Pleura

The lungs are contained within the thoracic cavity, but each lung is surrounded by a separate **pleural** (ploor′ăl; relating to the ribs) **cavity** formed by the pleural serous membranes (figure 23.12). The **mediastinum** (mē′dē-as-tī′nŭm), a midline partition formed by the heart, trachea, esophagus, and associated structures, separates the pleural cavities. The **parietal pleura** covers the inner thoracic wall, the superior surface of the diaphragm, and the mediastinum. At the hilum, the parietal pleura is continuous with the **visceral pleura,** which covers the surface of the lung.

The pleural cavity is filled with pleural fluid, which is produced by the pleural membranes. The pleural fluid does two things: (1) it acts as a lubricant, allowing the parietal and visceral pleural membranes to slide past each other as the lungs and the thorax change shape during respiration, and (2) it helps hold the parietal and visceral pleural membranes together. When thoracic volume changes during respiration, lung volume changes because the parietal pleura is attached to the diaphragm and inner thoracic wall, and the visceral pleura is attached to the lungs. The pleural fluid is analogous to a thin film of water between two sheets of glass (the visceral and parietal pleurae); the glass sheets can easily slide over each other, but it's difficult to separate them.

Blood Supply

Blood that has passed through the lungs and picked up oxygen is called **oxygenated blood,** and blood that has passed through the tissues and released some of its oxygen is called **deoxygenated blood.** Two blood flow routes to the lungs exist. The major route brings deoxygenated blood to the lungs, where it is oxygenated (see chapter 21 and figure 23.12*b*). The deoxygenated blood flows through pulmonary arteries to pulmonary capillaries, becomes oxygenated, and returns to the heart through pulmonary veins. The other route brings oxygenated blood to the tissues of the bronchi down to the respiratory bronchioles. The oxygenated blood flows from the thoracic aorta through bronchial arteries to capillaries, where oxygen is released. Deoxygenated blood from the proximal part of the bronchi returns to the heart through the bronchial veins and the azygos venous system (see chapter 21). More distally, the venous drainage from the bronchi enters the pulmonary veins. Thus, the oxygenated blood returning from the alveoli in the pulmonary veins is mixed with a small amount of deoxygenated blood returning from the bronchi.

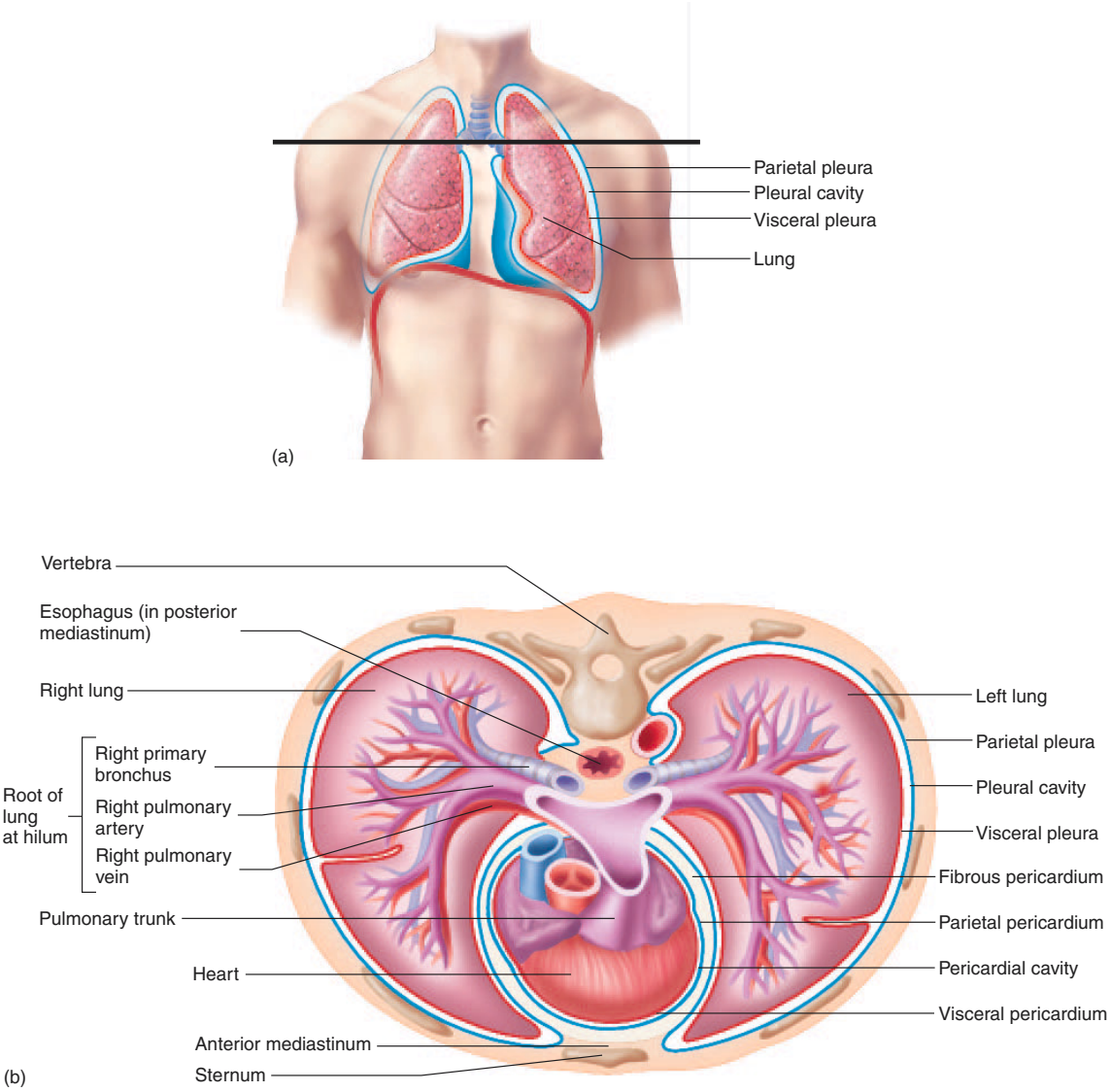


Figure 23.12 Pleural Cavities and Membranes

(*a*) Each lung is surrounded by a pleural cavity. The parietal pleura lines the wall of each pleural cavity, and the visceral pleura covers the surface of the lungs. The space between the parietal and visceral pleurae is small and filled with pleural fluid. (*b*) Transverse section of the thorax, at the level indicated in part (*a*), showing the relationship of the pleural cavities to the thoracic organs.

Lymphatic Supply

The lungs have two lymphatic supplies. The **superficial lymphatic vessels** are deep to the visceral pleura and function to drain lymph from the superficial lung tissue and the visceral pleura. The **deep lymphatic vessels** follow the bronchi and function to drain lymph from the bronchi and associated connective tissues. No lymphatic vessels are located in the walls of the alveoli. Both the superficial and deep lymphatic vessels exit the lung at the hilum.

Phagocytic cells pick up carbon particles and other debris from inspired air and move them to the lymphatic vessels. In older people, the surface of the lungs can appear gray to black because of the accumulation of these particles, especially if the person smokes or has lived most of his or her life in a city with air pollution. Cancer cells from the lungs can spread to other parts of the body through the lymphatic vessels.

14. *List the muscles of respiration and describe their role in quiet inspiration and expiration. How does this change during labored breathing?*
15. *Name the pleurae of the lungs. What is their function?*
16. *What are the two major routes of blood flow to and from the lungs? What is the function of each route?*
17. *Describe the lymphatic supply of the lungs.*

Clinical Focus Cough and Sneeze Reflexes

The function of both the cough reflex and the sneeze reflex is to dislodge foreign matter or irritating material from respiratory passages. The bronchi and trachea contain sensory receptors that are sensitive to foreign particles and irritating substances. The cough reflex is initiated when the sensory receptors detect such substances and initiate action potentials that pass along the vagus nerves to the medulla oblongata, where the cough reflex is triggered.

The movements resulting in a cough occur as follows: approximately 2.5 L of air is inspired; the vestibular and vocal folds close tightly to trap the inspired air in the lungs; the abdominal muscles contract to force the abdominal contents up against the diaphragm; and the muscles of expiration contract forcefully. As a consequence, the pressure in the lungs increases to 100 mm Hg or more. Then the vestibular and vocal folds open suddenly, the soft palate is elevated, and the air rushes from the lungs and out the oral cavity at a high velocity, carrying foreign particles with it.

The sneeze reflex is similar to the cough reflex, but it differs in several ways. The source of irritation that initiates the sneeze reflex is in the nasal passages instead of in the trachea and bronchi, and the action potentials are conducted along the trigeminal nerves to the medulla oblongata, where the reflex is triggered. During the sneeze reflex the soft palate is depressed so that air is directed primarily through the nasal passages, although a considerable amount passes through the oral cavity. The rapidly flowing air dislodges particulate matter from the nasal passages and can propel it a considerable distance from the nose.

Ventilation

Objectives

- ***Describe the factors that affect the flow of air through a tube and the factors that determine the pressure of a gas in a container.***
- ***Explain the movement of air into and out of the lungs.***
- ***Describe the factors that cause the alveoli to collapse and expand.***

Pressure Differences and Airflow

Ventilation is the process of moving air into and out of the lungs. The flow of air into the lungs requires a pressure gradient from the outside of the body to the alveoli, and airflow from the lungs requires a pressure gradient in the opposite direction. The physics of airflow in tubes, such as the ones that make up the respiratory passages, is the same as the flow of blood in blood vessels (see chapter 21). Thus, the following relationships hold:

$$F = \frac{P_1 - P_2}{R}$$

where F is airflow (milliliters per minute) in a tube, P_1 is pressure at point one, P_2 is pressure at point two, and R is resistance to airflow.

Air moves through tubes because of a pressure difference. When P_1 is greater than P_2, gas flows from P_1 to P_2 at a rate that's proportional to the pressure difference. For example, during inspiration, air pressure outside the body is greater than air pressure in the alveoli, and air flows through the trachea and bronchi to the alveoli.

Disorders That Decrease the Radius of Air Passageways

The flow of air decreases when the resistance to airflow is increased by conditions that reduce the radius of the respiratory passageways. According to Poiseuille's law (see chapter 21), the resistance to airflow is proportional to the radius (r) of a tube raised to the fourth power (r^4). Thus, a small change in radius results in a large change in resistance, which greatly decreases airflow. For example, asthma results in the release of inflammatory chemicals such as leukotrienes that cause severe constriction of the bronchioles. Emphysema produces increased airway resistance because the bronchioles are obstructed as a result of inflammation and because damaged bronchioles collapse during expiration, thus trapping air within the alveoli. Cancer can also occlude respiratory passages as the tumor replaces lung tissue. Increasing the pressure difference between alveoli and the atmosphere can help to maintain airflow despite increased resistance. Within limits, this can be accomplished by increased contraction of the muscles of respiration.

Pressure and Volume

The pressure in a container, such as the thoracic cavity or an alveolus, is described according to the **general gas law.**

$$P = \frac{nRT}{V}$$

where P is pressure, n is the number of gram moles of gas (a measure of the number of molecules present), R is the gas constant, T is absolute temperature, and V is volume.

The value of R is a constant, and the values of n and T (body temperature) are considered constants in humans. Thus, the general gas law reveals that air pressure is inversely proportional to volume. As volume increases, pressure decreases; and as volume decreases, pressure increases (table 23.1).

Table 23.1 Gas Law

Description	Importance
General Gas Law	
The pressure of a gas is inversely proportional to its volume (at a constant temperature, this is referred to as Boyle's law).	Air flows from areas higher to lower pressure. When alveolar volume increases, causing pleural pressure to decrease below atmosphereic pressure, air moves into the lungs. When alveolar volume decreases, causing pleural pressure to increase above atmospheric pressure, air moves out of the lungs.
Dalton's Law	
The partial pressure of a gas in a mixture of gases is the percentage of the gas in the mixture times the total pressure of the mixture of gases.	Gases move from areas of higher to areas of lower partial pressures. The greater the differernce in partial pressure between two points, the greater the rate of gas movement. Maintaining partial pressure differences ensures gas movements.
Henry's Law	
The concentration of a gas dissolved in a liquid is equal to the partial pressure of the gas over the liquid times the solubility coefficient of the gas.	Only a small amount of the gases in air dissolves in the fluid lining the alveoli. Carbon dioxide, however, is 24 times more soluble than oxygen; therefore, carbon dioxide passes out through the respiratory membrane more readily than oxygen enters.

18. *Define the term ventilation.*
19. *How do pressure differences and resistance affect airflow through a tube?*
20. *What happens to the pressure within a container when the volume of the container increases?*

Airflow into and out of Alveoli

Respiratory physiologists use three conventions to help simplify the numbers used to express pressures. First, **barometric air pressure (P_B),** which is atmospheric air pressure outside the body, is assigned a value of zero. Thus, whether at sea level with a pressure of 760 mm Hg or at 10,000 feet above sea level on a mountaintop with a pressure of 523 mm Hg, P_B is always zero. Second, the small pressures in respiratory physiology are usually expressed in centimeters of water (cm H_2O). A pressure of 1 cm H_2O is equal to 0.74 mm Hg. Third, other pressures are measured in reference to barometric air pressure. For example, **alveolar pressure (P_{alv})** is the pressure inside an alveolus. An alveolar pressure of 1 cm H_2O is 1 cm H_2O greater pressure than barometric air pressure, and an alveolar pressure of −1 cm H_2O is 1 cm H_2O less pressure than barometric air pressure.

Movement of air into and out of the lungs results from changes in thoracic volume, which cause changes in alveolar volume. The changes in alveolar volume produce changes in alveolar pressure. The pressure difference between barometric air pressure and alveolar pressure ($P_B - P_{alv}$) results in air movement. The details of this process during quiet breathing are described as follows:

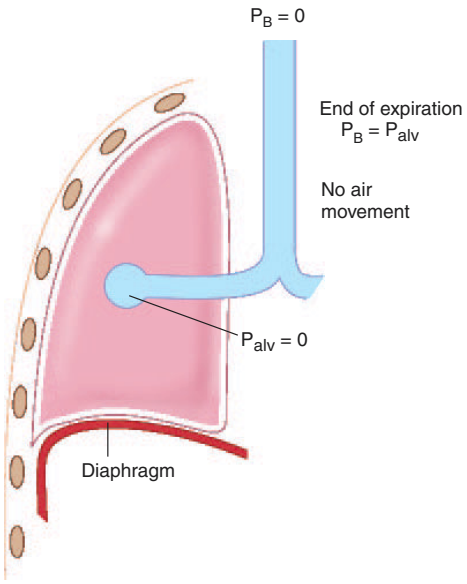
1. *End of expiration* (figure 23.13 *1*). At the end of expiration, barometric air pressure and alveolar pressure are equal. Therefore, no movement of air into or out of the lungs takes place.
2. *During inspiration* (figure 23.13 *2*). As inspiration begins, contraction of inspiratory muscles increases thoracic volume, which results in expansion of the lungs and an increase in alveolar volume (see following section on "Changing Alveolar Volume"). The increased alveolar volume causes a decrease in alveolar pressure below barometric air pressure to approximately −1cm H_2O. Air flows into the lungs because barometric air pressure is greater than alveolar pressure.
3. *End of inspiration* (figure 23.13 *3*). At the end of inspiration, the thorax stops expanding, the alveoli stop expanding, and alveolar pressure becomes equal to barometric air pressure because of airflow into the lungs. No movement of air occurs after alveolar pressure becomes equal to barometric pressure, but the volume of the lungs is larger than at the end of expiration.
4. *During expiration* (figure 23.13 *4*). During expiration, the volume of the thorax decreases as the diaphragm relaxes, and the thorax and lungs recoil. The decreased thoracic volume results in a decrease in alveolar volume and an increase in alveolar pressure over barometric air pressure to approximately 1cm H_2O. Air flows out of the lungs because alveolar pressure is greater than barometric air pressure. As expiration ends, the decrease in thoracic volume stops and the alveoli stop changing size. The process repeats beginning at step 1.

Changing Alveolar Volume

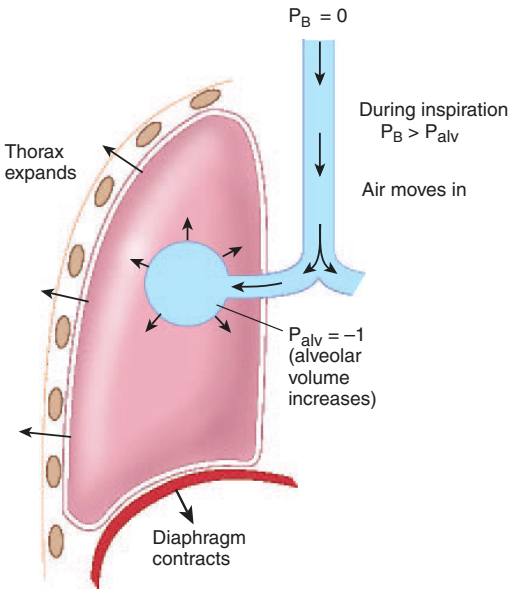
It's important to understand how alveolar volume is changed because these changes cause the pressure differences resulting in ventilation. In addition, many respiratory disorders affect how alveolar volume changes. Lung recoil and changes in pleural pressure cause changes in alveolar volume.

Lung Recoil

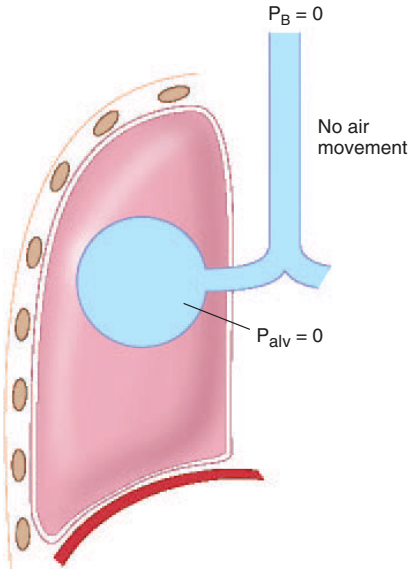
Lung recoil causes the alveoli to collapse, and it results from (1) elastic recoil caused by the elastic fibers in the alveolar walls and (2) surface tension of the film of fluid that lines the alveoli. Surface tension occurs at the boundary between water and air because the polar water molecules are attracted to one another more than they



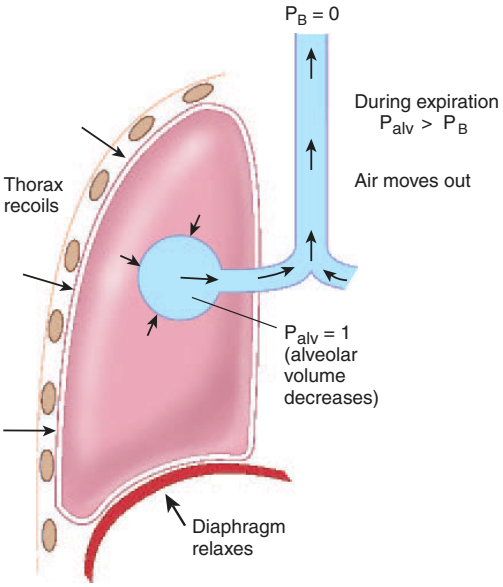
1. Barometric air pressure (P_B) is equal to alveolar pressure (P_{alv}) and there is no air movement.



2. Increased thoracic volume results in increased alveolar volume and decreased alveolar pressure. Barometric air pressure is greater than alveolar pressure, and air moves into the lungs.



3. End of inspiration.



4. Decreased thoracic volume results in decreased alveolar volume and increased alveolar pressure. Alveolar pressure is greater than barometric air pressure, and air moves out of the lungs.

