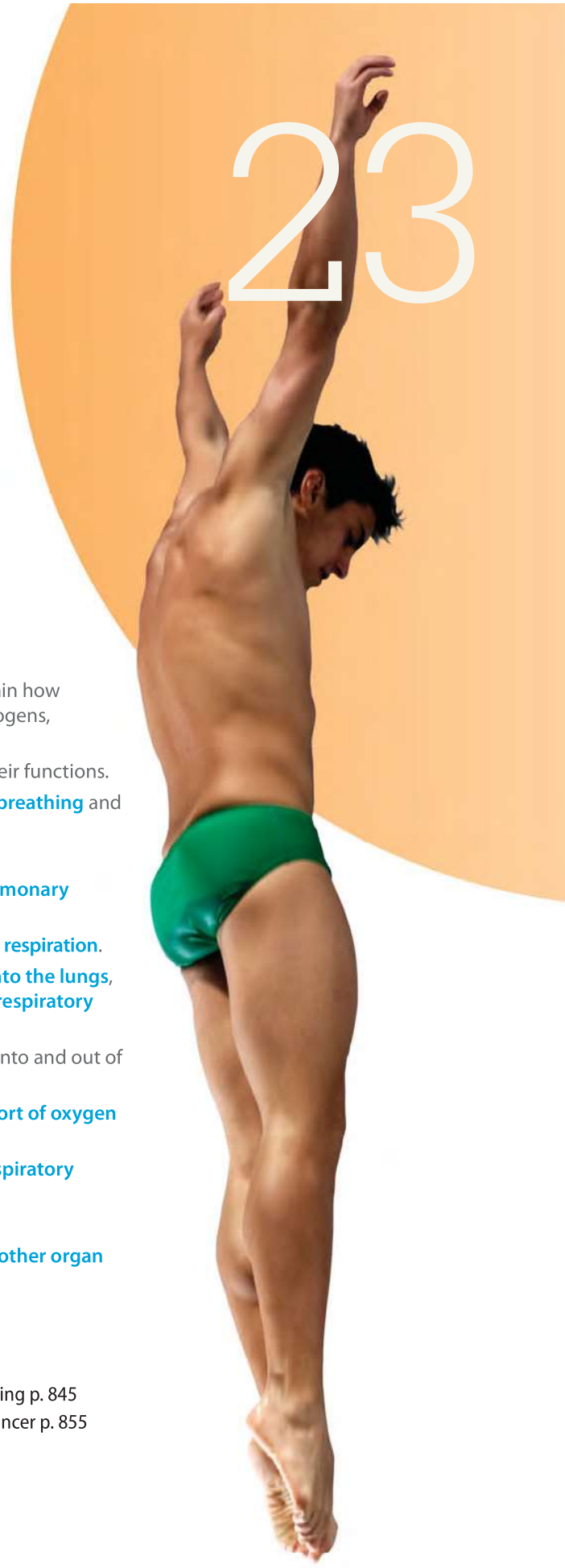
23 The Respiratory System



Learning Outcomes

These Learning Outcomes correspond by number to this chapter's sections and indicate what you should be able to do after completing the chapter.

23-1 Describe the **primary functions of the respiratory system**, and explain how the delicate **respiratory exchange surfaces** are protected from pathogens, debris, and other hazards.

23-2 Identify the organs of the **upper respiratory system**, and describe their functions.

23-3 Describe the **structure of the larynx**, and discuss its **roles in normal breathing** and in the **production of sound**.

23-4 Discuss the structure of the **extrapulmonary airways**.

23-5 Describe the **superficial anatomy of the lungs**, the structure of a **pulmonary lobule**, and the **functional anatomy of alveoli**.

23-6 Define and compare the processes of **external respiration and internal respiration**.

23-7 Summarize the physical principles governing the **movement of air into the lungs**, and describe the origins and actions of the **muscles responsible for respiratory movements**.

23-8 Summarize the physical principles governing the **diffusion of gases** into and out of the blood and body tissues.

23-9 Describe the **structure and function of hemoglobin**, and the **transport of oxygen and carbon** dioxide in the blood.

23-10 List the **factors that influence respiration rate**, and discuss **reflex respiratory activity** and the **brain centers** involved in the control of respiration.

23-11 Describe **age-related changes in the respiratory system**.

23-12 Give examples of **interactions between the respiratory system and other organ systems** studied so far.

Clinical Notes

Spotlight

An Introduction to the Respiratory System

When we think of the respiratory system, we generally think of breathing—pulling air into and out of our bodies. However, an efficient respiratory system must do more than merely move air. Cells need energy for maintenance, growth, defense, and division. Our cells obtain that energy mainly through aerobic mechanisms that require oxygen and produce carbon dioxide.

Many aquatic organisms can obtain oxygen and excrete carbon dioxide by diffusion across the surface of the skin or specialized structures, such as the gills of a fish. But such arrangements are poorly suited for life on land. The exchange surfaces must be very thin to permit rapid diffusion. In air, these exposed membranes collapse, evaporation and dehydration reduce blood volume, and the delicate surfaces become vulnerable to attack by pathogens. The respiratory exchange surfaces of humans are just as thin and delicate as those of an aquatic organism, but they are confined to the inside of the *lungs*—a warm, moist, protected environment. Under these conditions, diffusion can take place between the air and the blood.

The cardiovascular system is the link between your interstitial fluids and the exchange surfaces of your lungs. Circulating blood carries oxygen from the lungs to peripheral tissues. Your blood also accepts and transports the carbon dioxide generated by those tissues, delivering it to the lungs. In this chapter we describe how air enters the lungs as a result of the actions of respiratory muscles, and how oxygen and carbon dioxide are exchanged across delicate epithelial surfaces within the lungs.

23-1 The respiratory system, organized into an upper respiratory system and a lower respiratory system, has several basic functions

The **respiratory system** is composed of structures involved in ventilation and gas exchange. In this section we consider this body system's functions and structural organization.

Functions of the Respiratory System

The respiratory system has five basic functions:

1. Providing an extensive surface area for gas exchange between air and circulating blood.
2. Moving air to and from the exchange surfaces of the lungs along the respiratory passageways.
3. Protecting respiratory surfaces from dehydration, temperature changes, or other environmental variations, and defending the respiratory system and other tissues from invasion by pathogens.
4. Producing sounds for speaking, singing, and other forms of communication.
5. Facilitating the detection of odors by olfactory receptors in the superior portions of the nasal cavity.