Process Figure 23.13 Alveolar Pressure Changes During Inspiration and Expiration

The combined space of all the alveoli is represented by a large "bubble." The alveoli are actually microscopic in size and cannot be seen in the illustration.

are attracted to the air molecules. Consequently, the water molecules are drawn together, tending to form a droplet. Because the water molecules of the alveolar fluid are also attracted to the surface of the alveoli, formation of a droplet causes the alveoli to collapse, thus producing fluid-filled alveoli with smaller volumes than air-filled alveoli.

Surfactant (ser-fak′tănt) is a mixture of lipoprotein molecules produced by the type II pneumocytes of the alveolar epithelium. The surfactant molecules form a monomolecular layer over the surface of the fluid within the alveoli to reduce the surface tension. With surfactant, the force produced by surface tension is approximately 4 cm H_2O; without surfactant, the force can be as high as 40 cm H_2O. Thus, surfactant greatly reduces the tendency of the lungs to collapse.

Respiratory Distress Syndrome

In premature infants, **respiratory distress syndrome,** or **hyaline** (hī′ă-lin) **membrane disease,** is common, especially for infants with a gestation age of less than 7 months. This occurs because surfactant is not produced in adequate quantities until approximately 7 months of development. Thereafter, the amount produced increases as the fetus matures. Cortisol can be given to pregnant women who are likely to deliver prematurely, because it crosses the placenta into the fetus and stimulates surfactant synthesis.

If insufficient surfactant is produced by a newborn, the lungs tend to collapse. Thus, a great deal of energy must be exerted by the muscles of respiration to keep the lungs inflated, and even then inadequate ventilation occurs. Without specialized treatment, most babies with this disease die soon after birth as a result of inadequate ventilation of the lungs and fatigue of the respiratory muscles. Positive end-expiratory pressure delivers oxygen-rich, pressurized air to the lungs through a tube passed through the respiratory passages. The pressure helps to keep the alveoli inflated. In addition, human surfactant administered with the pressurized air can reduce surface tension in the alveoli.

Pleural Pressure

Pleural pressure (P_{pl}) is the pressure in the pleural cavity. When pleural pressure is less than alveolar pressure, the alveoli tend to expand. This principle can be understood by considering a balloon. The balloon expands when the pressure outside the balloon is less than the pressure inside. This pressure difference is normally achieved by increasing the pressure inside the balloon when a person forcefully blows into it. This pressure difference, however, can also be achieved by decreasing the pressure outside the balloon. For example, if the balloon is placed in a chamber from which air is removed, the pressure around the balloon becomes lower than atmospheric pressure, and the balloon expands. The lower the pressure outside the balloon, the greater the tendency for the higher pressure inside the balloon to cause it to expand. In a similar fashion, decreasing pleural pressure can result in expansion of the alveoli.

Normally the alveoli are expanded because of a negative pleural pressure that is lower than alveolar pressure. At the end of a normal expiration, pleural pressure is −5 cm H_2O, and alveolar pressure is 0 cm H_2O. Pleural pressure is lower than alveolar pressure because of a "suction effect" caused by lung recoil. As the lungs recoil, the visceral and parietal pleurae tend to be pulled apart. Normally the lungs don't pull away from the thoracic wall because pleural fluid holds the visceral and parietal pleurae together. Nonetheless, this pull decreases pressure in the pleural cavity, an effect that can be appreciated by putting water on the palms of the hands and putting them together. A sensation of negative pressure is felt as the hands are gently pulled apart.

When pleural pressure is lower than alveolar pressure, the alveoli tend to expand. This expansion is opposed by the tendency of the lungs to recoil. If the pleural pressure is sufficiently low, lung recoil is overcome and the alveoli expand. If the pleural pressure is not low enough to overcome lung recoil, then the alveoli collapse.

Pneumothorax

A **pneumothorax** is the introduction of air into the pleural cavity through an opening in the thoracic wall or lung. Pneumothorax can result from penetrating trauma by a knife, bullet, broken rib, or other object; nonpenetrating trauma such as a blow to the chest; medical procedures such as inserting a catheter to withdraw pleural fluid; disease, such as infections or emphysema; or can be of unknown cause.

Pleural pressure becomes equal to barometric air pressure when the pleural cavity is connected to the outside through an opening in the thoracic wall or the surface of the lung. The alveoli, therefore, don't tend to expand, lung recoil is unopposed, and the lung collapses and pulls away from the thoracic wall. Pneumothorax can occur in one lung while the lung on the opposite side remains inflated because the two pleural cavities are separated by the mediastinum.

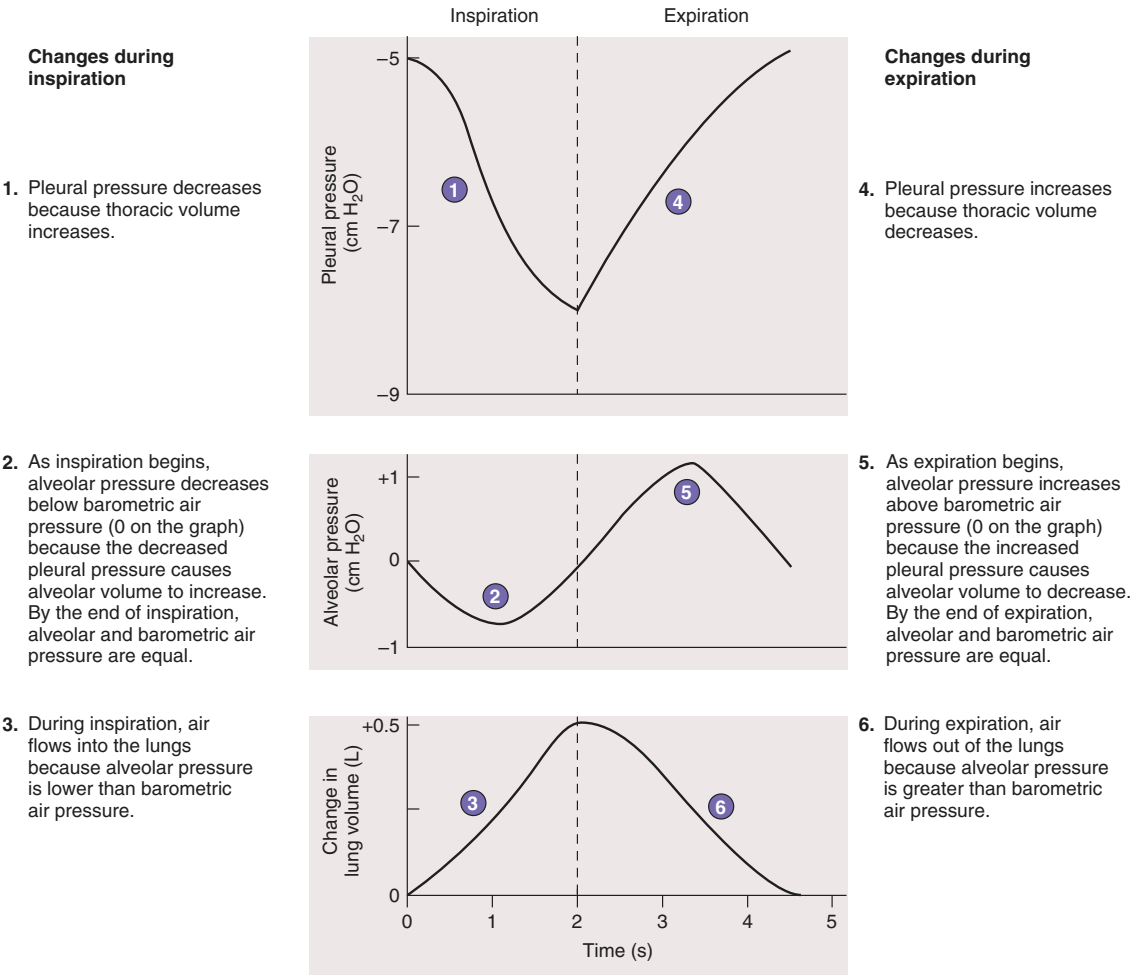
The most common symptoms of pneumothorax are chest pain and shortness of breath. Treatment of pneumothorax depends upon its cause and severity. In patients with mild symptoms, the pneumothorax may resolve on its own. In other cases, a chest tube that aspirates the pleural cavity and restores a negative pressure can cause re-expansion of the lung. Surgery may also be necessary to close the opening into the pleural cavity.

In a **tension pneumothorax,** the pressure within the thoracic cavity is always higher than barometric air pressure. A tissue flap or air passageway forms a flutter valve that allows air to enter the pleural cavity during inspiration but not exit during expiration. The result is an increase in air and pressure within the pleural cavity that can compress blood vessels returning blood to the heart, causing decreased venous return, low blood pressure, and inadequate delivery of oxygen to tissues. Insertion of a large bore needle into the pleural cavity allows air to escape and releases the pressure.

Pressure Changes During Inspiration and Expiration

At the end of a normal expiration, pleural pressure is −5 cm H_2O, and alveolar pressure is equal to barometric pressure (0 cm H_2O) (figure 23.14). During normal, quiet inspiration, pleural pressure decreases to −8 cm H_2O. Consequently, the alveolar volume increases, alveolar pressure decreases below barometric air pressure, and air flows into the lungs. As air flows into the lungs, alveolar pressure increases and becomes equal to barometric pressure at the end of inspiration.

The decrease in pleural pressure during inspiration occurs for two reasons. First, because of the effect of changing volume on pressure (general gas law), when the volume of the thoracic cavity increases, pleural pressure decreases. Second, as the thoracic cavity



Process Figure 23.14 Dynamics of a Normal Breathing Cycle

expands, the lungs expand because they adhere to the inner thoracic wall through the pleurae. As the lungs expand, the tendency for the lungs to recoil increases, resulting in an increased suction effect and a lowering of pleural pressure. The tendency for the lungs to recoil increases as the lungs are stretched, similar to the increased force generated in a stretched rubber band.

During expiration, pleural pressure increases because of decreased thoracic volume and decreased lung recoil (see figure 23.14). As pleural pressure increases, alveolar volume decreases, alveolar pressure increases above barometric air pressure, and air flows out of the lungs. As air flows out of the lungs, alveolar pressure decreases and becomes equal to barometric pressure at the end of expiration.

21. *Define barometric and alveolar pressures.*
22. *Explain how changes in alveolar volume cause air to move into and out of the lungs.*
23. *Name two things that cause the lungs to recoil. How does surfactant reduce lung recoil? What happens if there are inadequate amounts of surfactant in the alveoli?*
24. *Define pleural pressure. What happens to alveolar volume when pleural pressure decreases? Name two things that cause pleural pressure to decrease.*
25. *How does an opening in the chest wall cause the lung to collapse?*

PREDICT 4

How does the pleural pressure at the end of expiration in a newborn with respiratory distress syndrome compare to that of a healthy newborn? How does the pleural pressure compare during inspiration? Explain.

Measuring Lung Function

Objectives

- *Define the term compliance, and explain its significance.*
- *List the pulmonary volumes and capacities, and define each of them.*
- *Explain the significance of forced expiratory volume in one second, minute ventilation, and alveolar ventilation.*

A variety of measurements can be used to assess lung function. Each of these tests compares a subject's measurements to a normal range. These measurements can be used to diagnose diseases, track the progress of diseases, or track recovery from diseases.

Compliance of the Lungs and the Thorax

Compliance is a measure of the ease with which the lungs and the thorax expand. The compliance of the lungs and thorax is the volume by which they increase for each unit of pressure change in alveolar pressure. It is usually expressed in liters (volume of air) per centimeter of water (pressure), and for the normal person the compliance of the lungs and thorax is 0.13 L/cm H_2O. That is, for every 1 cm H_2O change in alveolar pressure, the volume changes by 0.13 L.

The greater the compliance, the easier it is for a change in pressure to cause expansion of the lungs and thorax. For example, one possible result of emphysema is the destruction of elastic lung tissue. This reduces the elastic recoil force of the lungs, thereby making expansion of the lungs easier and resulting in a higher-than-normal compliance. A lower-than-normal compliance means that it's harder to expand the lungs and thorax. Conditions that decrease compliance include deposition of inelastic fibers in lung tissue (pulmonary fibrosis), collapse of the alveoli (respiratory distress syndrome and pulmonary edema), increased resistance to airflow caused by airway obstruction (asthma, bronchitis, and lung cancer), and deformities of the thoracic wall that reduce the ability of the thoracic volume to increase (kyphosis and scoliosis).

Effects of Decreased Compliance

Pulmonary diseases can markedly affect the total amount of energy required for ventilation, as well as the percentage of the total amount of energy expended by the body. Diseases that decrease compliance can increase the energy required for breathing up to 30% of the total energy expended by the body.

Pulmonary Volumes and Capacities

Spirometry (spī-rom′ĕ-trē) is the process of measuring volumes of air that move into and out of the respiratory system, and a **spirometer** (spī-rom′ĕ-ter) is a device used to measure these pulmonary volumes (figure 23.15*a*). The four pulmonary volumes and representative values (figure 23.15*b*) for a young adult male follow:

1. **Tidal volume** is the volume of air inspired or expired during a normal inspiration or expiration (approximately 500 mL).
2. **Inspiratory reserve volume** is the amount of air that can be inspired forcefully after inspiration of the normal tidal volume (approximately 3000 mL).
3. **Expiratory reserve volume** is the amount of air that can be forcefully expired after expiration of the normal tidal volume (approximately 1100 mL).
4. **Residual volume** is the volume of air still remaining in the respiratory passages and lungs after the most forceful expiration (approximately 1200 mL).

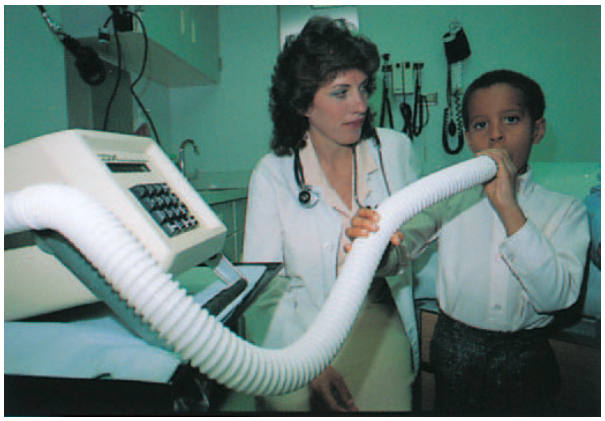
Pulmonary capacities are the sum of two or more pulmonary volumes (see figure 23.15*b*). Some pulmonary capacities follow:

1. **Inspiratory capacity** is the tidal volume plus the inspiratory reserve volume, which is the amount of air that a person can inspire maximally after a normal expiration (approximately 3500 mL).
2. **Functional residual capacity** is the expiratory reserve volume plus the residual volume, which is the amount of air remaining in the lungs at the end of a normal expiration (approximately 2300 mL).
3. **Vital capacity** is the sum of the inspiratory reserve volume, the tidal volume, and the expiratory reserve volume, which is the maximum volume of air that a person can expel from the respiratory tract after a maximum inspiration (approximately 4600 mL).
4. **Total lung capacity** is the sum of the inspiratory and expiratory reserve volumes plus the tidal volume and the residual volume (approximately 5800 mL).

Factors like sex, age, body size, and physical conditioning cause variations in respiratory volumes and capacities from one individual to another. For example, the vital capacity of adult females is usually 20%–25% less than that of adult males. The vital capacity reaches its maximum amount in the young adult and gradually decreases in the elderly. Tall people usually have a greater vital capacity than short people, and thin people have a greater vital capacity than obese people. Well-trained athletes can have a vital capacity 30%–40% above that of untrained people. In patients whose respiratory muscles are paralyzed by spinal cord injury or diseases like poliomyelitis or muscular dystrophy, vital capacity can be reduced to values not consistent with survival (less than 500–1000 mL). Factors that reduce compliance also reduce vital capacity.

The **forced expiratory vital capacity** is a simple and clinically important pulmonary test. The individual inspires maximally and then exhales maximally into a spirometer as rapidly as possible. The volume of air expired at the end of the test is the person's vital capacity. The spirometer also records the volume of air that enters it per second. The **forced expiratory volume in one second (FEV_1)** is the amount of air expired during the first second of the test. In some conditions, the vital capacity may not be dramatically affected, but how rapidly air is expired can be greatly decreased. Airway obstruction, caused by asthma, collapse of bronchi in emphysema, or a tumor, and disorders that reduce the ability of the

(a)



(b)

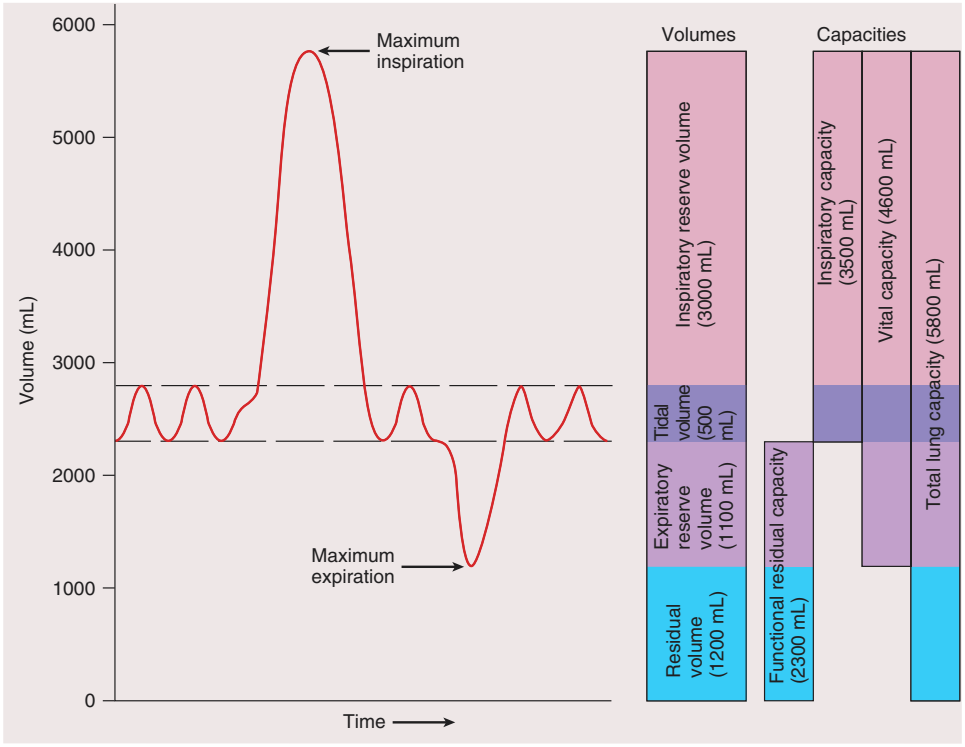


Figure 23.15 Spirometer, Lung Volumes, and Lung Capacities

(*a*) A spirometer used to measure lung volumes and capacities. (*b*) Lung volumes and capacities. The tidal volume in the figure is the tidal volume during resting conditions.

lungs or chest wall to deflate, such as pulmonary fibrosis, silicosis, kyphosis, and scoliosis, can cause a decreased FEV_1.

Minute Ventilation and Alveolar Ventilation

Minute ventilation is the total amount of air moved into and out of the respiratory system each minute, and it is equal to tidal volume times the respiratory rate. **Respiratory rate,** or **respiratory frequency,** is the number of breaths taken per minute. Because resting tidal volume is approximately 500 mL and respiratory rate is approximately 12 breaths per minute, minute ventilation averages approximately 6 L/min.

Although minute ventilation measures the amount of air moving into and out of the lungs per minute, it's not a measure of the amount of air available for gas exchange because gas exchange takes place mainly in the alveoli and to a lesser extent in the alveolar ducts and the respiratory bronchioles. The part of the respiratory system where gas exchange does not take place is called the dead space. A distinction can be made between anatomic and physiologic dead space. **Anatomic dead space,** which measures 150 mL, is formed by the nasal cavity, pharynx, larynx, trachea, bronchi, bronchioles, and terminal bronchioles. **Physiologic dead space** is anatomic dead space plus the volume of any alveoli in

which gas exchange is less than normal. In a healthy person, anatomic and physiologic dead spaces are nearly the same, meaning that few nonfunctional alveoli exist.

Emphysema and Dead Space

In patients with **emphysema,** alveolar walls degenerate, and small alveoli combine to form larger alveoli. The result is fewer alveoli, but alveoli with an increased volume and decreased surface area. Although the enlarged alveoli are still ventilated, surface area is inadequate for complete gas exchange, and the physiologic dead space increases.

During inspiration, much of the inspired air fills the dead space first before reaching the alveoli and, thus, is unavailable for gas exchange. The volume of air available for gas exchange per minute is called **alveolar ventilation ($\dot{V}_A$),** and it is calculated as follows:

$$\dot{V}_A = f(V_T - V_D)$$

where $\dot{V}_A$ is alveolar ventilation (milliliters per minute), f is respiratory rate (frequency; breaths per minute), V_T is tidal volume (milliliters per respiration), and V_D is dead space (milliliters per respiration).

26. *Define the term compliance. What is the effect on lung expansion when compliance increases or decreases?*
27. *Define the terms tidal volume, inspiratory reserve volume, expiratory reserve volume, and residual volume.*
28. *Define the terms inspiratory capacity, functional residual capacity, vital capacity, and total lung capacity.*
29. *What is forced expiratory volume in one second, and why is it clinically important?*
30. *Define the terms minute ventilation and alveolar ventilation.*
31. *What is dead space? What is the difference between anatomic and physiologic dead space?*

PREDICT 5

What is the alveolar ventilation of a resting person with a tidal volume of 500 mL, a dead space of 150 mL, and a respiratory rate of 12 breaths per minute? If the person exercises and tidal volume increases to 4000 mL, dead space increases to 300 mL as a result of dilation of the respiratory passageways, and respiratory rate increases to 24 breaths per minute, what is the alveolar ventilation? How is the change in alveolar ventilation beneficial for doing exercise?

Physical Principles of Gas Exchange

Objectives

- *Define the terms partial pressure of a gas and water vapor pressure.*
- *Describe the factors affecting the movement of gas into and through a liquid.*
- *Explain the factors that affect gas movement through the respiratory membrane.*
- *Describe the effect that ventilation and pulmonary capillary blood flow have on gas exchange.*

Ventilation supplies atmospheric air to the alveoli. The next step in the process of respiration is the diffusion of gases between alveoli and blood in the pulmonary capillaries. The molecules of gas move randomly, and if a gas is in a higher concentration at one point than at another, random motion ensures that the net movement of gas is from the higher concentration toward the lower concentration until a homogeneous mixture of gases is achieved. One measurement of the concentration of gases is partial pressure.

Partial Pressure

At sea level, atmospheric pressure is approximately 760 mm Hg, which means that the mixture of gases that constitute atmospheric air exerts a total pressure of 760 mm Hg. The major components of dry air are nitrogen (approximately 79%) and oxygen (approximately 21%). According to **Dalton's law,** in a mixture of gases, the part of the total pressure resulting from each type of gas is determined by the percentage of the total volume represented by each gas type (see table 23.1). The pressure exerted by each type of gas in a mixture is referred to as the **partial pressure** of that gas. Because nitrogen makes up 78.62% of the volume of atmospheric air, the partial pressure resulting from nitrogen is 0.7862 times 760 mm Hg, or 597.5 mm Hg. Because oxygen is 20.84% of the volume of atmospheric air, the partial pressure resulting from oxygen is 0.2084 times 760 mm Hg, or 158.4 mm Hg. It's traditional to designate the partial pressure of individual gases in a mixture with a capital P followed by the symbol for the gas. Thus, the partial pressure of nitrogen is denoted P_{N_2}, oxygen is P_{O_2}, and carbon dioxide is P_{CO_2}.

When air comes into contact with water, some of the water turns into a gas and evaporates into the air. Water molecules in gaseous form also exert a partial pressure. This partial pressure (P_{H_2O}) is sometimes referred to as **water vapor pressure.** The composition of dry, humidified, alveolar, and expired air is presented in table 23.2. The composition of alveolar air and of expired air is not identical to the composition of dry atmospheric air for three reasons. First, air entering the respiratory system during inspiration is humidified; second, oxygen diffuses from the alveoli into the blood, and carbon dioxide diffuses from the pulmonary capillaries into the alveoli; and third, the air within the alveoli is only partially replaced with atmospheric air during each inspiration.

Diffusion of Gases Through Liquids

When a gas comes into contact with a liquid such as water, it tends to dissolve in the liquid. At equilibrium, the concentration of a gas in the liquid is determined by its partial pressure in the gas and by its solubility in the liquid. This relationship is described by **Henry's law** (see table 23.1).

$$\text{Concentration of dissolved gas} = \text{Partial pressure of gas} \times \text{Solubility coefficient}$$

The solubility coefficient is a measure of how easily the gas dissolves in the liquid. In water, the solubility coefficient for oxygen is 0.024, and for carbon dioxide it is 0.57. Thus, carbon dioxide is approximately 24 times more soluble in water than is oxygen.

Table 23.2 Partial Pressures of Gases at Sea Level

	Dry Air		Humidified Air		Alveolar Air		Expired Air	
Gases	**mm Hg**	**%**	**mm Hg**	**%**	**mm Hg**	**%**	**mm Hg**	**%**
Nitrogen	597.5	78.62	563.4	74.09	569.0	74.9	566.0	74.5
Oxygen	158.4	20.84	149.3	19.67	104.0	13.6	120.0	15.7
Carbon dioxide	0.3	0.04	0.3	0.04	40.0	5.3	27.0	3.6
Water vapor	0.0	0.0	47.0	6.20	47.0	6.2	47.0	6.2

Gases don't actually produce a partial pressure in a liquid as they do when in the gaseous state. Using the general gas law equation and the concentration of a gas in a liquid, however, the partial pressure of the gas if it were in a gaseous state can be calculated. Because the calculated partial pressure of a gas in a liquid is a measure of concentration, it can be used to determine the direction of diffusion of the gas through the liquid: the gas moves from areas of higher to areas of lower partial pressure.

PREDICT 6

As a SCUBA diver descends, the pressure of the water on the body prevents normal expansion of the lungs. To compensate, the diver breathes pressurized air, which has a greater pressure than air at sea level. What effect does the increased pressure have on the amount of gas dissolved in the diver's body fluids? A SCUBA diver who suddenly ascends to the surface from a great depth can develop decompression sickness (the bends) in which bubbles of nitrogen gas form. The expanding bubbles damage tissues or block blood flow through small blood vessels. Explain the development of the bubbles.

Diffusion of Gases Through the Respiratory Membrane

The factors that influence the rate of gas diffusion across the respiratory membrane include (1) the thickness of the membrane; (2) the diffusion coefficient of the gas in the substance of the membrane, which is approximately the same as the diffusion coefficient for the gas through water; (3) the surface area of the membrane; and (4) the difference of the partial pressures of the gas between the two sides of the membrane.

Respiratory Membrane Thickness

Increasing the thickness of the respiratory membrane decreases the rate of diffusion. The thickness of the respiratory membrane normally averages 0.6 μm, but diseases can cause an increase in the thickness. If the thickness of the respiratory membrane increases two or three times, the rate of gas exchange markedly decreases. Pulmonary edema caused by failure of the left side of the heart is the most common cause of an increase in the thickness of the respiratory membrane. Left side heart failure increases venous pressure in the pulmonary capillaries and results in the accumulation of fluid in the alveoli. Conditions such as tuberculosis, pneumonia, or advanced silicosis that result in inflammation of the lung tissues can also cause fluid accumulation within the alveoli.

Diffusion Coefficient

The **diffusion coefficient** is a measure of how easily a gas diffuses through a liquid or tissue, taking into account the solubility of the gas in the liquid and the size of the gas molecule (molecular weight). If the diffusion coefficient of oxygen is assigned a value of 1, then the relative diffusion coefficient of carbon dioxide is 20, which means carbon dioxide diffuses through the respiratory membrane about 20 times more readily than oxygen does.

When the respiratory membrane becomes progressively damaged as a result of disease, its capacity for allowing the movement of oxygen into the blood is often impaired enough to cause death from oxygen deprivation before the diffusion of carbon dioxide is dramatically reduced. If life is being maintained by extensive oxygen therapy, which increases the concentration of oxygen in the lung alveoli, the reduced capacity for the diffusion of carbon dioxide across the respiratory membrane can result in substantial increases in carbon dioxide in the blood.

Surface Area

In a healthy adult, the total surface area of the respiratory membrane is approximately 70 m^2 (approximately the floor area of a 25- by 30-foot room). Several respiratory diseases, including emphysema and lung cancer, cause a decrease in the surface area of the respiratory membrane. Even small decreases in this surface area adversely affect the respiratory exchange of gases during strenuous exercise. When the total surface area of the respiratory membrane is decreased to one-third or one-fourth of normal, the exchange of gases is significantly restricted even under resting conditions.

A decreased surface area for gas exchange can also result from the surgical removal of lung tissue, the destruction of lung tissue by cancer, the degeneration of the alveolar walls by

emphysema, or the replacement of lung tissue by connective tissue caused by tuberculosis. More acute conditions that cause the alveoli to fill with fluid also reduce the surface area for gas exchange. Examples include pneumonia and pulmonary edema resulting from failure of the left ventricle.

Partial Pressure Difference

The partial pressure difference of a gas across the respiratory membrane is the difference between the partial pressure of the gas in the alveoli and the partial pressure of the gas in the blood of the pulmonary capillaries. When the partial pressure of a gas is greater on one side of the respiratory membrane than on the other side, net diffusion occurs from the higher to the lower partial pressure (see figure 23.8*b*). Normally, the partial pressure of oxygen (P_{O_2}) is greater in the alveoli than in the blood of the pulmonary capillaries, and the partial pressure of carbon dioxide (P_{CO_2}) is greater in the blood than in the alveolar air.

By increasing alveolar ventilation, the partial pressure difference for oxygen and carbon dioxide can be raised. The greater volume of atmospheric air exchanged with the residual volume raises alveolar P_{O_2}, lowers alveolar P_{CO_2}, and thus promotes gas exchange. Conversely, inadequate ventilation causes a lower-than-normal partial pressure difference for oxygen and carbon dioxide, resulting in inadequate gas exchange.

Relationship Between Ventilation and Pulmonary Capillary Blood Flow

Under normal conditions, ventilation of the alveoli and blood flow through pulmonary capillaries is such that effective gas exchange occurs between the air and the blood. During exercise, effective gas exchange is maintained because both ventilation and cardiac output increase.

The normal relationship between ventilation and pulmonary capillary blood flow can be disrupted in two different ways. One way occurs when ventilation exceeds the ability of the blood to pick up oxygen, which can happen because of inadequate cardiac output after a heart attack. Another way occurs when ventilation is not great enough to provide the oxygen needed to oxygenate the blood flowing through the pulmonary capillaries. For example, constriction of the bronchioles in asthma can decrease air delivery to the alveoli.

Blood that isn't completely oxygenated is called shunted blood. Two sources of shunted blood exist in the lungs. An **anatomic shunt** results when deoxygenated blood from the bronchi and bronchioles mixes with blood in the pulmonary veins (see section on "Blood Supply" on p. 826). The other source of shunted blood is blood that passes through pulmonary capillaries but doesn't become fully oxygenated. The **physiologic shunt** is the combination of deoxygenated blood from the anatomic shunt and the pulmonary capillaries. Normally, 1%–2% of cardiac output passes through the physiologic shunt.

Disorders That Increase Shunted Blood

Any condition that decreases gas exchange between the alveoli and the blood can increase the amount of shunted blood. For example, obstruction of the bronchioles in conditions such as asthma can decrease ventilation beyond the obstructed areas. The result is a large increase in shunted blood because the blood flowing through the pulmonary capillaries in the obstructed area remains unoxygenated. In pneumonia or pulmonary edema, a buildup of fluid in the alveoli results in poor gas diffusion and less oxygenated blood.

When a person is standing, greater blood flow and ventilation occur in the base of the lung than in the top of the lung because of the effects of gravity. Arterial pressure at the base of the lung is 22 mm Hg greater than at the top of the lung because of hydrostatic pressure caused by gravity (see chapter 21). This greater pressure increases blood flow and distends blood vessels. The decreased pressure at the top of the lung results in less blood flow and vessels that are less distended, some of which are even collapsed during diastole.

During exercise, cardiac output and ventilation increase. The increased cardiac output increases pulmonary blood pressure throughout the lung, which increases blood flow. Blood flow increases most at the top of the lung, however, because the increased pressure expands the less distended vessels and opens the collapsed vessels. Thus, the effectiveness of gas exchange at the top of the lung increases because of greater blood flow.

Although gravity is the major factor affecting regional blood flow in the lung, under certain circumstances alveolar P_{O_2} can have an effect also. In most tissues, low P_{O_2} results in increased blood flow through the tissues (see chapter 21). In the lung, low P_{O_2} has the opposite effect, causing arterioles to constrict and reducing blood flow. This response reroutes blood away from areas of low oxygen toward parts of the lung that are better oxygenated. For example, if a bronchus becomes partially blocked, ventilation of alveoli past the blockage site decreases, which decreases gas exchange between the air and blood. The effect of this decreased gas exchange on overall gas exchange in the lungs is reduced by rerouting the blood to better-ventilated alveoli.

32. *According to Dalton's law, what is the partial pressure of a gas? What is water vapor pressure?*
33. *Why is the composition of inspired, alveolar, and expired air different?*
34. *According to Henry's law, how does the partial pressure and solubility of a gas affect its concentration in a liquid?*
35. *Describe four factors that affect the diffusion of gases across the respiratory membrane. Give examples of diseases that decrease diffusion by altering these factors.*
36. *Does oxygen or carbon dioxide diffuse most easily through the respiratory membrane?*
37. *What effect do ventilation and pulmonary capillary blood flow have on gas exchange? What is the physiologic shunt?*
38. *What are the effects of gravity and alveolar P_{O_2} on blood flow in the lung?*

PREDICT 7

Even people in "good shape" can have trouble breathing at high altitudes. Explain how this can happen, even when ventilation of the lungs increases.

Oxygen and Carbon Dioxide Transport in the Blood

Objectives

- ***Describe the partial pressures of oxygen and carbon dioxide in the alveoli, lung capillaries, tissue capillaries, and tissues.***
- ***Explain the significance of the oxygen–hemoglobin dissociation curve, and illustrate how it is affected by changes in carbon dioxide, pH, temperature, and BPG.***
- ***Describe how carbon dioxide is transported in the blood, and discuss the chloride shift and how respiration can affect blood pH.***

Once oxygen diffuses across the respiratory membrane into the blood, most of it combines reversibly with hemoglobin, and a smaller amount dissolves in the plasma. Hemoglobin transports oxygen from the pulmonary capillaries through the blood vessels to the tissue capillaries, where some of the oxygen is released. The oxygen diffuses from the blood to tissue cells, where it is used in aerobic respiration.

Cells produce carbon dioxide during aerobic metabolism, and it diffuses from the cells into the tissue capillaries. Once carbon dioxide enters the blood, it is transported dissolved in the plasma, in combination with hemoglobin, and in the form of bicarbonate ions.

Oxygen Diffusion Gradients

The P_{O_2} within the alveoli averages approximately 104 mm Hg, and as blood flows into the pulmonary capillaries, it has a P_{O_2} of approximately 40 mm Hg (figure 23.16). Consequently, oxygen diffuses from the alveoli into the pulmonary capillary blood because the P_{O_2} is greater in the alveoli than in the capillary blood. By the time blood flows through the first third of the pulmonary capillary beds, an equilibrium is achieved, and the P_{O_2} in the blood is 104 mm Hg, which is equivalent to the P_{O_2} in the alveoli. Even with the greater velocity of blood flow associated with exercise, by the time blood reaches the venous ends of the pulmonary capillaries, the P_{O_2} in the capillaries has achieved the same value as that in the alveoli.

Blood leaving the pulmonary capillaries has a P_{O_2} of 104 mm Hg, but blood leaving the lungs in the pulmonary veins has a P_{O_2} of approximately 95 mm Hg. The decrease in the P_{O_2} occurs because the blood from the pulmonary capillaries mixes with deoxygenated (shunted) blood from the bronchial veins.

The blood that enters the arterial end of the tissue capillaries has a P_{O_2} of approximately 95 mm Hg. The P_{O_2} of the interstitial spaces, in contrast, is close to 40 mm Hg and is probably near 20 mm Hg in the individual cells. Oxygen diffuses from the tissue capillaries to the interstitial fluid and from the interstitial fluid into the cells of the body, where it's used in aerobic metabolism. Because oxygen is continuously used by cells, a constant diffusion gradient exists for oxygen from the tissue capillaries to the cells.

Carbon Dioxide Diffusion Gradients

Carbon dioxide is continually produced as a by-product of cellular respiration, and a diffusion gradient is established from tissue cells to the blood within the tissue capillaries. The intracellular P_{CO_2} is approximately 46 mm Hg, and the interstitial fluid P_{CO_2} is approximately 45 mm Hg. At the arterial end of the tissue capillaries, the P_{CO_2} is close to 40 mm Hg. As blood flows through the tissue capillaries, carbon dioxide diffuses from a higher P_{CO_2} to a lower P_{CO_2} until an equilibrium in P_{CO_2} is established. At the venous end of the capillaries, blood has a P_{CO_2} of 45 mm Hg (see figure 23.16).

After blood leaves the venous end of the capillaries, it's transported through the cardiovascular system to the lungs. At the arterial end of the pulmonary capillaries, the P_{CO_2} is 45 mm Hg. Because the P_{CO_2} is approximately 40 mm Hg in the alveoli, carbon dioxide diffuses from the pulmonary capillaries into the alveoli. At the venous end of the pulmonary capillaries, the P_{CO_2} has again decreased to 40 mm Hg.

39. Describe the partial pressures of oxygen and carbon dioxide in the alveoli, lung capillaries, tissue capillaries, and tissues. How do these partial pressures account for the movement of oxygen and carbon dioxide between air and blood and between blood and tissues?