In addition, the capillaries of the lungs indirectly help to regulate blood volume and blood pressure. They do so through the conversion of angiotensin I to angiotensin II. ↩ p. 624

Organization of the Respiratory System

We can organize the respiratory system from either an anatomical or a functional perspective. Anatomically, we can divide the system into an upper respiratory system and a lower respiratory system (**Figure 23–1**). The **upper respiratory system** consists of the nose, nasal cavity, paranasal sinuses, and pharynx (throat). These passageways filter, warm, and humidify incoming air, protecting the more delicate surfaces of the lower respiratory system. They also cool and dehumidify outgoing air. The **lower respiratory system** includes the larynx (voice box), trachea (windpipe), bronchi, bronchioles, and alveoli of the lungs.

Tips & Tricks

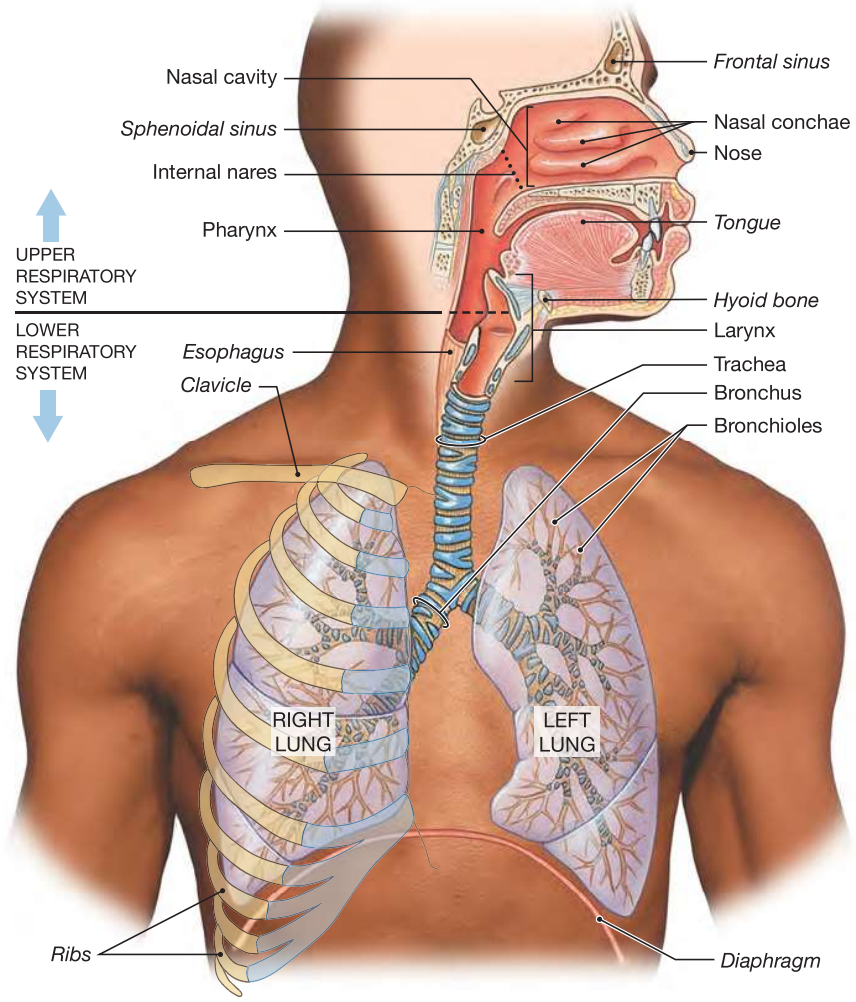
To recall the boundary between the upper and lower respiratory systems, remember that the ***l***ower respiratory system begins at the ***l***arynx.

The term **respiratory tract** refers to the passageways that carry air to and from the exchange surfaces of the lungs. The *conducting portion* of the respiratory tract begins at the entrance to the nasal cavity and extends through the pharynx, larynx, trachea, bronchi, and larger bronchioles. The *respiratory portion* of the tract includes the smallest, most delicate *bronchioles* and the associated **alveoli** (al-VĒ-ō-lī), air-filled pockets within the lungs where all gas exchange between air and blood takes place.

Gas exchange can take place quickly and efficiently because the distance between the blood in an alveolar capillary and the air inside an alveolus is generally less than 1 μm. In some cases this distance is as short as 0.1 μm. To meet the metabolic requirements of peripheral tissues, the surface area for gas exchange in the lungs must be very large. It is about 35 times the surface area of your body. Estimates of the surface area involved in gas exchange range from 70 m^2 to 140 m^2 (753 ft^2 to 1506 ft^2).

Filtering, warming, and humidifying inhaled air begin at the entrance to the respiratory tract and continue as air passes along the conducting portion. By the time air reaches the alveoli, most foreign particles and pathogens have been removed, and the humidity and temperature are within acceptable limits. The success of this "conditioning process" is due to the respiratory mucosa.

Figure 23–1 The Components of the Respiratory System. Only the conducting portion of the respiratory tract is shown; the smaller bronchioles and alveoli have been omitted. ATLAS: Plate 47a,b



The Respiratory Mucosa

The **respiratory mucosa** (mū-KŌ-suh) lines the conducting portion of the respiratory system. A *mucosa* is a *mucous membrane*, one of the four types of membranes introduced in Chapter 4. It consists of an epithelium and an underlying layer of areolar tissue. ↩ p. 131 The **lamina propria** (LAM-i-nuh PRŌ-prē-uh) is the underlying layer of areolar tissue that supports the respiratory epithelium. In the upper respiratory system, trachea, and bronchi, the lamina propria contains mucous glands that discharge their secretions onto the epithelial surface (**Figure 23–2**). The lamina propria in the conducting portions of the lower respiratory system contains bundles of smooth muscle cells. At the bronchioles, the smooth muscles form thick bands that encircle or spiral around the lumen.

The structure of the respiratory epithelium changes along the respiratory tract. A pseudostratified ciliated columnar epithelium with numerous mucous cells lines the nasal cavity and the superior portion of the pharynx. ↩ p. 117 The epithelium lining inferior portions of the pharynx is a stratified squamous epithelium similar to that of the oral cavity. These portions of the pharynx conduct air to the larynx and also convey food to the esophagus. The pharyngeal epithelium must therefore protect against abrasion and chemical attack.

A pseudostratified ciliated columnar epithelium, comparable to that of the nasal cavity, lines the superior portion of the lower respiratory system. The smaller bronchioles have a cuboidal epithelium with scattered cilia. The exchange surfaces of the alveoli are lined by a very delicate simple squamous epithelium. Other, more specialized cells are scattered among the squamous cells and together they form the *alveolar epithelium*.

The Respiratory Defense System

Debris or pathogens in inhaled air can severely damage the delicate exchange surfaces of the respiratory system. A series of filtration mechanisms that make up the **respiratory defense system** prevent such contamination.

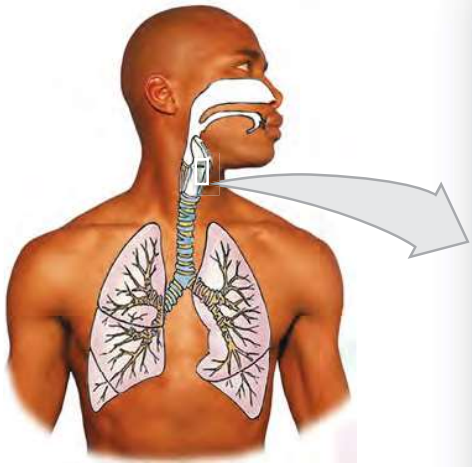
Along much of the respiratory tract, mucous cells in the epithelium and mucous glands in the lamina propria produce a sticky mucus that bathes exposed surfaces. In the nasal cavity, cilia sweep that mucus and any trapped debris or microorganisms toward the pharynx. There it is swallowed and exposed to the acids and enzymes of the stomach. In the lower respiratory system, the cilia beat toward the pharynx, moving a carpet of mucus in that direction and cleaning the respiratory surfaces. This process is often called a *mucus escalator* (**Figure 23–2b, c**).

Tips & Tricks

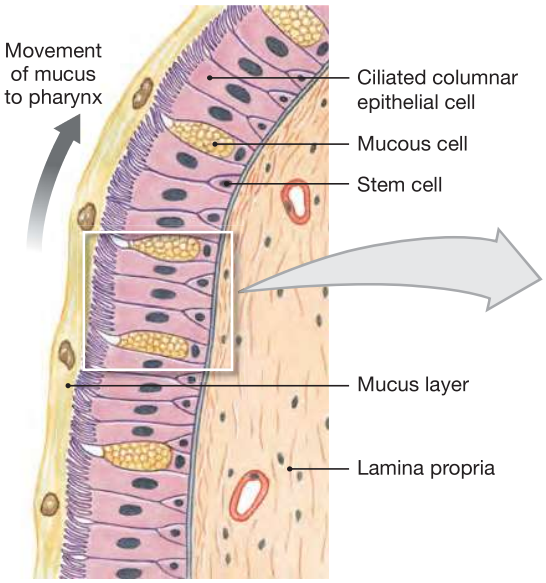
The mucus layer of the respiratory epithelium functions like sticky flypaper, but instead of flies, it traps particles and debris from the air moving past it.

Filtration in the nasal cavity removes virtually all particles larger than about 10 μm from the inhaled air. Smaller particles may be trapped by the mucus of the nasopharynx or by secretions of the pharynx. The rate of mucus production in the nasal cavity and paranasal sinuses speeds up upon exposure to unpleasant stimuli, such as noxious vapors, large quantities of dust and debris, allergens, or pathogens. (The familiar signs and

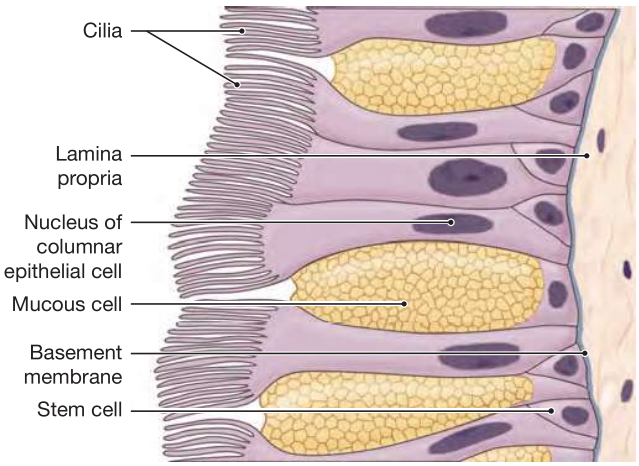
Figure 23–2 The Respiratory Epithelium of the Nasal Cavity and Conducting System.



a A surface view of the epithelium. The cilia of the epithelial cells form a dense layer that resembles a shag carpet. The movement of these cilia propels mucus across the epithelial surface.



b A diagrammatic view of the respiratory epithelium of the trachea, indicating the direction of mucus transport inferior to the pharynx.



c The sectional appearance of the respiratory epithelium, a pseudostratified ciliated columnar epithelium.

symptoms of the "common cold" appear when any of more than 200 types of viruses invades the respiratory epithelium.)

Most particles 1–5 μm in diameter are trapped in the mucus coating the respiratory bronchioles or in the liquid covering the alveolar surfaces. These areas are outside of the mucus escalator, but the foreign particles can be engulfed by alveolar macrophages. Most particles smaller than about 0.5μm remain suspended in the air.

Checkpoint

1. **Identify several functions of the respiratory system.**
2. **List the two anatomical divisions of the respiratory system.**
3. **What membrane lines the conducting portion of the respiratory tract?**

See the blue Answers tab at the back of the book.

Clinical Note

Breakdown of the Respiratory Defense System Large quantities of airborne particles may overload the respiratory defenses and produce a variety of illnesses. For example, irritants in the lining of the conducting passageways can provoke the formation of mucus plugs that block airflow and reduce pulmonary function, and damage to the epithelium in the affected area may allow irritants to enter the surrounding tissues of the lung. The irritants then produce local inflammation. Airborne irritants—such as those in cigarette smoke—are known to promote the development of lung cancer (p. 855).

Aggressive pathogens can also overwhelm respiratory defenses. **Tuberculosis** (tū-ber-kū-LŌ-sis), or **TB,** results from an infection of the lungs by the bacterium *Mycobacterium tuberculosis.* Other organs may be invaded as well. Bacteria may colonize the respiratory passageways, the interstitial spaces, the alveoli, or a combination of the three. Signs and symptoms are variable, but generally include coughing and chest pain, plus fever, night sweats, fatigue, and weight loss. In 1900, TB, then known as "consumption," was the leading cause of death. It remains among the most common and serious infectious diseases, and an estimated one-third of the world's population is infected with TB. According to the Centers for Disease Control and Prevention (CDC), there are nearly 2 million TB-related deaths worldwide each year.

The respiratory defense system can also fail due to inherited congenital defects affecting mucus production or transport. For example, **cystic fibrosis (CF)** is the most common lethal inherited disease in individuals of Northern European descent. It occurs in 1 birth in 2500. The respiratory mucosa in these individuals produces dense, viscous mucus that cannot be transported by the respiratory defense system. The mucus escalator stops working, leading to frequent infections. Mucus also blocks the smaller respiratory passageways, making breathing difficult. The average predicted age of survival for individuals with CF is now 37.4 years. Death generally results from heart failure associated with a massive chronic bacterial infection of the lungs.