Hemoglobin and Oxygen Transport

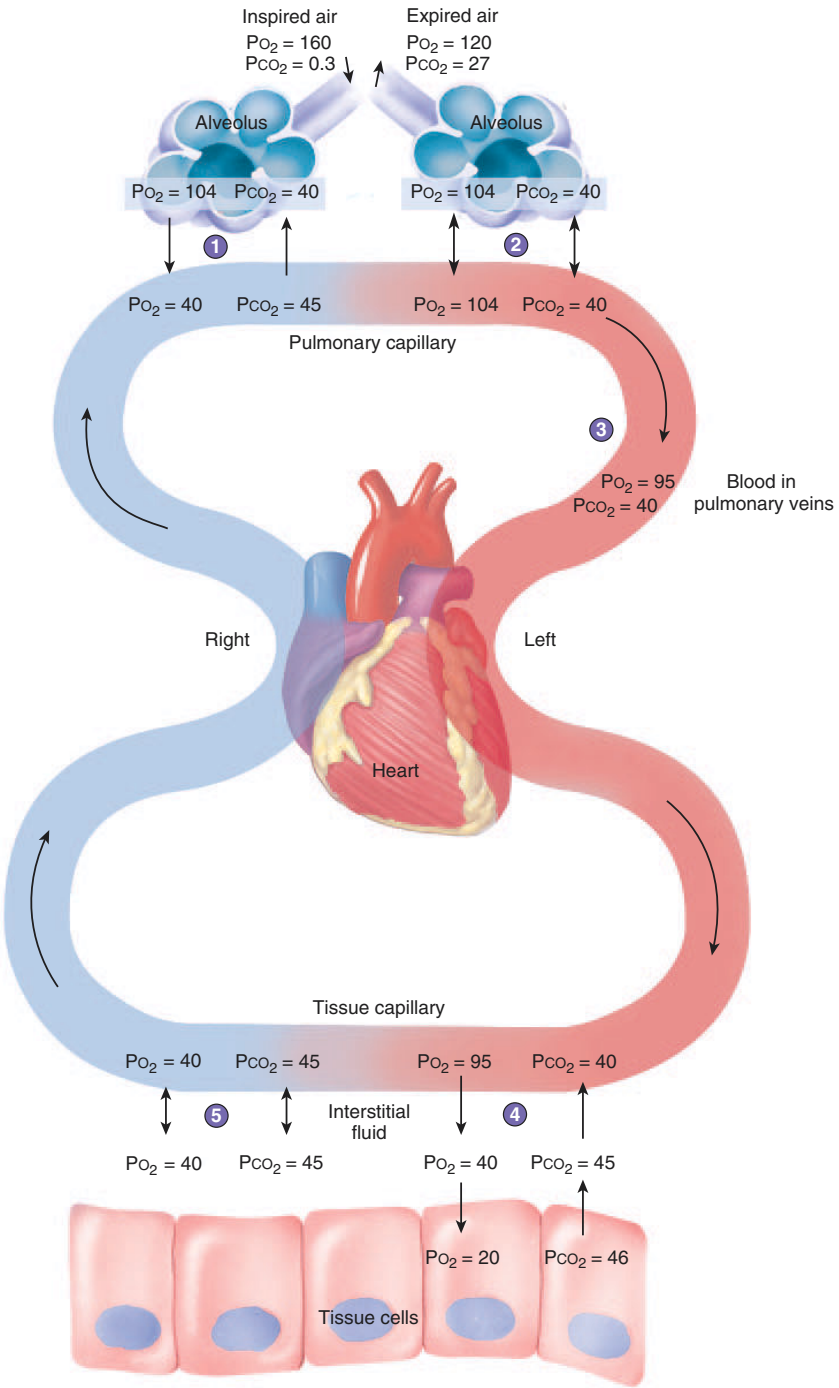
Approximately 98.5% of the oxygen transported in the blood from the lungs to the tissues is transported in combination with hemoglobin in red blood cells, and the remaining 1.5% is dissolved in the water part of the plasma. The combination of oxygen with hemoglobin is reversible. In the pulmonary capillaries, oxygen binds to hemoglobin, and in the tissue spaces oxygen diffuses away from hemoglobin and enters the tissues.

Effect of P_{O_2}

The **oxygen–hemoglobin dissociation curve** describes the percentage of hemoglobin saturated with oxygen at any given P_{O_2}. Hemoglobin is saturated when an oxygen molecule is bound to each of its four heme groups (see chapter 19). At any P_{O_2} above 80 mm Hg, approximately 95% of the hemoglobin is saturated with oxygen (figure 23.17). Because the P_{O_2} in the pulmonary capillaries is normally 104 mm Hg, the hemoglobin is 98% saturated.

In a resting person, the normal P_{O_2} of blood leaving the tissue capillaries of skeletal muscle is 40 mm Hg. At a P_{O_2} of 40 mm Hg, hemoglobin is approximately 75% saturated. Thus, approximately 23% of the oxygen bound to hemoglobin is released into the blood and can diffuse into the tissue spaces. During conditions of vigorous exercise, the blood P_{O_2} can decline to levels as low as

1. Oxygen diffuses into the arterial ends of pulmonary capillaries and carbon dioxide diffuses into the alveoli because of differences in partial pressures.
2. As a result of diffusion at the venous ends of pulmonary capillaries, the P_{O_2} in the blood is equal to the P_{O_2} in the alveoli and the P_{CO_2} in the blood is equal to the P_{CO_2} in the alveoli.
3. The P_{O_2} of blood in the pulmonary veins is less than in the pulmonary capillaries because of mixing with deoxygenated blood from veins draining the bronchi and bronchioles.
4. Oxygen diffuses out of the arterial ends of tissue capillaries and carbon dioxide diffuses out of the tissue because of differences in partial pressures.
5. As a result of diffusion at the venous ends of tissue capillaries, the P_{O_2} in the blood is equal to the P_{O_2} in the tissue and the P_{CO_2} in the blood is equal to the P_{CO_2} in the tissue. Go back to step 1.



Process Figure 23.16 Changes in the Partial Pressures of Oxygen and Carbon Dioxide

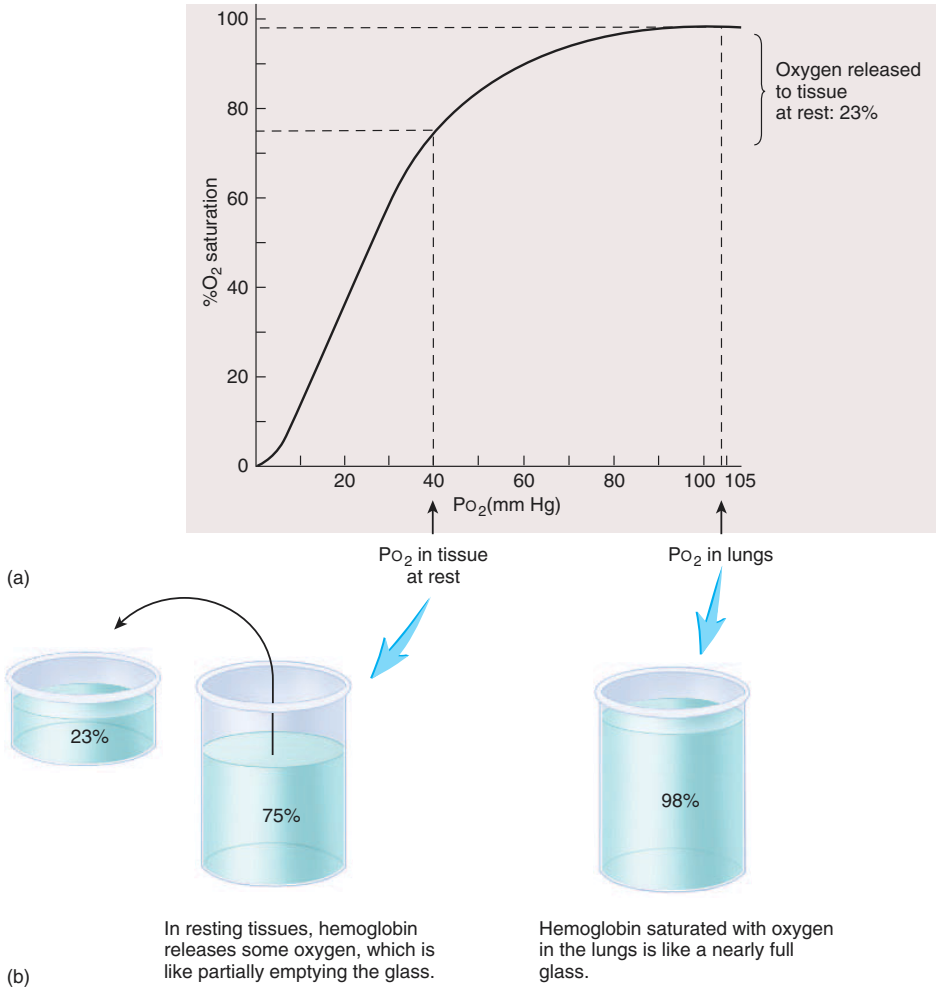


Figure 23.17 Oxygen–Hemoglobin Dissociation Curve at Rest

(*a*) At the P_{O_2} in the lungs, hemoglobin is 98% saturated. At the P_{O_2} of resting tissues, hemoglobin is 75% saturated. Consequently 23% of the oxygen picked up in the lungs is released to the tissues. (*b*) The ability of hemoglobin to pick up and release oxygen is like a glass filling and emptying.

15 mm Hg because the skeletal muscle cells are using the oxygen in aerobic respiration (see chapter 9). At a P_{O_2} of 15 mm Hg, approximately 25% of the hemoglobin is saturated with oxygen, and it releases 73% of the bound oxygen (figure 23.18). Thus, when the oxygen needs of tissues increase, blood P_{O_2} decreases, and more oxygen is released for use by the tissues.

Effect of pH, P_{CO_2}, and Temperature

In addition to P_{O_2}, other factors influence the degree to which oxygen binds to hemoglobin. As the pH of the blood declines, the amount of oxygen bound to hemoglobin at any given P_{O_2} also declines. This occurs because decreased pH results from an increase in hydrogen ions, and the hydrogen ions combine with the protein part of the hemoglobin molecule and change its three-dimensional structure, causing a decrease in the ability of hemoglobin to bind oxygen. Conversely, an increase in blood pH results in an increased ability of hemoglobin to bind oxygen. The effect of pH (hydrogen ions) on the oxygen–hemoglobin dissociation curve is called the **Bohr effect** after its discoverer, Christian Bohr.

An increase in P_{CO_2} also decreases the ability of hemoglobin to bind oxygen because of the effect of carbon dioxide on pH. Within red blood cells, an enzyme called **carbonic anhydrase** catalyzes this reversible reaction.

$$\underset{\text{Carbon dioxide}}{CO_2} + \underset{\text{Water}}{H_2O} \overset{\text{Carbonic anhydrase}}{\rightleftarrows} \underset{\text{Carbonic acid}}{H_2CO_3} \rightleftarrows \underset{\text{Hydrogen ion}}{H^+} + \underset{\text{Bicarbonate ion}}{HCO_3^-}$$

As carbon dioxide levels increase, more hydrogen ions are produced, and the pH declines. As carbon dioxide levels decline, the reaction proceeds in the opposite direction, resulting in a decrease in hydrogen ion concentration and an increase in pH.

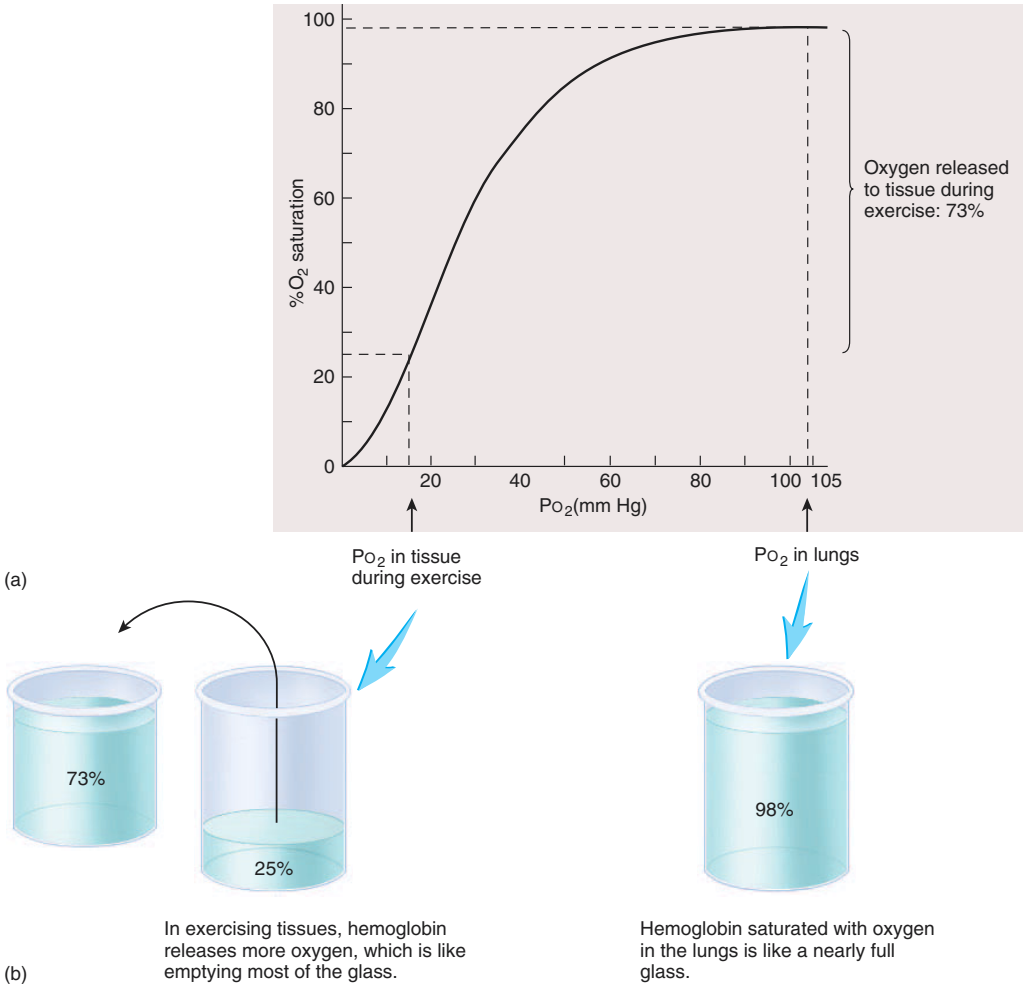


Figure 23.18 Oxygen–Hemoglobin Dissociation Curve During Exercise

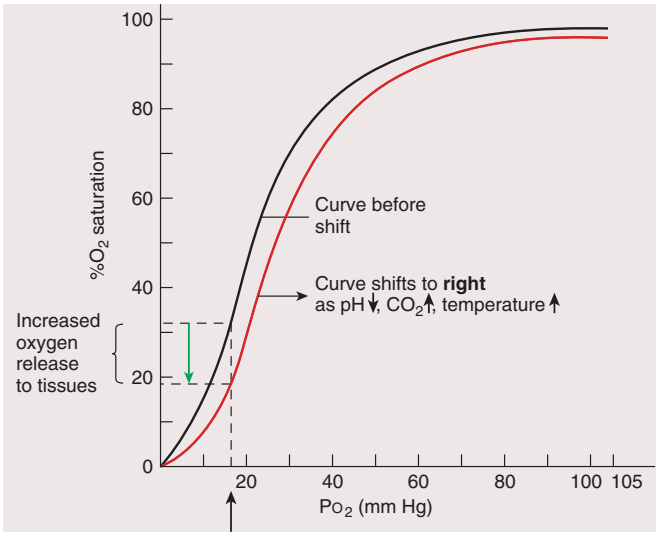
(*a*) At the P_{O_2} in the lungs, hemoglobin is 98% saturated. At the P_{O_2} of exercising tissues, hemoglobin is 25% saturated. Consequently 73% of the oxygen picked up in the lungs is released to the tissues. (*b*) The ability of hemoglobin to pick up and release oxygen is like a glass filling and emptying.

As blood passes through tissue capillaries, carbon dioxide enters the blood from the tissues. As a consequence, blood carbon dioxide levels increase, hemoglobin has less affinity for oxygen in the tissue capillaries, and a greater amount of oxygen is released in the tissue capillaries than would be released if carbon dioxide were not present. When blood is returned to the lungs and passes through the pulmonary capillaries, carbon dioxide leaves the capillaries and enters the alveoli. As a consequence, carbon dioxide levels in the pulmonary capillaries are reduced, and the affinity of hemoglobin for oxygen increases.

An increase in temperature also decreases the tendency for oxygen to remain bound to hemoglobin. Elevated temperatures resulting from increased metabolism, therefore, increase the amount of oxygen released into the tissues by hemoglobin. In less metabolically active tissues in which the temperature is lower, less oxygen is released from hemoglobin.

When the affinity of hemoglobin for oxygen decreases, the oxygen–hemoglobin dissociation curve is shifted to the right, and hemoglobin releases more oxygen (figure 23.19*a*). During exercise, when carbon dioxide and acidic substances, such as lactic acid, accumulate and the temperature increases in the tissue spaces, the oxygen–hemoglobin curve shifts to the right. Under these conditions, as much as 75%–85% of the oxygen is released from the hemoglobin. In the lungs, however, the curve shifts to the left because of the lower carbon dioxide levels, lower temperature, and lower lactic acid levels. The affinity of hemoglobin for oxygen, therefore, increases, and it becomes easily saturated (figure 23.19*b*).

During resting conditions, approximately 5 mL of oxygen is transported to the tissues in each 100 mL of blood, and cardiac output is approximately 5000 mL/min. Consequently, 250 mL of oxygen is delivered to the tissues each minute. During conditions of exercise, this value can increase up to 15 times. Oxygen transport



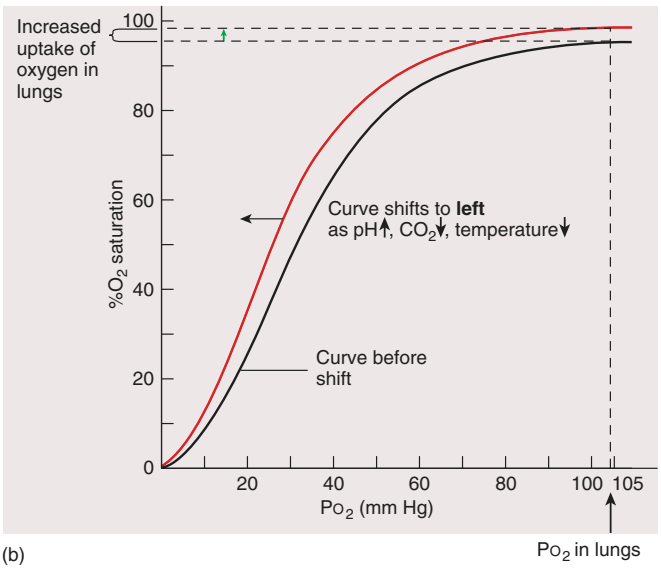


Figure 23.19 Effects of Shifting the Oxygen–Hemoglobin Dissociation Curve

(*a*) In the tissues, as pH decreases, P_{CO_2} increases, or temperature increases, the curve (*black*) shifts to the right (*red*), resulting in an increased release of oxygen. (*b*) In the lungs, as pH increases, P_{CO_2} decreases, or temperature decreases, the curve (*black*) shifts to the left (*red*), resulting in an increased ability of hemoglobin to pick up oxygen.

can be increased threefold because of a greater degree of oxygen release from hemoglobin in the tissue spaces, and the rate of oxygen transport is increased another five times because of the increase in cardiac output. Consequently, the volume of oxygen delivered to the tissues can be as high as 3750 mL/min (15 × 250 mL/min). Highly trained athletes can increase this volume to as high as 5000 mL/min.

40. Name two ways that oxygen is transported in the blood, and state the percentage of total oxygen transport for which each is responsible.

41. How does the oxygen–hemoglobin dissociation curve explain the uptake of oxygen in the lungs and the release of oxygen in tissues?

42. What is the Bohr effect? How is it related to blood carbon dioxide?

43. Why is it advantageous for the oxygen–hemoglobin dissociation curve to shift to the left in the lungs and to the right in tissues?

PREDICT 8

In carbon monoxide (CO) poisoning, CO binds to hemoglobin, thereby preventing the uptake of oxygen by hemoglobin. In addition, when CO binds to hemoglobin, the oxygen–hemoglobin dissociation curve shifts to the left. What are the consequences of this shift on the ability of tissues to get oxygen? Explain.

Effect of BPG

As red blood cells break down glucose for energy, they produce a substance called **2,3-bisphosphoglycerate (BPG;** formerly called diphosphoglycerate). BPG binds to hemoglobin and increases its ability to release oxygen. When BPG levels increase, hemoglobin releases more oxygen. When BPG levels decrease, hemoglobin releases less oxygen. For example, people living at high altitudes have increased levels of BPG, which increases oxygen delivery to tissues by causing hemoglobin to release more oxygen. On the other hand, when blood is removed from the body and stored in a blood bank, the BPG levels in the stored blood gradually decrease. As BPG levels decrease, the blood becomes unsuitable for transfusion purposes because the hemoglobin releases less oxygen to the tissues.