23-2 ◗ Located outside the thoracic cavity, the upper respiratory system consists of the nose, nasal cavity, paranasal sinuses, and pharynx

As we have noted, the upper respiratory system consists of the nose, nasal cavity, paranasal sinuses, and pharynx (**Figures 23–1** and **23–3**).

The Nose, Nasal Cavity, and Paranasal Sinuses

The nose is the primary passageway for air entering the respiratory system. Air normally enters through the paired **external nares** (NĀ-res), or *nostrils* (**Figure 23–3a**), which open into the *nasal cavity*. The **nasal vestibule** is the space contained within the flexible tissues of the nose (**Figure 23–3c**). The epithelium of the vestibule contains coarse hairs that extend across the external nares. Large airborne particles, such as sand, sawdust, or even insects, are trapped in these hairs and prevented from entering the nasal cavity.

The **nasal septum** divides the nasal cavity into left and right portions (**Figure 23–3b**). The bony portion of the nasal septum is formed by the fusion of the perpendicular plate of the ethmoid bone and the plate of the vomer (**Figure 7–3d**, p. 202). The anterior portion of the nasal septum is formed of hyaline cartilage. This cartilaginous plate supports the *dorsum nasi* (DOR-sum NĀ-zī), or bridge, and *apex* (tip) of the nose.

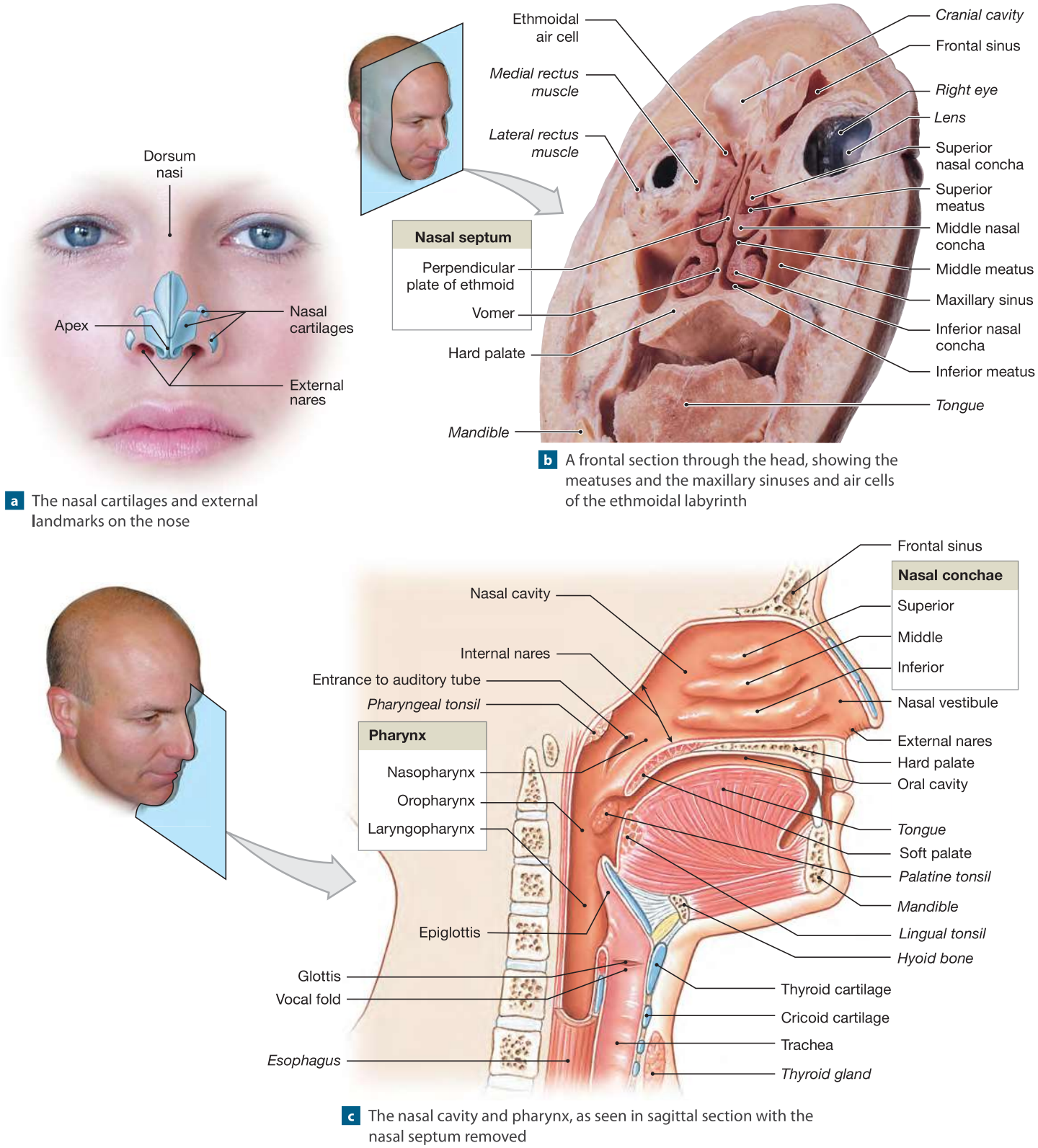
The maxillary, nasal, frontal, ethmoid, and sphenoid bones form the lateral and superior walls of the nasal cavity. The mucous secretions produced in the *paranasal sinuses* (sinuses of the frontal, sphenoid, ethmoid, and paired maxillary and palatine bones) help keep the surfaces of the nasal cavity moist and clean (**Figure 7–14**, p. 215). The tears draining through the nasolacrimal ducts do so as well.

The *olfactory region* is the superior portion of the nasal cavity. It includes the areas lined by olfactory epithelium: (1) the inferior surface of the cribriform plate, (2) the superior portion of the nasal septum, and (3) the superior nasal conchae. Receptors in the olfactory epithelium provide your sense of smell. ↩ p. 549

The *superior*, *middle*, and *inferior nasal conchae* project toward the nasal septum from the lateral walls of the nasal cavity. ↩ pp. 208, 211 To pass from the vestibule to the internal nares, air tends to flow between adjacent conchae, through the **superior, middle,** and **inferior meatuses** (mē-Ā-tus-ez; *meatus*, a passage) (**Figure 23–3b**). These are narrow grooves rather than open passageways. The incoming air bounces off the conchal surfaces and churns like a stream flowing over rocks. This turbulence serves several purposes. As the air swirls, small airborne particles are likely to come into contact with the mucus that coats the lining of the nasal cavity. In addition, the turbulence provides extra time for warming and humidifying incoming air. It also creates circular air currents that bring olfactory stimuli to the olfactory receptors.

The bony **hard palate** is made up of portions of the maxillary and palatine bones. The hard palate forms the floor of the nasal cavity and separates it from the oral cavity. A fleshy **soft palate** extends posterior to the hard palate, marking the boundary between the superior *nasopharynx* (nā-zō-FAR-ingks) and the rest of the pharynx. The nasal cavity opens into the nasopharynx through a connection known as the **internal nares.**

Figure 23–3 Structures of the Upper Respiratory System. ATLAS: Plate 19



a The nasal cartilages and external landmarks on the nose

b A frontal section through the head, showing the meatuses and the maxillary sinuses and air cells of the ethmoidal labyrinth

c The nasal cavity and pharynx, as seen in sagittal section with the nasal septum removed

The Nasal Mucosa

The mucosa of the nasal cavity prepares inhaled air for arrival at the lower respiratory system. Throughout much of the nasal cavity, the lamina propria contains an abundance of arteries, veins, and capillaries that bring nutrients and water to the secretory cells. The lamina propria of the nasal conchae also contains an extensive network of large and highly expandable veins. This vascularization warms and humidifies the incoming air (and cools and dehumidifies the outgoing air as well). As cool, dry air passes inward over the exposed surfaces of the nasal cavity, the warm epithelium radiates heat, and water in the mucus evaporates. In this way, air moving from your nasal cavity to your lungs is heated almost to body temperature. It is also nearly saturated with water vapor. These changes protect more delicate respiratory surfaces from chilling or drying out—two potentially disastrous events. If you breathe through your mouth, you eliminate much of this preliminary filtration, heating, and humidifying of the inhaled air. To avoid alveolar damage, patients breathing on a respirator (mechanical ventilator), which utilizes a tube to conduct air directly into the trachea, must receive air that has been externally filtered and humidified.

As air moves out of the respiratory tract, it again passes over the epithelium of the nasal cavity. This air is warmer and more humid than the air that enters. It warms the nasal mucosa, and moisture condenses on the epithelial surfaces. In this way, breathing through your nose helps prevent heat loss and water loss.

The extensive vascularization of the nasal cavity and the vulnerable position of the nose make a nosebleed, or *epistaxis* (ep-i-STAK-sis), a fairly common event. This bleeding generally involves vessels of the mucosa covering the cartilaginous portion of the septum. Possible causes include trauma (such as a punch in the nose), drying, infections, allergies, or clotting disorders. Hypertension can also bring on a nosebleed by rupturing small vessels of the lamina propria.

The Pharynx

The **pharynx** (FAR-ingks), or throat, is a chamber shared by the digestive and respiratory systems. It extends between the internal nares and the entrances to the larynx and esophagus. The curving superior and posterior walls of the pharynx are closely bound to the axial skeleton, but the lateral walls are flexible and muscular.

We can divide the pharynx into the nasopharynx, the oropharynx, and the laryngopharynx (**Figure 23–3c**):

1. The **nasopharynx** is the superior portion of the pharynx. It is connected to the posterior portion of the nasal cavity through the internal nares. The soft palate separates it from the oral cavity. The nasopharynx is lined by the same pseudostratified ciliated columnar epithelium as in the nasal cavity. The *pharyngeal tonsil* is located on the posterior wall of the nasopharynx. The left and right *auditory tubes* open into the nasopharynx on either side of this tonsil. pp. 575, 773
2. The **oropharynx** (*oris*, mouth) extends between the soft palate and the base of the tongue at the level of the hyoid bone. The posterior portion of the oral cavity communicates directly with the oropharynx, as does the posterior inferior portion of the nasopharynx. At the boundary between the nasopharynx and the oropharynx, the epithelium changes from pseudostratified columnar epithelium to stratified squamous epithelium.
3. The narrow **laryngopharynx** (la-rin-gō-FAR-ingks) is the inferior part of the pharynx. It includes that portion of the pharynx between the hyoid bone and the entrance to the larynx and esophagus. Like the oropharynx, the laryngopharynx is lined with a stratified squamous epithelium that resists abrasion, chemical attack, and invasion by pathogens.

Checkpoint

4. **Name the structures of the upper respiratory system.**
5. **Why is the vascularization of the nasal cavity important?**
6. **Why is the lining of the nasopharynx different from that of the oropharynx and the laryngopharynx?**

See the blue Answers tab at the back of the book.

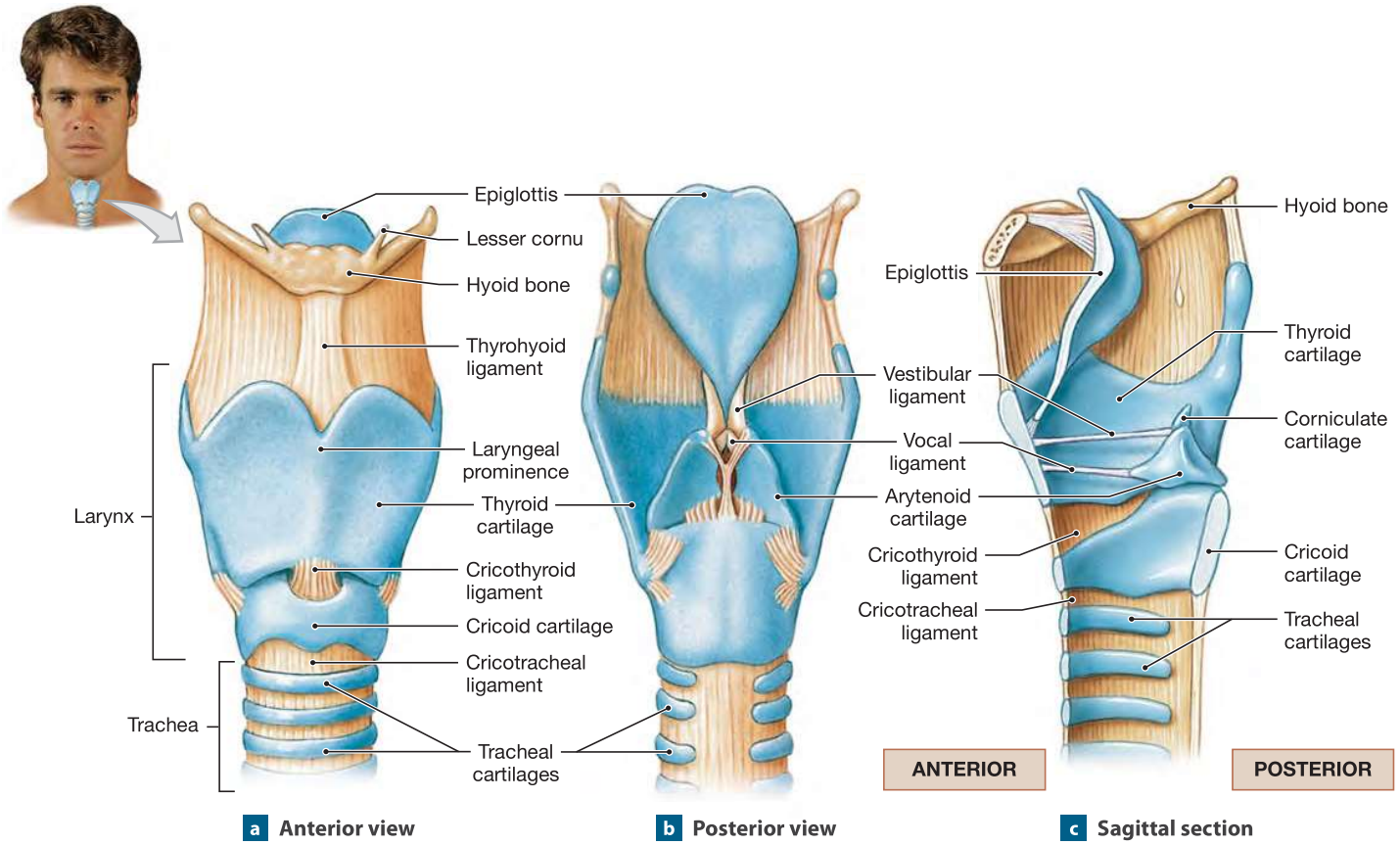
23-3 Composed of cartilages, ligaments, and muscles, the larynx produces sound