44. How does BPG affect the release of oxygen from hemoglobin?

PREDICT 9

If a person lacks the enzyme necessary for BPG synthesis, would she exhibit anemia (lower-than-normal number of red blood cells) or erythrocytosis (higher-than-normal number of red blood cells)? Explain.

Fetal Hemoglobin

As fetal blood circulates through the placenta, oxygen is released from the mother's blood into the fetal blood and carbon dioxide is released from fetal blood into the mother's blood. Fetal blood is very efficient at picking up oxygen for several reasons.

1. The concentration of fetal hemoglobin is approximately 50% greater than the concentration of maternal hemoglobin.
2. Fetal hemoglobin is different from maternal hemoglobin. It has an oxygen–hemoglobin dissociation curve that's to the left of the maternal oxygen–hemoglobin dissociation curve. Thus, for a given P_{O_2} fetal hemoglobin can hold more oxygen than maternal hemoglobin.
3. BPG has little effect on fetal hemoglobin. That is, BPG does not cause fetal hemoglobin to release oxygen.

4. The movement of carbon dioxide out of the fetal blood causes the fetal oxygen–hemoglobin dissociation curve to shift to the left. At the same time, the movement of carbon dioxide into the mother's blood causes the maternal oxygen–hemoglobin dissociation curve to shift to the right. Thus, the mother's blood releases more oxygen and the fetal blood picks up more oxygen. This is called the **double Bohr effect.**

45. How does the affinity for oxygen of fetal hemoglobin compare to maternal hemoglobin?
46. What is the double Bohr effect?

Transport of Carbon Dioxide

Carbon dioxide is transported in the blood in three major ways: approximately 7% is transported as carbon dioxide dissolved in the plasma, approximately 23% is transported in combination with blood proteins (mostly hemoglobin), and 70% is transported in the form of bicarbonate ions.

The most abundant protein to which carbon dioxide binds in the blood is hemoglobin. Carbon dioxide binds in a reversible fashion to the globin part of the hemoglobin molecule, and many carbon dioxide molecules can combine to a single hemoglobin molecule.

Hemoglobin that has released its oxygen binds more readily to carbon dioxide than hemoglobin that has oxygen bound to it. This is called the **Haldane effect.** In tissues, after hemoglobin has released oxygen, the hemoglobin has an increased ability to pick up carbon dioxide. In the lungs, as hemoglobin binds to oxygen, the hemoglobin more readily releases carbon dioxide.

Chloride Shift

Carbon dioxide from tissues diffuses into red blood cells within the capillaries (figure 23.20*a*). Some of the carbon dioxide binds to hemoglobin, but most of it reacts with water inside the red blood cells to form carbonic acid, a reaction catalyzed by carbonic anhydrase. The carbonic acid then dissociates to form bicarbonate and hydrogen ions. Thus, most of the carbon dioxide becomes part of a bicarbonate ion.

Lowering the amount of bicarbonate and hydrogen ions inside red blood cells promotes carbon dioxide transport, because as these reaction products are removed and their ion concentrations decrease, more carbon dioxide combines with water to form additional bicarbonate and hydrogen ions (see section on "Reversible Reactions" on p. 36). In a process called the **chloride shift** (see figure 23.20*a*), bicarbonate ion concentrations inside red blood cells are lowered by exchanging them for chloride ions (Cl^-). As bicarbonate ions are produced, carrier molecules in red blood cell membranes move bicarbonate ions out of the red blood cells and chloride ions into the red blood cells. The exchange of negatively charged ions maintains electrical balance in the red blood cells and the plasma. Hemoglobin, which binds hydrogen ions, decreases the concentration of hydrogen ions inside the red blood cells. Thus, hemoglobin functions as a buffer and resists an increase in pH within the red blood cells.

PREDICT 10

How is the ability of hemoglobin to release oxygen and pick up carbon dioxide in tissues affected by the change in the concentration of hydrogen ions inside red blood cells? Explain.

The reverse of the previous events occurs in the lungs (figure 23.20*b*). Carbon dioxide diffuses from the red blood cells into the alveoli. As carbon dioxide levels in the red blood cells decrease, carbonic acid is converted to carbon dioxide and water. In response, bicarbonate ions join with hydrogen ions to form carbonic acid. As the bicarbonate and hydrogen ions decrease because of this reaction, they are replaced. Bicarbonate ions enter the red blood cell in exchange for chloride ions, and hydrogen ions are released from hemoglobin.

Carbon Dioxide and Blood pH

Blood pH refers to the pH in plasma, not inside red blood cells. In plasma, carbon dioxide can combine with water to form carbonic acid, a reaction that is catalyzed by carbonic anhydrase on the surface of capillary endothelial cells. The carbonic acid then dissociates to form bicarbonate and hydrogen ions. Thus, as plasma carbon dioxide levels increase, hydrogen ion levels increase, and blood pH decreases. An important function of the respiratory system is to regulate blood pH by changing plasma carbon dioxide levels (see chapter 27). Hyperventilation decreases plasma carbon dioxide, and hypoventilation increases it.

47. List three ways that carbon dioxide is transported in the blood, and state the percentage of total carbon dioxide transport for which each is responsible.
48. What is the Haldane effect?
49. Where and why does the chloride shift take place?

PREDICT 11

What effect does hyperventilation and holding one's breath have on blood pH? Explain.

Rhythmic Ventilation

Objective

- ***Describe the brainstem structures that regulate respiration, and explain how rhythmic ventilation is produced.***

The generation of the basic rhythm of ventilation is controlled by neurons within the medulla oblongata that stimulate the muscles of respiration. Recruitment of muscle fibers and the increased frequency of stimulation of muscle fibers result in stronger contractions of the muscles and an increased depth of respiration. The rate of respiration is determined by how frequently the respiratory muscles are stimulated.

Respiratory Areas in the Brainstem

The classic view of respiratory areas held that distinct inspiratory and expiratory centers were located in the brainstem. This view is now known to be too simplistic. Although neurons involved with respiration are aggregated in certain parts of the brainstem, neurons that are active during inspiration are intermingled with neurons that are active during expiration. Modern imaging techniques, such as positron emission tomography (PET), also confirm that much of the historical work on animals doesn't apply to humans.

The **medullary respiratory center** consists of two **dorsal respiratory groups,** each forming a longitudinal column of cells located bilaterally in the dorsal part of the medulla oblongata, and

(a) In the tissue capillaries, carbon dioxide enters red blood cells and reacts with water to form carbonic acid, which dissociates to form bicarbonate and hydrogen ions. Bicarbonate ions are exchanged for chloride ions in the chloride shift. Hydrogen ions combine with hemoglobin. Lowering the concentration of bicarbonate and hydrogen ions inside red blood cells promotes the conversion of carbon dioxide to bicarbonate ions.

(b) In the pulmonary capillaries, carbon dioxide leaves red blood cells, resulting in the formation of additional carbon dioxide from carbonic acid. Bicarbonate and hydrogen ions combine to replace the carbonic acid. The bicarbonate ions are exchanged for chloride ions, and the hydrogen ions are released from hemoglobin.

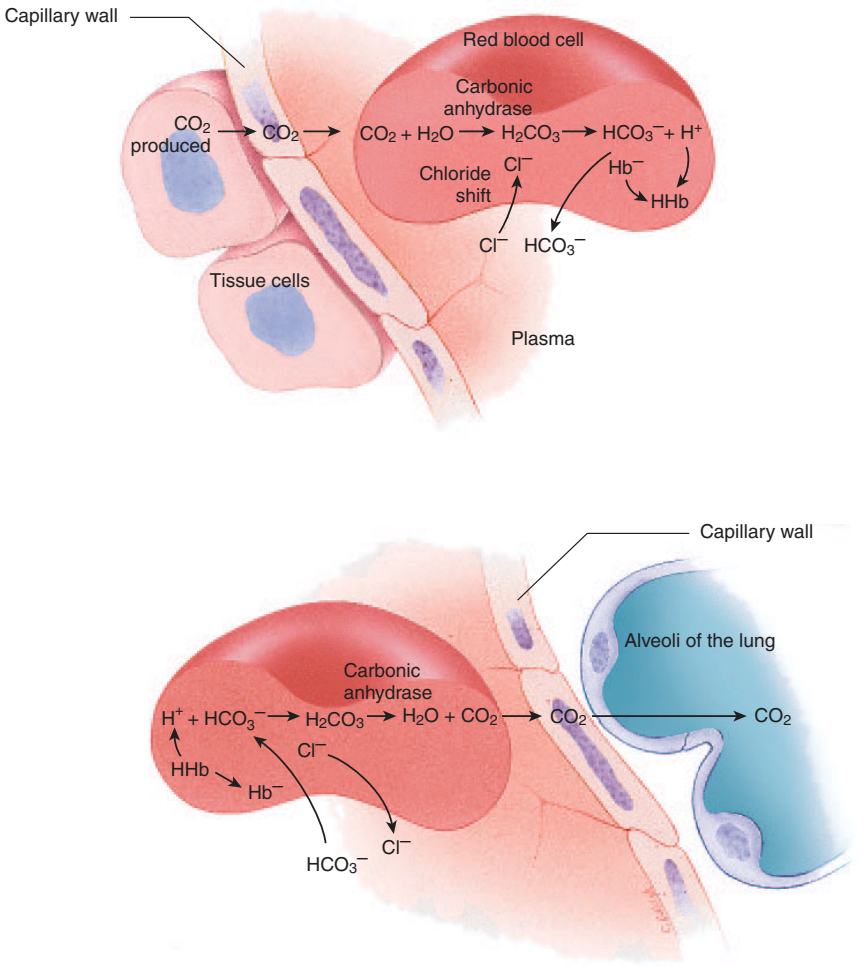


Figure 23.20 Carbon Dioxide Transport and Chloride Movement

two **ventral respiratory groups,** each forming a longitudinal column of cells located bilaterally in the ventral part of the medulla oblongata (figure 23.21). Although the dorsal and ventral respiratory groups are bilaterally paired, cross communication exists between the pairs so that respiratory movements are symmetric. In addition, communication exists between the dorsal and ventral respiratory groups.

Each dorsal respiratory group is a collection of neurons that are most active during inspiration, but some are active during expiration. The dorsal respiratory groups are primarily responsible for stimulating contraction of the diaphragm. They receive input from other parts of the brain and peripheral receptors that allows modification of respiration.

Each ventral respiratory group is a collection of neurons that are active during inspiration and expiration. These neurons primarily stimulate the external intercostal, internal intercostal, and abdominal muscles.

The **pontine respiratory group,** formerly called the pneumotaxic center, is a collection of neurons in the pons (see figure 23.21). Some of the neurons are only active during inspiration, some only during expiration, and some during both inspiration and expiration. The precise function of the pontine respiratory group is unknown, but it has connections with the medullary respiratory center and appears to play a role in switching between inspiration and expiration. It's not considered to be essential for the generation of the respiratory rhythm.

Generation of Rhythmic Ventilation

The exact locations of neurons in the medullary respiratory center responsible for rhythmic ventilation are unknown. Nor is it well understood how they generate the basic pattern of spontaneous, rhythmic ventilation at rest. One explanation involves integration of stimuli that start and stop inspiration.

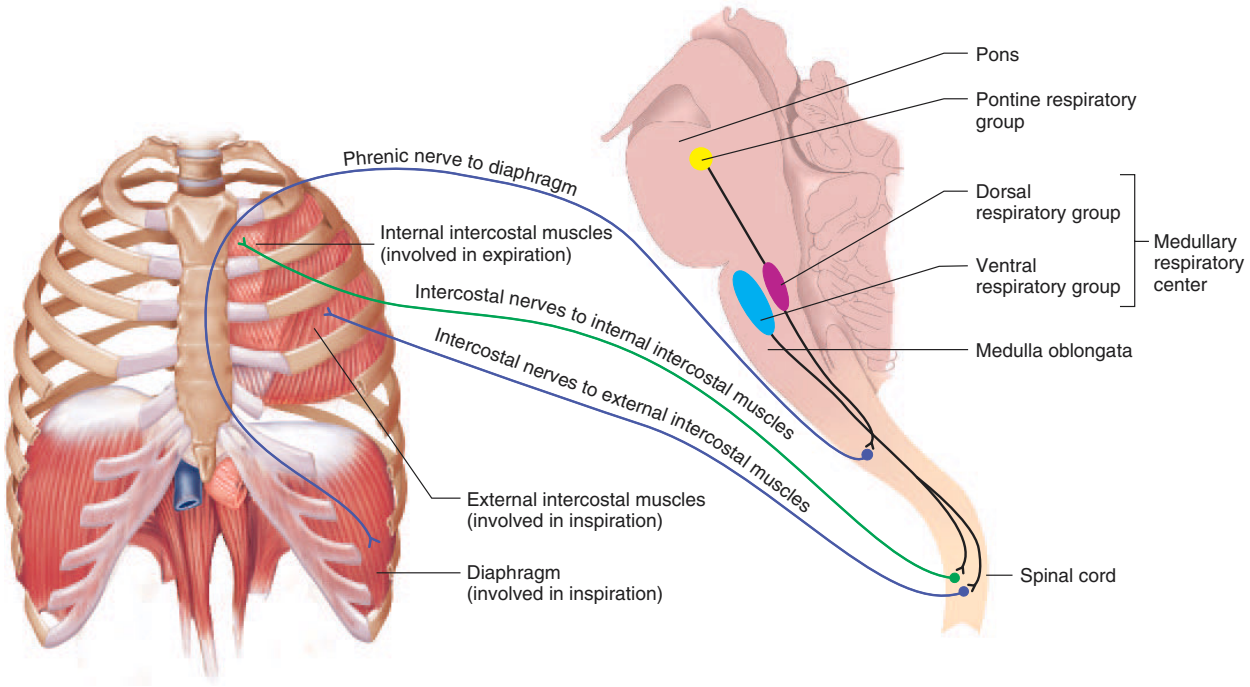


Figure 23.21 Respiratory Structures in the Brainstem

The relationship of respiratory structures to each other and to the nerves innervating the muscles of respiration.

1. *Starting inspiration.* Certain neurons in the medullary respiratory center that promote inspiration are continuously active. The medullary respiratory center constantly receives stimulation from receptors that monitor blood gas levels, blood temperature, and movements of muscles and joints. In addition, stimulation from parts of the brain concerned with voluntary respiratory movements and emotions can occur. Inspiration starts when the combined input from all these sources causes the production of action potentials in the neurons that stimulate respiratory muscles.
2. *Increasing inspiration.* Once inspiration begins, more and more neurons are gradually activated. The result is progressively stronger stimulation of the respiratory muscles that lasts for approximately 2 seconds.
3. *Stopping inspiration.* The neurons stimulating the muscles of respiration also stimulate other neurons in the medullary respiratory center that are responsible for stopping inspiration. The neurons responsible for stopping inspiration also receive input from the pontine respiratory group, stretch receptors in the lungs, and probably other sources. When these inhibitory neurons are activated, they cause the neurons stimulating respiratory muscles to be inhibited. Relaxation of respiratory muscles results in expiration, which lasts approximately 3 seconds. For the next inspiration, go back to step 1.

50. Name the three respiratory groups and describe their main functions.
51. How is rhythmic ventilation generated?

Modification of Ventilation

Objective

- ***Describe the different ways by which rhythmic ventilation can be altered.***

Although the medullary neurons establish the basic rate and depth of breathing, their activities can be influenced by input from other parts of the brain and by input from peripherally located receptors.

Cerebral and Limbic System Control

Through the cerebral cortex, it's possible to consciously or unconsciously increase or decrease the rate and depth of the respiratory movements (figure 23.22). For example, during talking or singing, air movement is controlled to produce sounds as well as to facilitate gas exchange.

Apnea (ap′nē-ă) is the absence of breathing. A person may stop breathing voluntarily. As the period of voluntary apnea increases, a greater and greater urge to breathe develops. That urge is primarily associated with increasing P_{CO_2} levels in the arterial

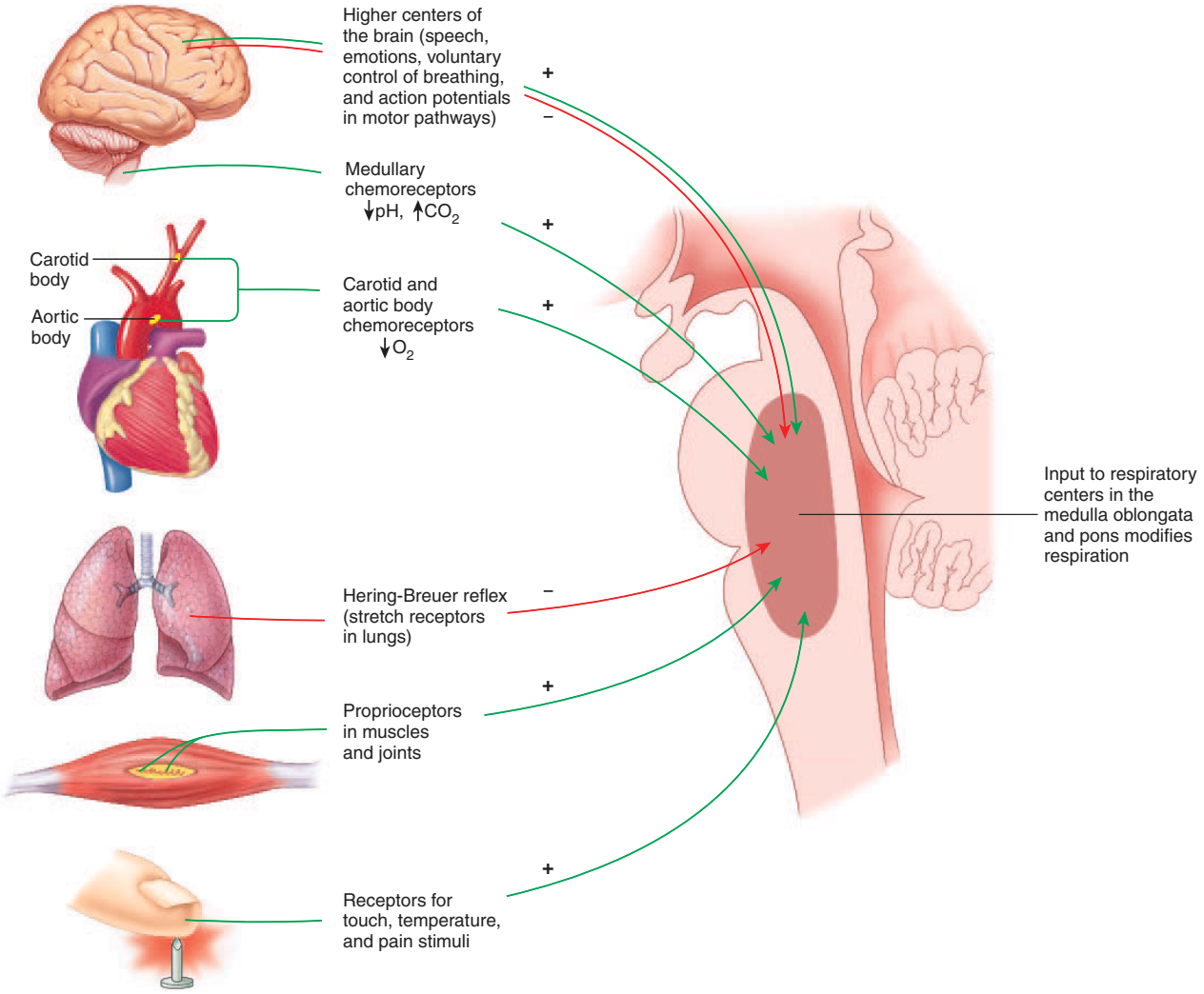


Figure 23.22 Modifying Respiration

Voluntary control; emotions; changes in blood pH, carbon dioxide, and oxygen levels; stretch of the lungs; movements of the limbs (proprioception); and stimuli such as touch, temperature, and pain can affect the respiratory center and modify respiration. A *plus sign (+)* indicates an increase in respiration, and a *minus (–) sign* indicates a decrease in respiration.

blood. Finally, the P_{CO_2} reaches levels that cause the respiratory center to override the conscious influence from the cerebrum. Occasionally, people are able to hold their breath until the blood P_{O_2} declines to a level low enough that they lose consciousness. After consciousness is lost, the respiratory center resumes its normal function in automatically controlling respiration.

Voluntary hyperventilation can decrease blood P_{CO_2} levels sufficiently to cause vasodilation of the peripheral blood vessels and a decrease in blood pressure (see chapter 21). Dizziness or a giddy feeling can result because of decreased delivery of oxygen to the brain caused by the decreased rate of blood flow to the brain after blood pressure drops.

Emotions acting through the limbic system of the brain can also affect the respiratory center (see figure 23.22). For example, strong emotions can cause hyperventilation or produce the sobs and gasps of crying.

Chemical Control of Ventilation

The respiratory system maintains blood oxygen and carbon dioxide concentrations and blood pH within a normal range of values. A deviation by any of these parameters from their normal range has a marked influence on respiratory movements. The effect of changes in oxygen and carbon dioxide concentrations and in pH is superimposed on the neural mechanisms that establish rhythmic ventilation.

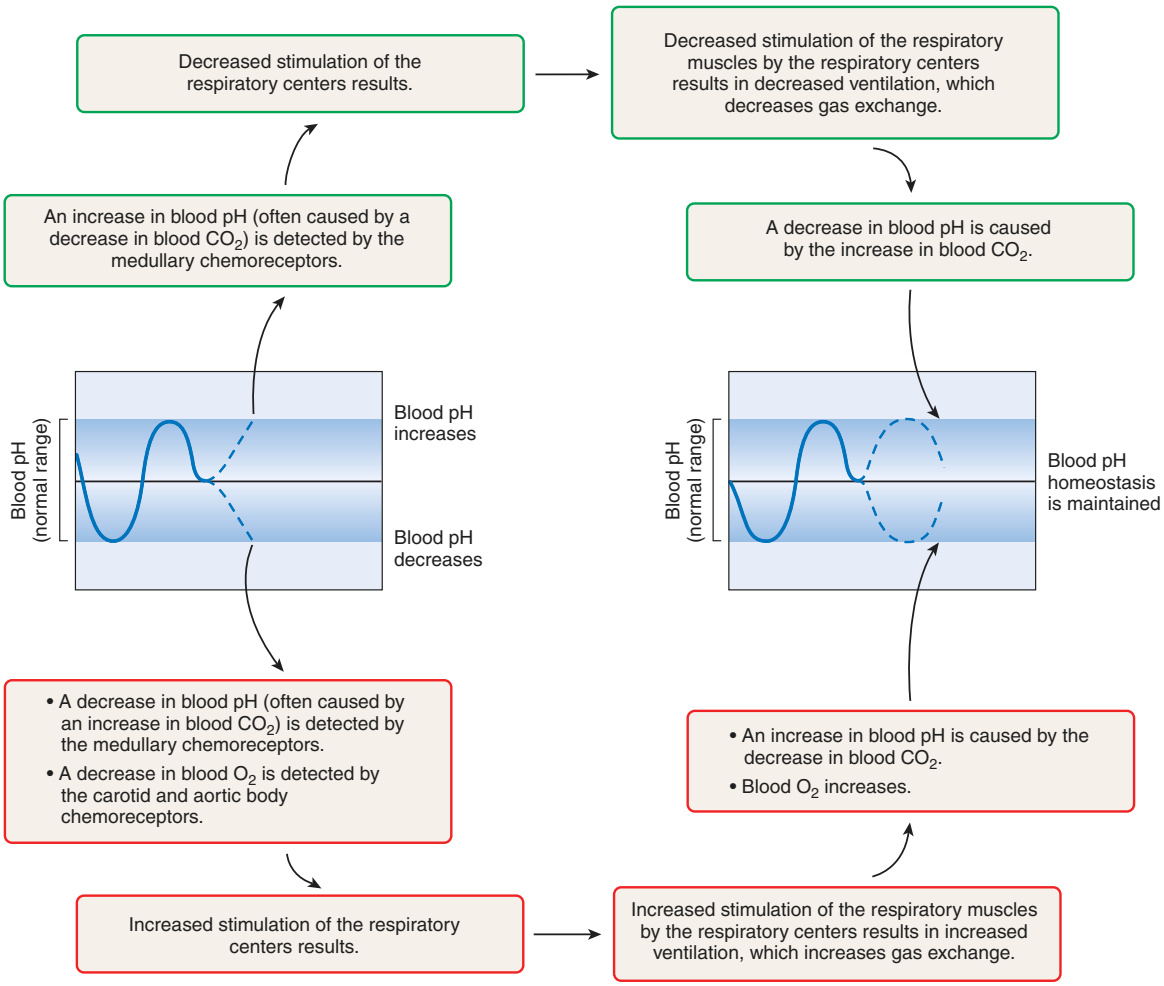
Chemoreceptors

Chemoreceptors are specialized neurons that respond to changes in chemicals in solution. The chemoreceptors involved with the regulation of respiration respond to changes in hydrogen ion concentrations or changes in P_{O_2} (or both) (see figures 23.22 and 23.23). **Central chemoreceptors** are located bilaterally and ventrally in the **chemosensitive area** of the medulla oblongata, and they are connected to the respiratory center. **Peripheral chemoreceptors** are found in the carotid and aortic bodies. These structures are small vascular sensory organs, which are encapsulated in connective tissue and located near the carotid sinuses and the aortic arch (see chapter 21). The respiratory center is connected to the carotid body chemoreceptors through the glossopharyngeal nerve (IX) and to the aortic body chemoreceptors by the vagus nerve (X).

Effect of pH

The chemosensitive area is bathed by cerebrospinal fluid and is sensitive to changes in the pH of the fluid. Because the blood–brain barrier separates the chemosensitive area from the blood, this area doesn't directly detect changes in blood pH. Changes in blood pH can alter cerebrospinal fluid pH, however, so the chemosensitive area responds indirectly to changes in blood pH. In addition, the carotid and aortic bodies have a rich vascular supply and are directly sensitive to changes in blood pH.

Maintaining body pH levels within normal parameters is necessary for the proper functioning of cells. Because changes in carbon dioxide levels can change pH, the respiratory system plays an important role in acid–base balance. For example, if blood pH decreases, the respiratory center is stimulated, resulting in elimination of carbon dioxide and an increase in blood pH back to normal



Homeostasis Figure 23.23 Regulation of Blood pH and Gases

levels. Conversely, if blood pH increases, the respiratory rate decreases, and carbon dioxide levels increase, causing blood pH to decrease back to normal levels. The role of the respiratory system in maintaining pH is considered in greater detail in chapter 27.

Effect of Carbon Dioxide

Blood carbon dioxide levels are a major regulator of respiration during resting conditions and conditions when the carbon dioxide levels are elevated, for example, during intense exercise. Even a small increase in carbon dioxide in the circulatory system triggers a large increase in the rate and depth of respiration. An increase in P_{CO_2} of 5 mm Hg, for example, causes an increase in ventilation of 100%. A greater-than-normal amount of carbon dioxide in the blood is called **hypercapnia** (hī-per-kap′nē-ă). Conversely, lower-than-normal carbon dioxide levels, a condition called **hypocapnia** (hī-pō-kap′nē-ă), result in periods in which respiratory movements are reduced or do not occur.

Carbon dioxide apparently doesn't directly affect the chemosensitive area. Instead, it exerts its effect by changing pH levels, which can affect the chemosensitive area (see figure 23.23). For example, if blood carbon dioxide levels increase, carbon dioxide diffuses across the blood–brain barrier into the cerebrospinal fluid. The carbon dioxide combines with water to form carbonic acid, which dissociates into hydrogen ions and bicarbonate ions. The increased concentration of hydrogen ions lowers the pH and stimulates the chemosensitive area, which then stimulates the respiratory center, resulting in a greater rate and depth of breathing. Consequently, carbon dioxide levels decrease as carbon dioxide is eliminated from the body.

P R E D I C T 12

Explain why a person who breathes rapidly and deeply (hyperventilates) for several seconds experiences a short period during which respiration does not occur (apnea) before normal breathing resumes.

The chemoreceptors in the carotid and aortic bodies also respond to changes in carbon dioxide because of the effects of carbon dioxide on blood pH. The carotid and aortic bodies, however, are responsible for, at most, 15%–20% of the total response to changes in P_{CO_2} or pH. The chemosensitive area in the medulla oblongata is far more important for the regulation of P_{CO_2} and pH than are the carotid and aortic bodies. During intense exercise, however, the carotid bodies respond more rapidly to changes in blood pH than does the chemosensitive area of the medulla.

Effect of Oxygen

Changes in P_{O_2} can affect respiration (see figure 23.23), although P_{CO_2} levels detected by the chemosensitive area are responsible for most changes in respiration. A decrease in oxygen levels below normal values is called **hypoxia** (hī-pok′sē-ă). If P_{O_2} levels in the arterial blood are markedly reduced while the pH and P_{CO_2} are held constant, an increase in ventilation occurs. Within a normal range of P_{O_2} levels, however, the effect of oxygen on the regulation of respiration is small. Only after arterial P_{O_2} decreases to approximately 50% of its normal value does it begin to have a large stimulatory effect on respiratory movements.

At first, it's somewhat surprising that small changes in P_{O_2} don't cause changes in respiratory rate. Consideration of the oxygen–hemoglobin dissociation curve, however, provides an explanation. Because of the S shape of the curve, at any P_{O_2} above 80 mm Hg nearly all of the hemoglobin is saturated with oxygen. Consequently, until P_{O_2} levels change significantly, the oxygen-carrying capacity of the blood is unaffected.

The carotid and aortic body chemoreceptors respond to decreased P_{O_2} by increased stimulation of the respiratory center, which can keep it active, despite decreasing oxygen levels. If P_{O_2} decreases sufficiently, however, the respiratory center can fail to function, resulting in death.

Importance of Reduced P_{O_2}

Carbon dioxide is much more important than oxygen as a regulator of normal alveolar ventilation, but under certain circumstances a reduced P_{O_2} in the arterial blood does play an important stimulatory role. During conditions of shock in which blood pressure is very low, the P_{O_2} in arterial blood can drop to levels sufficiently low to strongly stimulate carotid and aortic body sensory receptors. At high altitudes where barometric air pressure is low, the P_{O_2} in arterial blood can also drop to levels sufficiently low to stimulate carotid and aortic bodies. Although P_{O_2} levels in the blood are reduced, the ability of the respiratory system to eliminate carbon dioxide is not greatly affected by low barometric air pressure. Thus, blood carbon dioxide levels become lower than normal because of the increased alveolar ventilation initiated in response to low P_{O_2}.

A similar situation exists in people who have emphysema. Because carbon dioxide diffuses across the respiratory membrane more readily than oxygen, the decreased surface area of the respiratory membrane caused by the disease results in low arterial P_{O_2} without elevated arterial P_{CO_2}. The elevated rate and depth of respiration are due, to a large degree, to the stimulatory effect of low arterial P_{O_2} levels on carotid and aortic bodies. More severe emphysema, in which the surface area of the respiratory membrane is reduced to a minimum, can also result in elevated P_{CO_2} levels in arterial blood.

Hering-Breuer Reflex

The **Hering-Breuer** (her′ing-broy′er) **reflex** limits the degree to which inspiration proceeds and prevents overinflation of the lungs (see figure 23.22). This reflex depends on stretch receptors in the walls of the bronchi and bronchioles of the lung. Action potentials are initiated in these stretch receptors when the lungs are inflated and are passed along sensory neurons within the vagus nerves to the medulla oblongata. The action potentials have an inhibitory influence on the respiratory center and result in expiration. As expiration proceeds, the stretch receptors are no longer stimulated, and the decreased inhibitory effect on the respiratory center allows inspiration to begin again.

In infants, the Hering-Breuer reflex plays a role in regulating the basic rhythm of breathing and in preventing overinflation of the lungs. In adults, however, the reflex is important only when the tidal volume is large, such as during exercise.

Effect of Exercise on Ventilation

The mechanisms by which ventilation is regulated during exercise are controversial, and no one factor can account for all of the observed responses. Ventilation during exercise is divided into two phases.

1. *Ventilation increases abruptly.* At the onset of exercise, ventilation immediately increases. This initial increase can be as much as 50% of the total increase that occurs during exercise. The immediate increase in ventilation occurs too quickly to be explained by changes in metabolism or blood gases. As axons pass from the motor cortex of the cerebrum through the motor pathways, numerous collateral fibers project into the reticular formation of the brain. During exercise, action potentials in the motor pathways stimulate skeletal muscle contractions, and action potentials in the collateral fibers stimulate the respiratory center (see figure 23.22).

   Furthermore, during exercise, body movements stimulate proprioceptors in the joints of the limbs. Action potentials from the proprioceptors pass along sensory nerve fibers to the spinal cord and along ascending nerve tracts (the dorsal-column/medial-lemniscal system) of the spinal cord to the brain. Collateral fibers project from these ascending pathways to the respiratory center in the medulla oblongata. Movement of the limbs has a strong stimulatory influence on the respiratory center (see figure 23.22).

   A learned component may also exist to the ventilation response during exercise. After a period of training, the brain "learns" to match ventilation with the intensity of the exercise. Well-trained athletes match their respiratory movements more efficiently with their level of physical activity than do untrained individuals. Thus, centers of the brain involved in learning have an indirect influence on the respiratory center, but the exact mechanism for this kind of regulation is unclear.
2. *Ventilation increases gradually.* After the immediate increase in ventilation, a gradual increase occurs that levels off within 4–6 minutes after the onset of exercise. Factors responsible for the immediate increase in ventilation may play a role in the gradual increase as well.

   Despite large changes in oxygen consumption and carbon dioxide production during exercise, the *average* arterial P_{O_2}, P_{CO_2}, and pH remain constant and close to resting levels as long as the exercise is aerobic (see chapter 9). This suggests that changes in blood gases and pH do not play an important role in regulating ventilation during aerobic exercise. During exercise, however, the values of arterial P_{O_2}, P_{CO_2}, and pH rise and fall more than at rest. Thus, even though their average values don't change, their oscillations may be a signal for helping to control ventilation.

   The highest level of exercise that can be performed without causing a significant change in blood pH is called the **anaerobic threshold.** If the exercise intensity is high enough to exceed the anaerobic threshold, then skeletal muscles produce and release lactic acid into the blood. The resulting change in blood pH stimulates the carotid bodies, resulting in increased ventilation. In fact, ventilation can increase so much that arterial P_{CO_2} decreases below resting levels and arterial P_{O_2} increases above resting levels.

Other Modifications of Ventilation

The activation of touch, thermal, and pain receptors can also affect the respiratory center (see figure 23.22). For example, irritants in the nasal cavity can initiate a sneeze reflex, and irritants in the lungs can stimulate a cough reflex. An increase in body temperature can stimulate increased ventilation.

52. ***Describe cerebral and limbic system control of ventilation.***
53. ***Define central and peripheral chemoreceptors. Which are most important for the regulation of blood pH and carbon dioxide?***
54. ***Define hypercapnia and hypocapnia.***
55. ***What effect does a decrease in blood pH or carbon dioxide have on respiratory rate?***
56. ***Describe the Hering-Breuer reflex and its function.***
57. ***Define hypoxia. Why must arterial P_{O_2} change significantly before it affects respiratory rate?***
58. ***What mechanisms regulate ventilation at the onset of exercise and during exercise? What is the anaerobic threshold?***

P R E D I C T 13

Describe the respiratory response when cold water is splashed onto a person. In the past, newborn babies were sometimes swatted on the buttocks. Explain the rationale for this procedure.

Respiratory Adaptations to Exercise

Objective

- ***Describe respiratory adaptations that occur in response to training.***

In response to training, athletic performance increases because the cardiovascular and respiratory systems become more efficient at delivering oxygen and picking up carbon dioxide. Ventilation in most individuals does not limit performance because ventilation can increase to a greater extent than does cardiovascular function.

After training, vital capacity increases slightly and residual volume decreases slightly. Tidal volume at rest and during submaximal exercise does not change. At maximal exercise, however, tidal volume increases. After training, the respiratory rate at rest or during submaximal exercise is slightly lower than in an untrained person, but at maximal exercise respiratory rate is generally increased.

Minute ventilation is affected by the changes in tidal volume and respiratory rate. After training, minute ventilation is essentially unchanged or slightly reduced at rest and is slightly reduced during submaximal exercise. Minute ventilation is greatly increased at maximal exercise. For example, an untrained person with a minute ventilation of 120 L/min can increase to 150 L/min after training. Increases to 180 L/min are typical of highly trained athletes.

Gas exchange between the alveoli and blood increases at maximal exercise following training. The increased minute ventilation results in increased alveolar ventilation. In addition, increased cardiovascular efficiency results in greater blood flow through the lungs, especially in the superior parts of the lungs.

59. ***What effect does training have on resting, submaximal, and maximal tidal volumes and on minute ventilation?***

Clinical Focus Disorders of the Respiratory System

Bronchi and Lungs

Bronchitis (brong-kī′tis) is an inflammation of the bronchi caused by irritants, such as cigarette smoke, air pollution, or infections. The inflammation results in swelling of the mucous membrane lining the bronchi, increased mucus production, and decreased movement of mucus by cilia. Consequently, the diameter of the bronchi is decreased, and ventilation is impaired. Bronchitis can progress to emphysema.

Emphysema (em-fi-zē′mă) results in the destruction of the alveolar walls. Many smokers have both bronchitis and emphysema, which are often referred to as **chronic obstructive pulmonary disease (COPD).** Chronic inflammation of the bronchioles, usually caused by cigarette smoke or air pollution, probably initiates emphysema. Narrowing of the bronchioles restricts air movement, and air tends to be retained in the lungs. Coughing to remove accumulated mucus increases pressure in the alveoli, resulting in rupture and destruction of alveolar walls. Loss of alveolar walls has two important consequences. The respiratory membrane has a decreased surface area, which decreases gas exchange, and loss of elastic fibers decreases the ability of the lungs to recoil and expel air. Symptoms of emphysema include shortness of breath and enlargement of the thoracic cavity. Treatment involves removing sources of irritants (e.g., stopping smoking), promoting the removal of bronchial secretions, using bronchiodilators, retraining people to breathe so that expiration of air is maximized, and using antibiotics to prevent infections. The progress of emphysema can be slowed, but no cure exists.

Cystic fibrosis is an inherited disease that affects the secretory cells lining the lungs, pancreas, sweat glands, and salivary glands. The defect produces an abnormal chloride transport protein that doesn't reach the cell surface or doesn't function normally if it does reach the cell surface. The result is decreased chloride ion secretion out of cells and increased sodium ion movement into cells. Normally, the presence of chloride and sodium ions outside of the cells causes water to move to the outside by osmosis. In the lungs, the water forms a thin fluid layer over which mucus is moved by ciliated cells. In cystic fibrosis, the decreased chloride and sodium ions outside the cells results in dehydrated respiratory secretions. The mucus is more viscous, resisting movement by cilia, and it accumulates in the lungs. For reasons not completely understood, the mucus accumulation increases the likelihood of infections. Chronic airflow obstruction causes difficulty in breathing, and coughing in an attempt to remove the mucus can result in pneumothorax and bleeding within the lungs. Once fatal during early childhood, many victims of cystic fibrosis are now surviving into young adulthood. Future treatments could include the development of drugs that correct or assist the normal ion transport mechanism. Alternatively, cystic fibrosis may someday be cured through genetic engineering by inserting a functional copy of the defective gene into a person with the disease. Research on this exciting possibility is currently underway.

Pulmonary fibrosis is the replacement of lung tissue with fibrous connective tissue, thereby making the lungs less elastic and breathing more difficult. Exposure to asbestos, silica (silicosis), or coal dust is the most common cause.