Inhaled air leaves the pharynx and enters the larynx through a narrow opening called the **glottis** (GLOT-is). The **larynx** (LAR-ingks) is a cartilaginous tube that surrounds and protects the glottis. The larynx begins at the level of vertebra C_4 or C_5 and ends at the level of vertebra C_6. Essentially a cylinder, the larynx has incomplete cartilaginous walls that are stabilized by ligaments and skeletal muscles (**Figure 23–4**).

Cartilages and Ligaments of the Larynx

Three large, unpaired cartilages form the larynx: (1) the thyroid cartilage, (2) the cricoid cartilage, and (3) the epiglottis (**Figure 23–4**). The **thyroid cartilage** (*thyroid*, shield shaped) is the largest laryngeal cartilage. Made of hyaline cartilage, it forms most of the anterior and lateral walls of the larynx. In section, this cartilage is U-shaped, and posteriorly, it is incomplete. You can easily see and feel the prominent anterior surface of the thyroid cartilage, called the *laryngeal prominence* or *Adam's apple*.

Figure 23–4 The Anatomy of the Larynx.



The inferior surface articulates with the cricoid cartilage. The superior surface has ligamentous attachments to the hyoid bone and to the epiglottis and smaller laryngeal cartilages.

The thyroid cartilage sits superior to the **cricoid** (KRĪ-koyd; ring shaped) **cartilage,** another hyaline cartilage. The posterior portion of the cricoid is greatly expanded, providing support in the absence of the thyroid cartilage. The cricoid and thyroid cartilages protect the glottis and the entrance to the trachea. Their broad surfaces provide sites for the attachment of important laryngeal muscles and ligaments. Ligaments attach the inferior surface of the cricoid cartilage to the first tracheal cartilage. The superior surface of the cricoid cartilage articulates with the small, paired *arytenoid cartilages*.

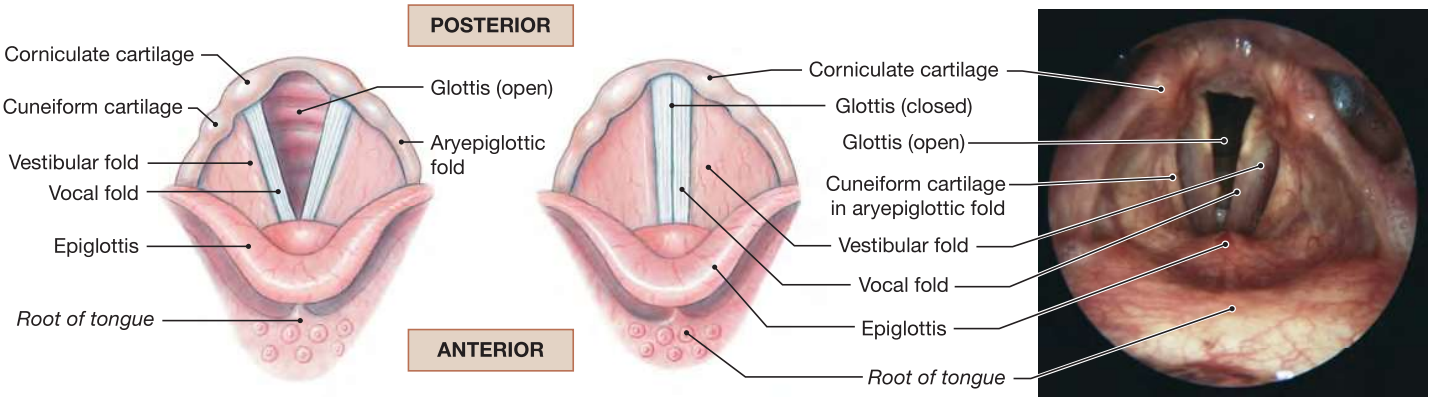
The shoehorn-shaped **epiglottis** (ep-i-GLOT-is) projects superior to the glottis and forms a lid over it. The epiglottis is composed of elastic cartilage. It has ligamentous attachments to the anterior and superior borders of the thyroid cartilage and the hyoid bone. During swallowing, the larynx is elevated and the epiglottis folds back over the glottis, preventing both liquids and solid food from entering the respiratory tract.

The larynx also contains three pairs of smaller hyaline cartilages: (1) The **arytenoid** (ar-i-TĒ-noyd; ladle shaped) **cartilages** articulate with the superior border of the enlarged portion of the cricoid cartilage. (2) The **corniculate** (kor-NIK-ū-lāt; horn shaped) **cartilages** articulate with the arytenoid cartilages. The corniculate and arytenoid cartilages function in the opening and closing of the glottis and the production of sound. (3) Elongated, curving **cuneiform** (kū-NĒ-i-form; wedge shaped) **cartilages** lie within folds of tissue (the *aryepiglottic folds*) that extend between the lateral surface of each arytenoid cartilage and the epiglottis (**Figures 23–4c** and **23–5**).