Lung, or **bronchiogenic, cancer** arises from the epithelium of the respiratory tract. Cancers arising from tissues other than respiratory epithelium are not called lung cancer, even though they occur in the lungs. Lung cancer is the most common cause of cancer death in males and females in the United States, and almost all cases occur in smokers. Because of the rich lymph and blood supply in the lungs, cancer in the lung can readily spread to other parts of the lung or body. In addition, the disease is often advanced before symptoms become severe enough for the victim to seek medical aid. Typical symptoms include coughing, sputum production, and blockage of the airways. Treatments include removal of part or all of the lung, chemotherapy, and radiation.

Nervous System

Sudden infant death syndrome (SIDS), or crib death, is the most frequent cause of death of infants between 2 weeks and 1 year of age. Death results when the infant stops breathing during sleep. Although the cause of SIDS remains controversial, evidence exists that damage to the respiratory center during development is a factor. No treatment has yet been found, but at-risk babies can be placed on a monitor that sounds an alarm if the baby stops breathing.

Paralysis of the respiratory muscles can result from damage of the spinal cord in the cervical or thoracic regions. The damage interrupts nerve tracts that transmit action potentials to the muscles of respiration. Transection of the spinal cord can result from trauma,

Effects of Aging on the Respiratory System

Objective

- ***Describe the effects of aging on the respiratory system.***

Almost all aspects of the respiratory system are affected by aging. Even though vital capacity, maximum ventilation rates, and gas exchange decrease with age, the elderly can engage in light to moderate exercise because the respiratory system has a large reserve capacity.

Vital capacity decreases with age because of a decreased ability to fill the lungs (decreased inspiratory reserve volume) and a decreased ability to empty the lungs (decreased expiratory reserve volume). As a result, maximum minute ventilation rates decrease, which in turn decreases the ability to perform intense exercise. These changes are related to weakening of respiratory muscles and to decreased compliance of the thoracic cage caused by stiffening of cartilage and ribs. Lung compliance actually increases with age, but this effect is offset by the decreased thoracic cage compliance. Lung compliance decreases because alveoli become shallower with age, which

such as automobile accidents or diving into water that is too shallow. Another cause of paralysis is poliomyelitis, a viral infection that damages neurons of the respiratory center or motor neurons that stimulate the muscles of respiration. Anesthetics or central nervous system depressants can also depress the function of the respiratory center if they are taken or administered in large enough doses.

Diseases of the Upper Respiratory Tract

Strep throat is caused by a streptococcal bacteria *(Streptococcus pyogenes)* and is characterized by inflammation of the pharynx and by fever. Frequently, inflammation of the tonsils and middle ear is involved. Without a throat analysis, the infection cannot be distinguished from viral causes of pharyngeal inflammation. Current techniques allow rapid diagnosis within minutes to hours, and antibiotics are an effective treatment.

Diphtheria (dif-thē′rē-ă) was once a major cause of death among children. It is caused by a bacterium *(Corynebacterium diphtheriae)*. A grayish membrane forms in the throat and can block the respiratory passages totally. A vaccine against diphtheria is part of the normal immunization program for children in the United States.

The **common cold** is the result of a viral infection. Symptoms include sneezing, excessive nasal secretions, and congestion. The infection can easily spread to sinus cavities, lower respiratory passages, and the middle ear. Laryngitis and middle ear infections are common complications. The common cold usually runs its course to recovery in about 1 week.

Diseases of the Lower Respiratory Tract

Laryngitis (lar-in-jī′tis) is an inflammation of the larynx, especially the vocal folds, and **bronchitis** is an inflammation of the bronchi. Bacterial or viral infections can move from the upper respiratory tract to cause laryngitis or bronchitis. Bronchitis is also often caused by continually breathing air containing harmful chemicals, such as those found in cigarette smoke.

Whooping cough (pertussis; per-tŭs′is) is a bacterial infection *(Bordetella pertussis)* that causes a loss of cilia of the respiratory epithelium. Mucus accumulates, and the infected person attempts to cough up the mucous accumulations. The coughing can be severe. A vaccine for whooping cough is part of the normal vaccination procedure for children in the United States.

Tuberculosis (tū-ber′kyū-lō′sis) is caused by a tuberculosis bacterium *(Mycobacterium tuberculosis)*. In the lung, the bacteria form lesions called tubercles. The small lumps contain degenerating macrophages and tuberculosis bacteria. An immune reaction is directed against the tubercles, which causes the formation of larger lesions and inflammation. The tubercles can rupture and release bacteria that infect other parts of the lung or body. Recently, a strain of the tuberculosis bacteria has developed that is resistant to treatment, and this strain is increasing concern that tuberculosis will again become a widespread infectious disease.

Pneumonia (noo-mō′nē-ă) is a general term that refers to many infections of the lung. Most pneumonias are caused by bacteria, but some result from viral, fungal, or protozoan infections. Symptoms include fever, difficulty in breathing, and chest pain. Inflammation of the lungs results in the accumulation of fluid within alveoli (pulmonary edema) and poor inflation of the lungs with air. A fungal infection *(Pneumocystis carinii)* that results in pneumocystosis pneumonia is rare, except in persons who have a compromised immune system. This type of pneumonia has become one of the infections commonly suffered by persons who have AIDS.

Flu (influenza) is a viral infection of the respiratory system and does not affect the digestive system as is commonly assumed. Flu is characterized by chills, fever, headache, and muscular aches, in addition to coldlike symptoms. Several strains of flu viruses have been identified. The mortality rate from flu is approximately 1%, and most of those deaths occur among the very old and very young. During a flu epidemic, the infection rate is so rapid and the disease so widespread that the total number of deaths is substantial, even though the percentage of deaths is relatively low. Flu vaccines can provide some protection against the flu.

A number of fungal diseases, such as **histoplasmosis** (his′tō-plaz-mō′sis) and **coccidioidomycosis** (kok-sid-ē-oy′dō-mī-kō′sis), affect the respiratory system. The fungal spores *(Histoplasma capsulatum; Coccidioides immitis)* usually enter the respiratory system through dust particles. Spores in soil and feces of certain animals make the rate of infection higher in farm workers and in gardeners. The infections usually result in minor respiratory infections, but in some cases they can cause infections throughout the body.

reduces the surface tension of the water lining the alveoli. There are no significant age-related changes in lung elastic fibers or surfactant.

Residual volume increases with age as the alveolar ducts and many of the larger bronchioles increase in diameter. This increases the dead space, which decreases the amount of air available for gas exchange (alveolar ventilation). In addition, gas exchange across the respiratory membrane is reduced because parts of the alveolar walls are lost, which decreases the surface area available for gas exchange, and the remaining walls thicken, which decreases diffusion of gases. A gradual increase in resting tidal volume with age compensates for these changes.

With age, mucus accumulates within the respiratory passageways. The mucus-cilia escalator is less able to move the mucus because it becomes more viscous and because the number of cilia and their rate of movement decrease. As a consequence, the elderly are more susceptible to respiratory infections and bronchitis.

60. ***Why do vital capacity, alveolar ventilation, and diffusion of gases across the respiratory membrane decrease with age?***
61. ***Why are the elderly more likely to develop respiratory infections and bronchitis?***

Systems Pathology

Asthma

Mr. W is an 18-year-old track athlete in seemingly good health. One day he came down with a common cold, resulting in the typical symptoms of nasal congestion and discomfort. After several days, he began to cough and wheeze, and he thought that his cold had progressed to his lungs. Determined not to get "out of shape" because of his cold, Mr. W took a few aspirins to relieve his discomfort and went to the track to jog. After a few minutes of exercise, he began to wheeze very forcefully and rapidly, and he felt that he could hardly get enough air. Even though he stopped jogging, his condition did not improve (figure A). Fortunately, a concerned friend who was also at the track took him to the emergency room.

Although Mr. W had no previous history of asthma, careful evaluation by the emergency room doctor convinced her that he probably was having an asthma attack. Mr. W inhaled a bronchiodilator drug, which resulted in rapid improvement in his condition. He was released from the emergency room and referred to his personal physician for further treatment and education about asthma.

Figure A Jogger with Asthma

Background Information

Asthma (az′mă) is a disease characterized by increased constriction of the trachea and bronchi in response to various stimuli, resulting in a narrowing of the air passageways and decreased ventilation efficiency. Symptoms include wheezing, coughing, and shortness of breath. In contrast to many other respiratory disorders, however, the symptoms of asthma typically reverse either spontaneously or with therapy.

It's estimated that the prevalence of asthma in the United States is from 3%–6% of the general population. Approximately half the cases first appear before age 10, and twice as many boys as girls develop asthma. Anywhere from 25%–50% of childhood asthmatics are symptom-free from adolescence onward.

The exact cause or causes of asthma are unknown, but asthma and allergies run strongly in some families. No definitive pathologic feature or diagnostic test for asthma has been discovered, but three important features of the disease are chronic airway inflammation, airway hyperreactivity, and airflow obstruction. The inflammatory response results in tissue damage, edema, and mucous buildup, which can block airflow through the bronchi. Airway hyperreactivity is greatly increased contraction of the smooth muscle in the trachea and bronchi in response to a stimulus. As a result of airway hyperactivity, the diameter of the airway decreases, and resistance to airflow increases. The effects of inflammation and airway hyperreactivity combine to cause airflow obstruction.

Many cases of asthma appear to be associated with a chronic inflammatory response by the immune system. The number of immune cells in the bronchi increases, including mast cells, eosinophils, neutrophils, macrophages, and lymphocytes. These cells release chemical mediators, such as interleukins, leukotrienes, prostaglandins, platelet-activating factor, thromboxanes, and chemotactic factors. These chemical mediators promote inflammation, increase mucous secretion, and attract additional immune cells to the bronchi, resulting in chronic airway inflammation. Airway hyperreactivity and inflammation appear to be linked by some of the chemical mediators, which increase the sensitivity of the airway to stimulation and cause smooth muscle contraction.

S U M M A R Y

Respiration includes the movement of air into and out of the lungs, the exchange of gases between the air and the blood, the transport of gases in the blood, and the exchange of gases between the blood and tissues.

Functions of the Respiratory System (p. 814)

Major functions associated with the respiratory system include gas exchange, regulation of blood pH, voice production, olfaction, and protection against some microorganisms.

System Interactions

System	Effect of Asthma on Other Systems
Integumentary	Cyanosis, a bluish skin color, results from a decreased blood oxygen content.
Muscular	Skeletal muscles are necessary for respiratory movements and the cough reflex. Increased muscular work during a severe asthma attack can cause metabolic acidosis because of anaerobic respiration and excessive lactic acid production.
Skeletal	Red bone marrow is the site of production of many of the immune cells responsible for the inflammatory response of asthma. The thoracic cage is necessary for respiration.
Nervous	Emotional upset or stress can evoke an asthma attack. Peripheral and central chemoreceptor reflexes affect ventilation. The cough reflex helps to remove mucus from respiratory passages. Pain, anxiety, and death from asphyxiation can result from the altered gas exchange caused by asthma. One theory of the cause of asthma is an imbalance in the autonomic nervous system (ANS) control of bronchiolar smooth muscle, and drugs that enhance sympathetic effects or block parasympathetic effects are used in asthma treatment.
Endocrine	Steroids from the adrenal gland play a role in regulating inflammation, and they are used in asthma therapy.
Cardiovascular	Increased vascular permeability of lung blood vessels results in edema. Blood carries ingested substances that provoke an asthma attack to the lungs. Blood carries immune cells from the red bone marrow to the lungs. Tachycardia commonly occurs, and the normal effects of respiration on venous return of blood to the heart are exaggerated, resulting in large fluctuations in blood pressure.
Lymphatic and immune	Immune cells release chemical mediators that promote inflammation, increase mucous production, and cause bronchiolar constriction (believed to be a major factor in asthma). Ingested allergens, such as aspirin or sulfites in food, can evoke an asthma attack.
Digestive	Reflux of stomach acid into the esophagus can evoke an asthma attack.
Urinary	Modifying hydrogen ion secretion into the urine helps to compensate for acid–base imbalances caused by asthma.

The stimuli that prompt airflow obstruction vary from one individual to another. Some asthmatics have reactions to particular allergens, which are foreign substances that evoke an inappropriate immune system response (see chapter 22). Examples include inhaled pollen, animal dander, and dust mites. Many cases of asthma may be caused by an allergic reaction to substances in the droppings and carcasses of cockroaches, which may explain the higher rate of asthma in poor, urban areas.

On the other hand, inhaled substances, such as chemicals in the workplace or cigarette smoke, can provoke an asthma attack without stimulating an allergic reaction. Over 200 substances have been associated with occupational asthma. An asthma attack can also be stimulated by ingested substances like aspirin, nonsteroidal anti-inflammatory compounds like ibuprofen (i-boo′prō-fen), sulfites in food preservatives, and tartrazine (tar′trā-zēn) in food colorings. Asthmatics can substitute acetaminophen (as-et-ă-mē′nō-fen; Tylenol) for aspirin.

Other stimuli, such as strenuous exercise, especially in cold weather, can precipitate an asthma attack. Such episodes can often be avoided by using a bronchiodilator drug prior to exercise. Viral infections, emotional upset, stress, and even reflux of stomach acid into the esophagus are known to elicit an asthma attack.

Treatment of asthma involves avoiding the causative stimulus and administering drug therapy. Steroids and mast cell–stabilizing agents, which prevent the release of chemical mediators from mast cells, are used to reduce airway inflammation. Theophylline (thē-of′i-lēn, thē-of′i-lin) and β-adrenergic agents (see chapter 16) are commonly used to cause bronchiolar dilation. Although treatment is generally effective in controlling asthma, in rare cases death by asphyxiation may occur. Earlier and more intensive therapy will in most cases prevent death by asphyxiation.

P R E D I C T 14

It is not usually necessary to assess arterial blood gases in the diagnosis and treatment of asthma. This information, however, can sometimes be useful in cases of severe asthma attacks. Suppose that Mr. W had a Po_2 of 60 mm Hg and a Pco_2 of 30 mm Hg when he first came to the emergency room. Explain how that could happen.

Anatomy and Histology of the Respiratory System (p. 814)

Nose

1. The nose consists of the external nose and the nasal cavity.
2. The bridge of the nose is bone, and most of the external nose is cartilage.
3. Openings of the nasal cavity
   - The nares open to the outside, and the choane lead to the pharynx.
   - The paranasal sinuses and the nasolacrimal duct open into the nasal cavity.
4. Parts of the nasal cavity
   - The nasal cavity is divided by the nasal septum.
   - The anterior vestibule contains hairs that trap debris.
   - The nasal cavity is lined with pseudostratified ciliated columnar epithelium that traps debris and moves it to the pharynx.
   - The superior part of the nasal cavity contains the olfactory epithelium.

Pharynx

1. The nasopharynx joins the nasal cavity through the internal nares and contains the openings to the auditory tube and the pharyngeal tonsils.
2. The oropharynx joins the oral cavity and contains the palatine and lingual tonsils.
3. The laryngopharynx opens into the larynx and the esophagus.

Larynx

1. Cartilage
   - Three unpaired cartilages exist. The thyroid cartilage and cricoid cartilage form most of the larynx. The epiglottis covers the opening of the larynx during swallowing.
   - Six paired cartilages exist. The vocal folds attach to the arytenoid cartilages.
2. Sounds are produced as the vocal folds vibrate when air passes through the larynx. Tightening the folds produces sounds of different pitches by controlling the length of the fold, which is allowed to vibrate.

Trachea

The trachea connects the larynx to the primary bronchi.

Tracheobronchial Tree

1. The conducting zone, from the trachea to the terminal bronchioles, is a passageway for air movement.
   - The area from the trachea to the terminal bronchioles is ciliated to facilitate removal of debris.
   - Cartilage helps to hold the tube system open (from the trachea to the bronchioles).
   - Smooth muscle controls the diameter of the tubes (terminal bronchioles).
2. The respiratory zone, from the respiratory bronchioles to the alveoli, is a site of gas exchange.
3. The components of the respiratory membrane include a film of water, the walls of the alveolus and the capillary, and an interstitial space.

Lungs

1. The body contains two lungs.
2. The lungs are divided into lobes, bronchopulmonary segments, and lobules.

Thoracic Wall and Muscles of Respiration

1. The thoracic wall consists of vertebrae, ribs, sternum, and muscles that allow expansion of the thoracic cavity.
2. Contraction of the diaphragm increases thoracic volume.
3. Muscles can elevate the ribs and increase thoracic volume or can depress the ribs and decrease thoracic volume.

Pleura

The pleural membranes surround the lungs and provide protection against friction.

Blood Supply

1. Deoxygenated blood is transported to the lungs through the pulmonary arteries, and oxygenated blood leaves through the pulmonary veins.
2. Oxygenated blood is mixed with a small amount of deoxygenated blood from the bronchi.

Lymphatic Supply

The superficial and deep lymphatic vessels drain lymph from the lungs.

Ventilation (p. 828)

Pressure Differences and Airflow

1. Ventilation is the movement of air into and out of the lungs.
2. Air moves from an area of higher pressure to an area of lower pressure.

Pressure and Volume

Pressure is inversely related to volume.

Airflow into and out of Alveoli

1. Inspiration results when barometric air pressure is greater than alveolar pressure.
2. Expiration results when barometric air pressure is less than alveolar pressure.

Changing Alveolar Volume

1. Lung recoil causes alveoli to collapse.
   - Lung recoil results from elastic fibers and water surface tension.
   - Surfactant reduces water surface tension.
2. Pleural pressure is the pressure in the pleural cavity.
   - A negative pleural pressure can cause the alveoli to expand.
   - Pneumothorax is an opening between the pleural cavity and the air that causes a loss of pleural pressure.
3. Changes in thoracic volume cause changes in pleural pressure, resulting in changes in alveolar volume, alveolar pressure, and airflow.

Measuring Lung Function (p. 833)

Compliance of the Lungs and the Thorax

1. Compliance is a measure of lung expansion caused by alveolar pressure.
2. Reduced compliance means that it's more difficult than normal to expand the lungs.

Pulmonary Volumes and Capacities

1. Four pulmonary volumes exist: tidal volume, inspiratory reserve volume, expiratory reserve volume, and residual volume.
2. Pulmonary capacities are the sum of two or more pulmonary volumes and include inspiratory capacity, functional residual capacity, vital capacity, and total lung capacity.
3. The forced expiratory vital capacity measures vital capacity as the individual exhales as rapidly as possible.

Minute Ventilation and Alveolar Ventilation

1. The minute ventilation is the total amount of air moved in and out of the respiratory system per minute.
2. Dead space is the part of the respiratory system in which gas exchange does not take place.
3. Alveolar ventilation is how much air per minute enters the parts of the respiratory system in which gas exchange takes place.

Physical Principles of Gas Exchange (p. 835)

Partial Pressure

1. Partial pressure is the contribution of a gas to the total pressure of a mixture of gases (Dalton's law).
2. Water vapor pressure is the partial pressure produced by water.
3. Atmospheric air, alveolar air, and expired air have different compositions.

Diffusion of Gases Through Liquids

The concentration of a gas in a liquid is determined by its partial pressure and by its solubility coefficient (Henry's law).

Diffusion of Gases Through the Respiratory Membrane

1. The respiratory membrane is thin and has a large surface area that facilitates gas exchange.
2. The rate of diffusion of gases through the respiratory membrane depends on its thickness, the diffusion coefficient of the gas, the surface area of the membrane, and the partial pressure of the gases in the alveoli and the blood.

Relationship Between Ventilation and Pulmonary Capillary Blood Flow

1. Increased ventilation or increased pulmonary capillary blood flow increases gas exchange.
2. The physiologic shunt is the deoxygenated blood returning from the lungs.