Ligaments bind together the various laryngeal cartilages. Additional ligaments attach the thyroid cartilage to the hyoid bone, and the cricoid cartilage to the trachea (cricotracheal ligament) (**Figure 23–4a, b**). The median cricothyroid ligament attaches the thyroid cartilage to the cricoid cartilage. This ligament is the common placement site for a tracheostomy, a tracheal incision to bypass an airway obstruction. The **vestibular ligaments** and the **vocal ligaments** extend between the thyroid cartilage and the arytenoid cartilages.

The vestibular and vocal ligaments are covered by folds of laryngeal epithelium that project into the glottis. The vestibular ligaments lie within the superior pair of folds, known as the **vestibular folds** (**Figure 23–5**). These folds are fairly inelastic. They help prevent foreign objects from entering the glottis. They also protect the more delicate **vocal folds.**

Figure 23–5 The Glottis and Surrounding Structures.



a Glottis in the open position. **b** Glottis in the closed position. **c** This photograph is a representative laryngoscopic view. For this view the camera is positioned within the oropharynx, just superior to the larynx.

The vocal folds, inferior to the vestibular folds, guard the entrance to the glottis. The vocal folds are highly elastic, because the vocal ligaments consist of elastic tissue. The vocal folds are involved with the production of sound. For this reason they are known as the **vocal cords.**

Sound Production

How do you produce sounds? Air passing through your glottis vibrates your vocal folds and produces sound waves. The pitch of the sound depends on the diameter, length, and tension in your vocal folds. The diameter and length are directly related to the size of your larynx. You control the tension by contracting voluntary muscles that reposition the arytenoid cartilages relative to the thyroid cartilage. When the distance increases, your vocal folds tense and the pitch rises. When the distance decreases, your vocal folds relax and the pitch falls.

Children have slender, short vocal folds, so their voices tend to be high-pitched. At puberty, the larynx of males enlarges much more than does that of females. The vocal cords of an adult male are thicker and longer. They produce lower tones than those of an adult female.

Sound production at the larynx is called *phonation* (fō-NĀ-shun; *phone*, voice). Phonation is one part of speech production. Clear speech also requires *articulation*, the modification of those sounds by other structures, such as the tongue, teeth, and lips. In a stringed instrument, such as a guitar, the quality of the sound produced does not depend solely on the nature of the vibrating string. Rather, the entire instrument becomes involved as the walls vibrate and the composite sound echoes within the hollow body. Similar amplification and resonance take place within your pharynx, oral cavity, nasal cavity, and paranasal sinuses. The combination gives you the particular and distinctive sound of your voice. When your nasal cavity and paranasal sinuses are filled with mucus rather than air, as in sinus infections, that sound changes.

Tips & Tricks

Intelligible sound requires both phonation and articulation. Saying "ahhhh" while your tongue is depressed during a tonsil examination is an example of phonation. Saying "hot" adds articulation to that sound.

The final production of distinct words depends further on voluntary movements of your tongue, lips, and cheeks. An infection or inflammation of the larynx is known as *laryngitis* (lar-in-JĪ-tis). It commonly affects the vibrational qualities of the vocal folds. Hoarseness is the most familiar result. Mild cases are temporary and seldom serious. However, bacterial or viral infections of the epiglottis can be very dangerous. The resulting swelling may close the glottis and cause suffocation. This condition, *acute epiglottitis* (ep-i-glot-TĪ-tis), can develop rapidly after a bacterial infection of the throat. Young children are most likely to be affected.

The Laryngeal Musculature

The larynx is associated with two sets of muscles. They include (1) muscles of the neck and pharynx, which position and stabilize the larynx (↩ pp. 336–338), and (2) smaller intrinsic muscles that control tension in the vocal folds or open and close the glottis. These smaller muscles insert on the thyroid, arytenoid, and corniculate cartilages. The opening or closing of the glottis involves rotational movements of the arytenoid cartilages that move the vocal folds.

When you swallow, both sets of muscles work together to prevent food or drink from entering the glottis. Food is crushed and chewed into a pasty mass, known as a *bolus*, before being swallowed. Muscles of the neck and pharynx then elevate the larynx, bending the epiglottis over the glottis, so that the bolus can glide across the epiglottis rather than falling into the larynx. While this movement is under way, the glottis is closed.

Food or liquids that touch the vestibular or vocal folds trigger the *coughing reflex*. In a cough, the glottis is kept closed while the chest and abdominal muscles contract, compressing the lungs. When the glottis is opened suddenly, a blast of air from the trachea ejects material that blocks the entrance to the glottis.

Checkpoint

7. **Identify the paired and unpaired cartilages associated with the larynx.**
8. **What are the highly elastic vocal folds of the larynx better known as?**
9. **When the tension in your vocal folds increases, what happens to the pitch of your voice?**

See the blue Answers tab at the back of the book.

23-4 ◗ The trachea and primary bronchi convey air to and from the lungs

Three large, extrapulmonary airways are associated with the lungs: the trachea and the right and left primary bronchi.

The Trachea

The **trachea** (TRĀ-kē-uh), or windpipe, is a tough, flexible tube with a diameter of about 2.5 cm (1 in.) and a length of about 11 cm (4.33 in.) (**Figure 23–6**). The trachea begins anterior to vertebra C_6 in a ligamentous attachment to the cricoid cartilage. It ends in the mediastinum, at the level of vertebra T_5, where it branches to form the *right* and *left primary bronchi*.

The epithelium of the trachea is continuous with that of the larynx. The mucosa of the trachea resembles that of the nasal cavity and nasopharynx (**Figure 23–2a**). The **submucosa** (sub-mū-KŌ-suh), a thick layer of connective tissue, surrounds the mucosa. The submucosa contains mucous glands that communicate with the epithelial surface through a number of secretory ducts. The trachea contains 15–20 **tracheal cartilages,** which serve to stiffen the tracheal walls and protect the airway (**Figure 23–6a**). They also prevent it from collapsing or overexpanding as pressures change in the respiratory system.

Each tracheal cartilage is C-shaped. The closed portion of the C protects the anterior and lateral surfaces of the trachea. The open portion of the C faces posteriorly, toward the esophagus (**Figure 23–6b**). Because these cartilages are not continuous, the posterior tracheal wall can easily distort when you swallow, allowing large masses of food to pass through the esophagus.

An elastic ligament and the **trachealis muscle,** a band of smooth muscle, connect the ends of each tracheal cartilage (**Figure 23–6b**). Contraction of the trachealis muscle reduces the diameter of the trachea. This narrowing increases the tube's resistance to airflow. The normal diameter of the trachea changes from moment to moment, primarily under the control of the sympathetic division of the ANS. Sympathetic stimulation increases the diameter of the trachea and makes it easier to move large volumes of air along the respiratory passageways.