Oxygen and Carbon Dioxide Transport in the Blood (p. 838)

Oxygen Diffusion Gradients

1. Oxygen moves from the alveoli (P_{O_2} = 104 mm Hg) into the blood (P_{O_2} = 40 mm Hg). Blood is almost completely saturated with oxygen when it leaves the capillary.
2. The P_{O_2} in the blood decreases (P_{O_2} = 95 mm Hg) because of mixing with deoxygenated blood.
3. Oxygen moves from the tissue capillaries (P_{O_2} = 95 mm Hg) into the tissues (P_{O_2} = 40 mm Hg).

Carbon Dioxide Diffusion Gradients

1. Carbon dioxide moves from the tissues (P_{CO_2} = 45 mm Hg) into tissue capillaries (P_{CO_2} = 40 mm Hg).
2. Carbon dioxide moves from the pulmonary capillaries (P_{CO_2} = 45 mm Hg) into the alveoli (P_{CO_2} = 40 mm Hg).

Hemoglobin and Oxygen Transport

1. Oxygen is transported by hemoglobin (98.5%) and is dissolved in plasma (1.5%).
2. The oxygen–hemoglobin dissociation curve shows that hemoglobin is almost completely saturated when P_{O_2} is 80 mm Hg or above. At lower partial pressures, the hemoglobin releases oxygen.
3. A shift of the oxygen–hemoglobin dissociation curve to the right because of a decrease in pH (Bohr effect), an increase in carbon dioxide, or an increase in temperature results in a decrease in the ability of hemoglobin to hold oxygen.
4. A shift of the oxygen–hemoglobin dissociation curve to the left because of an increase in pH (Bohr effect), a decrease in carbon dioxide, or a decrease in temperature results in an increase in the ability of hemoglobin to hold oxygen.
5. The substance 2,3-bisphosphoglycerate increases the ability of hemoglobin to release oxygen.
6. Fetal hemoglobin has a higher affinity for oxygen than does maternal hemoglobin.

Transport of Carbon Dioxide

1. Carbon dioxide is transported as bicarbonate ions (70%), in combination with blood proteins (23%), and in solution in plasma (7%).
2. Hemoglobin that has released oxygen binds more readily to carbon dioxide than hemoglobin that has oxygen bound to it (Haldane effect).
3. In tissue capillaries, carbon dioxide combines with water inside the red blood cells to form carbonic acid, which dissociates to form bicarbonate ions and hydrogen ions.
4. The chloride shift is the movement of chloride ions into red blood cells as bicarbonate ions move out.
5. In lung capillaries, bicarbonate ions and hydrogen ions move into red blood cells, and chloride ions move out. Bicarbonate ions combine with hydrogen ions to form carbonic acid. The carbonic acid is converted to carbon dioxide and water. The carbon dioxide diffuses out of the red blood cells.
6. Increased plasma carbon dioxide lowers blood pH. The respiratory system regulates blood pH by regulating plasma carbon dioxide levels.

Rhythmic Ventilation (p. 843)

Respiratory Areas in the Brainstem

1. The medullary respiratory center consists of the dorsal and ventral respiratory groups.
   - The dorsal respiratory groups stimulate the diaphragm.
   - The ventral respiratory groups stimulate the intercostal and abdominal muscles.
2. The pontine respiratory group is involved with switching between inspiration and expiration.

Generation of Rhythmic Ventilation

1. When stimuli from receptors or other parts of the brain exceed a threshold level, inspiration begins.
2. At the same time that respiratory muscles are stimulated, neurons that stop inspiration are stimulated. When the stimulation of these neurons exceeds a threshold level, inspiration is inhibited.

Modification of Ventilation (p. 845)

Cerebral and Limbic System Control

Respiration can be voluntarily controlled and can be modified by emotions.

Chemical Control of Ventilation

1. Carbon dioxide is the major regulator of respiration. An increase in carbon dioxide or a decrease in pH can stimulate the chemosensitive area, causing a greater rate and depth of respiration.
2. Oxygen levels in the blood affect respiration when a 50% or greater decrease from normal levels exists. Decreased oxygen is detected by receptors in the carotid and aortic bodies, which then stimulate the respiratory center.

Hering-Breuer Reflex

Stretch of the lungs during inspiration can inhibit the respiratory center and contribute to a cessation of inspiration.

Effect of Exercise on Ventilation

1. Collateral fibers from motor neurons and from proprioceptors stimulate the respiratory centers.
2. Chemosensitive mechanisms and learning fine-tune the effects produced through the motor neurons and proprioceptors.

Other Modifications of Ventilation

Touch, thermal, and pain sensations can modify ventilation.

Respiratory Adaptations to Exercise (p. 849)

Tidal volume, respiratory rate, minute ventilation, and gas exchange between the alveoli and blood remain unchanged or slightly lower at rest or during submaximal exercise but increase at maximal exercise.

Effects of Aging on the Respiratory System (p. 850)

1. Vital capacity and maximum minute ventilation decrease with age because of weakening of respiratory muscles and decreased thoracic cage compliance.
2. Residual volume and dead space increase because of increased diameter of respiratory passageways. As a result, alveolar ventilation decreases.
3. An increase in resting tidal volume compensates for decreased alveolar ventilation, loss of alveolar walls (surface area), and thickening of alveolar walls.
4. The ability to remove mucus from the respiratory passageways decreases with age.

REVIEW AND COMPREHENSION

1. The nasal cavity
   a. has openings for the paranasal sinuses.
   b. has a vestibule, which contains the olfactory epithelium.
   c. is connected to the pharynx by the nares.
   d. has passageways called conchae.
   e. is lined with squamous epithelium, except for the vestibule.
2. The nasopharynx
   a. is lined with moist stratified squamous epithelium.
   b. contains the pharyngeal tonsil.
   c. opens into the oral cavity through the fauces.
   d. extends to the tip of the epiglottis.
   e. is an area that food, drink, and air pass through.
3. The larynx
   a. connects the oropharynx to the trachea.
   b. has three unpaired and six paired cartilages.
   c. contains the vocal folds.
   d. contains the vestibular folds.
   e. all of the above.
4. The trachea contains
   a. skeletal muscle.
   b. pleural fluid glands.
   c. C-shaped pieces of cartilage.
   d. all of the above.
5. The conducting zone of the tracheobronchial tree ends at the
   a. alveolar duct.
   b. alveoli.
   c. bronchioles.
   d. respiratory bronchioles.
   e. terminal bronchioles.
6. During an asthma attack, the patient has difficulty breathing because of constriction of the
   a. trachea.
   b. bronchi.
   c. terminal bronchioles.
   d. alveoli.
   e. respiratory membrane.
7. During quiet expiration, the
   a. abdominal muscles relax.
   b. diaphragm moves inferiorly.
   c. external intercostal muscles contract.
   d. thorax and lungs passively recoil.
   e. all of the above.
8. The parietal pleura
   a. covers the surface of the lung.
   b. covers the inner surface of the thoracic cavity.
   c. is the connective tissue partition that divides the thoracic cavity into right and left pleural cavities.
   d. covers the inner surface of the alveoli.
   e. is the membrane across which gas exchange occurs.
9. Contraction of the bronchiolar smooth muscle has which of these effects?
   a. a smaller pressure gradient is required to get the same rate of airflow when compared to normal bronchioles
   b. increases airflow through the bronchioles
   c. increases resistance to airflow
   d. increases alveolar ventilation
10. During the process of expiration, the alveolar pressure is
    a. greater than the pleural pressure.
    b. greater than the barometric pressure.
    c. less than the barometric pressure.
    d. unchanged.
11. The lungs do not normally collapse because of
    a. surfactant.
    b. pleural pressure.
    c. elastic recoil.
    d. both a and b.
12. Immediately after the creation of an opening through the thorax into the pleural cavity,
    a. air flows through the hole and into the pleural cavity.
    b. air flows through the hole and out of the pleural cavity.
    c. air flows neither out nor in.
    d. the lung protrudes through the hole.
13. Compliance of the lungs and thorax
    a. is the volume by which the lungs and thorax change for each unit change of alveolar pressure.
    b. increases in emphysema.
    c. decreases because of lack of surfactant.
    d. all of the above.
14. Given these lung volumes:
    1. tidal volume = 500 mL
    2. residual volume = 1000 mL
    3. inspiratory reserve volume = 2500 mL
    4. expiratory reserve volume = 1000 mL
    5. dead space = 1000 mL

    The vital capacity is
    a. 3000 mL.
    b. 3500 mL.
    c. 4000 mL.
    d. 5000 mL.
    e. 6000 mL.
15. The alveolar ventilation is the
    a. tidal volume times respiratory rate.
    b. minute ventilation plus the dead space.
    c. amount of air available for gas exchange in the lungs.
    d. vital capacity divided by respiratory rate.
    e. inspiratory reserve volume times minute ventilation.
16. If the total pressure of a gas is 760 mm Hg and its composition is 20% oxygen, 0.04% carbon dioxide, 75% nitrogen, and 5% water vapor, the partial pressure of oxygen is
    a. 15.2 mm Hg.
    b. 20 mm Hg.
    c. 118 mm Hg.
    d. 152 mm Hg.
    e. 740 mm Hg.
17. The rate of diffusion of a gas across the respiratory membrane increases as the
    a. respiratory membrane becomes thicker.
    b. surface area of the respiratory membrane decreases.
    c. partial pressure difference of the gas across the respiratory membrane increases.
    d. diffusion coefficient of the gas decreases.
    e. all of the above.
18. In which of these sequences does P_{O_2} progressively decrease?
    a. arterial blood, alveolar air, body tissues
    b. body tissues, arterial blood, alveolar air
    c. body tissues, alveolar air, arterial blood
    d. alveolar air, arterial blood, body tissues
    e. arterial blood, body tissues, alveolar air
19. The partial pressure of carbon dioxide in the venous blood is
    a. greater than in the tissue spaces.
    b. less than in the tissue spaces.
    c. less than in the alveoli.
    d. less than in arterial blood.

20. Oxygen is mostly transported in the blood
    a. dissolved in plasma.
    b. bound to blood proteins.
    c. within bicarbonate ions.
    d. bound to the heme portion of hemoglobin.
21. The oxygen–hemoglobin dissociation curve is adaptive because it
    a. shifts to the right in the pulmonary capillaries and to the left in the tissue capillaries.
    b. shifts to the left in the pulmonary capillaries and to the right in the tissue capillaries.
    c. doesn't shift.
22. Carbon dioxide is mostly transported in the blood
    a. dissolved in plasma.
    b. bound to blood proteins.
    c. within bicarbonate ions.
    d. bound to the heme portion of hemoglobin.
    e. bound to the globin portion of hemoglobin.
23. When blood passes through the tissues, the hemoglobin in blood is better able to combine with carbon dioxide because of the
    a. Bohr effect.
    b. Haldane effect.
    c. chloride shift.
    d. Boyle effect.
    e. Dalton effect.
24. The chloride shift
    a. occurs primarily in pulmonary capillaries.
    b. occurs when chloride ions replace bicarbonate ions within erythrocytes.
    c. decreases the formation of bicarbonate ions.
    d. decreases the number of hydrogen ions.
25. Which of these parts of the brainstem is correctly matched with its main function?
    a. ventral respiratory groups—stimulate the diaphragm
    b. dorsal respiratory groups—limit inflation of the lungs
    c. pontine respiratory group—switching between inspiration and expiration
    d. all of the above
26. The chemosensitive area
    a. stimulates the respiratory center when blood carbon dioxide levels increase.
    b. stimulates the respiratory center when blood pH increases.
    c. is located in the pons.
    d. stimulates the respiratory center when blood oxygen levels increase.
    e. all of the above.
27. Blood oxygen levels
    a. are more important than carbon dioxide in the regulation of respiration.
    b. need to change only slightly to cause a change in respiration.
    c. are detected by sensory receptors in the carotid and aortic bodies.
    d. all of the above.
28. The Hering-Breuer reflex
    a. limits inspiration.
    b. limits expiration.
    c. occurs in response to changes in carbon dioxide levels in the blood.
    d. is stimulated when oxygen decreases in the blood.
    e. does not occur in infants.
29. At the onset of exercise, respiration rate and depth increases primarily because of
    a. increased blood carbon dioxide levels.
    b. decreased blood oxygen levels.
    c. decreased blood pH.
    d. input to the respiratory center from the cerebral motor cortex and proprioceptors.
30. In response to exercise training,
    a. the tidal volume at rest does not change.
    b. minute ventilation during maximal exercise increases.
    c. the brain learns to match ventilation to exercise intensity.
    d. all of the above.

Answers in Appendix F

CRITICAL THINKING

1. What effect does rapid (respiratory rate equals 24 breaths per minute), shallow (tidal volume equals 250 mL per breath) breathing have on minute ventilation, alveolar ventilation, and alveolar P_{O_2} and P_{CO_2}?
2. A person's vital capacity is measured while standing and while lying down. What difference, if any, in the measurement do you predict and why?
3. Ima Diver wanted to do some underwater exploration. She didn't want to buy expensive SCUBA equipment, however. Instead, she bought a long hose and an inner tube. She attached one end of the hose to the inner tube so that the end was always out of the water, and she inserted the other end of the hose in her mouth and went diving. What happened to her alveolar ventilation and why? How would she compensate for this change? How would diving affect lung compliance and the work of ventilation?
4. The bacteria that cause gangrene *(Clostridium perfringens)* are anaerobic microorganisms that don't thrive in the presence of oxygen. Hyperbaric oxygenation (HBO) treatment places a person in a chamber that contains oxygen at three to four times normal atmospheric pressure. Explain how HBO helps in the treatment of gangrene.
5. Cardiopulmonary resuscitation (CPR) has replaced older, less efficient methods of sustaining respiration. The back-pressure/arm-lift method is one such technique that's no longer used. This procedure is performed with the victim lying face down. The rescuer presses firmly on the base of the scapulae for several seconds and then grasps the arms and lifts them. The sequence is then repeated. Explain why this procedure results in ventilation of the lungs.
6. Another technique for artificial respiration is mouth-to-mouth resuscitation. The rescuer takes a deep breath, blows air into the victim's mouth, and then lets air flow out of the victim. The process is repeated. Explain the following: (1) Why do the victim's lungs expand? (2) Why does air move out of the victim's lungs? and (3) What effect do the P_{O_2} and the P_{CO_2} of the rescuer's air have on the victim?
7. During normal quiet respiration, when does the maximum rate of diffusion of oxygen in the pulmonary capillaries occur? The maximum rate of diffusion of carbon dioxide?
8. Is the oxygen–hemoglobin dissociation curve in humans who live at high altitudes to the left or to the right of a person who lives at low altitudes?
9. Predict what would happen to tidal volume if the vagus nerves were cut. The phrenic nerves? The intercostal nerves?
10. You and your physiology instructor are trapped in an overturned ship. To escape, you must swim underwater a long distance. You tell your instructor it would be a good idea to hyperventilate before making the escape attempt. Your instructor calmly replies, "What good would that do, since your pulmonary capillaries are already 100% saturated with oxygen?" What would you do and why?

Answers in Appendix G

ANSWERS TO PREDICT QUESTIONS

1. Air moving through the mouth is not as efficiently warmed and moistened as air moving through the nasal cavity, and the throat or lung tissue can become dehydrated or damaged by the cold air.
2. When food moves down the esophagus, the normally collapsed esophagus expands. If the cartilage rings were solid, expansion of the esophagus, and, therefore, swallowing, would be more difficult.
3. A foreign object is more likely to become lodged in the right primary bronchus because it has a larger diameter and is more directly in line with the trachea.
4. Respiratory distress syndrome results from inadequate surfactant, which results in increased water surface tension. Consequently, lung recoil is increased. At the end of expiration, pleural pressure is lower than normal because of the increased lung recoil. Although the decreased pleural pressure increases the tendency for the alveoli to expand, the alveoli don't expand because the increased force of expansion is only counteracting the increased lung recoil. The alveoli collapse if the lung recoil becomes larger than the force of expansion caused by the difference between alveolar and pleural pressure. During inspiration, pleural pressure has to be lower than normal to overcome the effect of the larger-than-normal lung recoil. A larger-than-normal increase in thoracic volume can cause a greater-than-normal decrease in pleural pressure. The effort of overcoming the increased lung recoil, however, can cause muscular fatigue and death.
5. The alveolar ventilation is 4200 mL/min ($12 \times [500 - 150]$). During exercise, the alveolar ventilation is 88,800 mL/min ($24 \times [4000 - 300]$), a 21-fold increase. The increased air exchange increases P_{O_2} and decreases P_{CO_2} in the alveoli, thus increasing gas exchange between the alveoli and the blood.
6. The air the diver is breathing has a greater total pressure than atmospheric pressure at sea level. Consequently, the partial pressure of each gas in the air increases. According to Henry's law, as the partial pressure of a gas increases, the amount (concentration) of gas dissolved in the liquid (e.g., body fluids) with which the gas is in contact increases. When the diver suddenly ascends, the partial pressure of gases in the body returns toward sea level barometric pressure. As a result, the amount (concentration) of gas that can be dissolved in body fluids suddenly decreases. When the fluids can no longer hold all the gas, gas bubbles form.
7. At high altitudes, the atmospheric P_{O_2} decreases because of a decrease in atmospheric pressure. The decreased atmospheric P_{O_2} results in a decrease in alveolar P_{O_2} and less oxygen diffusion into lung tissue. If the person's arterioles are especially sensitive to the decreased oxygen levels, constriction of the arterioles reduces blood flow through the lungs, and the ability to oxygenate blood decreases. Such generalized hypoxemia can also be caused by certain respiratory diseases, such as emphysema and cystic fibrosis.
8. Remember that the oxygen–hemoglobin dissociation curve normally shifts to the right in tissues. The shift of the curve to the left caused by CO reduces the ability of hemoglobin to release oxygen to tissues, which contributes to the detrimental effects of CO poisoning. In the lungs, the shift to the left could slightly increase the ability of hemoglobin to pick up oxygen, but this effect is offset by the decreased ability of hemoglobin to release oxygen to tissues.
9. A person who cannot synthesize BPG has mild erythrocytosis. Her hemoglobin releases less oxygen to tissues. Consequently, one would expect increased erythropoietin release from the kidneys and increased red blood cell production in red bone marrow.
10. In tissues, carbon dioxide moves into red blood cells, resulting in an increase in hydrogen ions. According to the Bohr effect, as hydrogen ions bind to hemoglobin the oxygen–hemoglobin dissociation curve shifts to the right and there is increased release of oxygen. According to the Haldane effect, hemoglobin that has released oxygen picks up more carbon dioxide.
11. Hyperventilation decreases blood carbon dioxide levels, causing an increase in blood pH. Holding one's breath increases blood carbon dioxide levels and decreases blood pH.
12. When a person hyperventilates, P_{CO_2} in the blood decreases. Consequently, carbon dioxide moves out of cerebrospinal fluid into the blood. As carbon dioxide levels in cerebrospinal fluid decrease, hydrogen ions and bicarbonate ions combine to form carbonic acid, which forms carbon dioxide. The result is a decrease in hydrogen ion concentration in cerebrospinal fluid and decreased stimulation of the respiratory center by the chemosensitive area. Until blood P_{CO_2} levels increase, the chemosensitive area is not stimulated, and apnea results.
13. Through touch, thermal, or pain receptors, the respiratory center can be stimulated to cause a sudden inspiration of air.
14. A P_{O_2} of 60 mm Hg and a P_{CO_2} of 30 mm Hg are both below normal. The movement of air into and out of the lungs is restricted because of the asthma and a mismatch occurs between ventilation of the alveoli and blood flow to the alveoli. Consequently, because of the ineffective ventilation, blood oxygen levels decrease. Mr. W hyperventilates, which helps to maintain blood oxygen levels but also results in lower-than-normal blood carbon dioxide levels. (If no hyperventilation occurred, one would expect decreased blood oxygen but increased blood carbon dioxide levels.)