The Primary Bronchi

The trachea branches within the mediastinum into the **right** and **left primary bronchi** (BRONG-kī; singular, *bronchus*). An internal ridge called the **carina** (ka-RĪ-nuh) separates the two bronchi (**Figure 23–6a**). Like the trachea, the primary bronchi have C-shaped rings, but the ends of the C overlap. The right primary bronchus supplies the right lung, and the left supplies the left lung. The right primary bronchus is larger in diameter than the left, and descends toward the lung at a steeper angle. For these reasons, most foreign objects that enter the trachea find their way into the right bronchus rather than the left.

Before branching further, each primary bronchus travels to a groove along the medial surface of its lung. This groove, the **hilum** of the lung, also provides access for entry to pulmonary vessels, nerves, and lymphatics (**Figure 23–7c**). The entire array is firmly anchored in a meshwork of dense connective tissue. This complex is the **root** of the lung (**Figure 23–6a**). The root attaches to the mediastinum and fixes the positions of the major nerves, blood vessels, and lymphatic vessels. The roots of the lungs are anterior to vertebrae T_5 (right) and T_6 (left).

Checkpoint

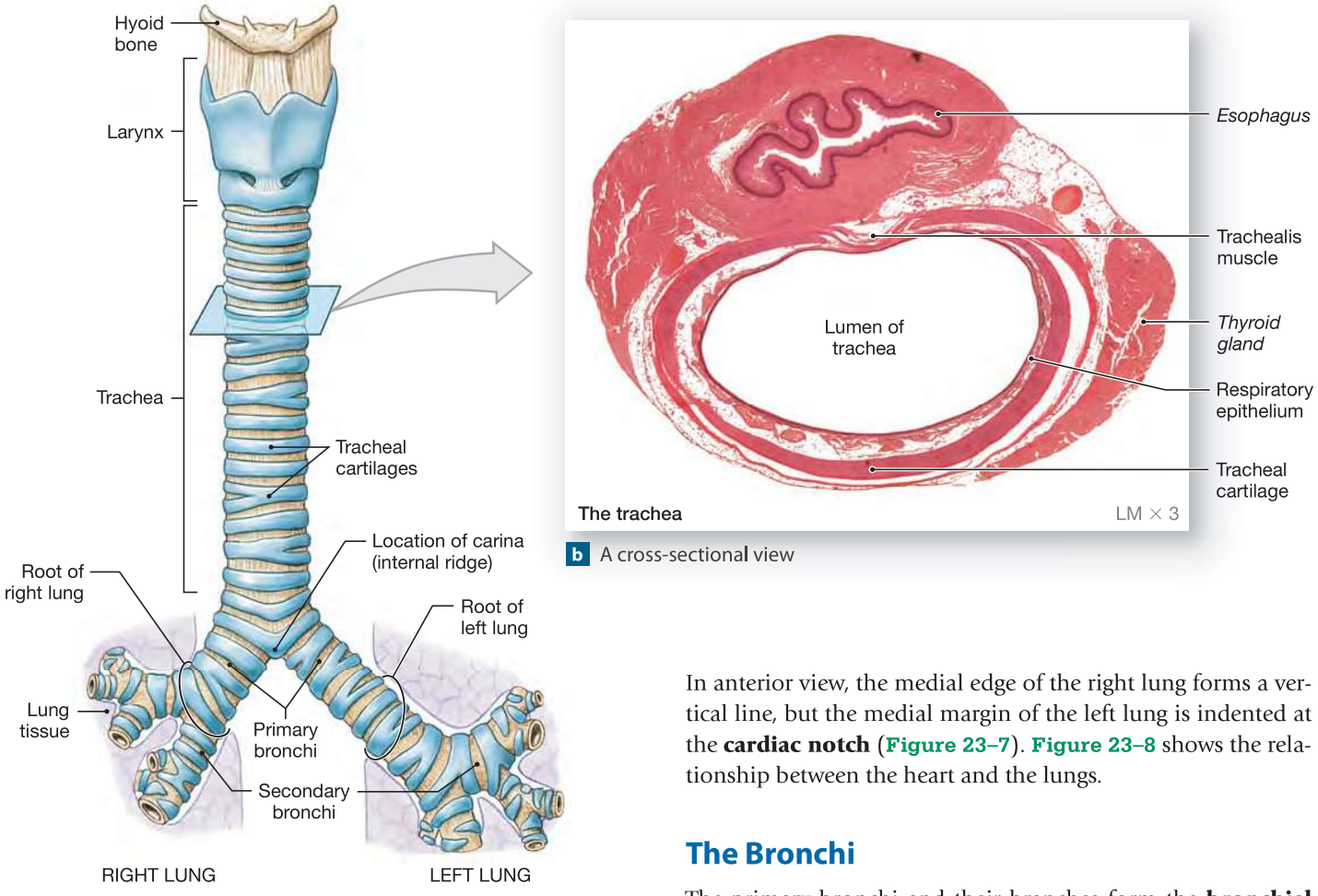
10. **List functions of the trachea.**
11. **Why are the cartilages that reinforce the trachea C-shaped?**
12. **If food accidentally enters the bronchi, in which bronchus is it more likely to lodge? Why?**

See the blue Answers tab at the back of the book.

23-5 ◗ Enclosed by a pleural membrane, the lungs are paired organs containing alveoli, which permit gaseous exchange

The left and right lungs are surrounded by the left and right pleural cavities, respectively (**Figure 23–7**). Each lung is a blunt cone. Its tip, or apex, points superiorly. The apex on each side extends superior to the first rib. The broad concave inferior por-

Figure 23–6 The Anatomy of the Trachea. ATLAS: Plate 42b,c



a A diagrammatic anterior view showing the plane of section for part (b)

b A cross-sectional view

tion, or base, of each lung rests on the superior surface of the diaphragm.

Lobes and Surfaces of the Lungs

The lungs have distinct **lobes** that are separated by deep fissures (**Figure 23–7**). The right lung has three lobes—*superior*, *middle*, and *inferior*—separated by the *horizontal* and *oblique fissures*. The left lung has only two lobes—*superior* and *inferior*—separated by the *oblique fissure*. The right lung is broader than the left, because most of the heart and great vessels project into the left thoracic cavity. However, the left lung is longer than the right lung, because the diaphragm rises on the right side to accommodate the mass of the liver. The lateral and medial lung surfaces are shown in **Figure 23–7b,c**.

The heart is located to the left of the midline, so its corresponding impression is larger in the left lung than in the right. In anterior view, the medial edge of the right lung forms a vertical line, but the medial margin of the left lung is indented at the **cardiac notch** (**Figure 23–7**). **Figure 23–8** shows the relationship between the heart and the lungs.

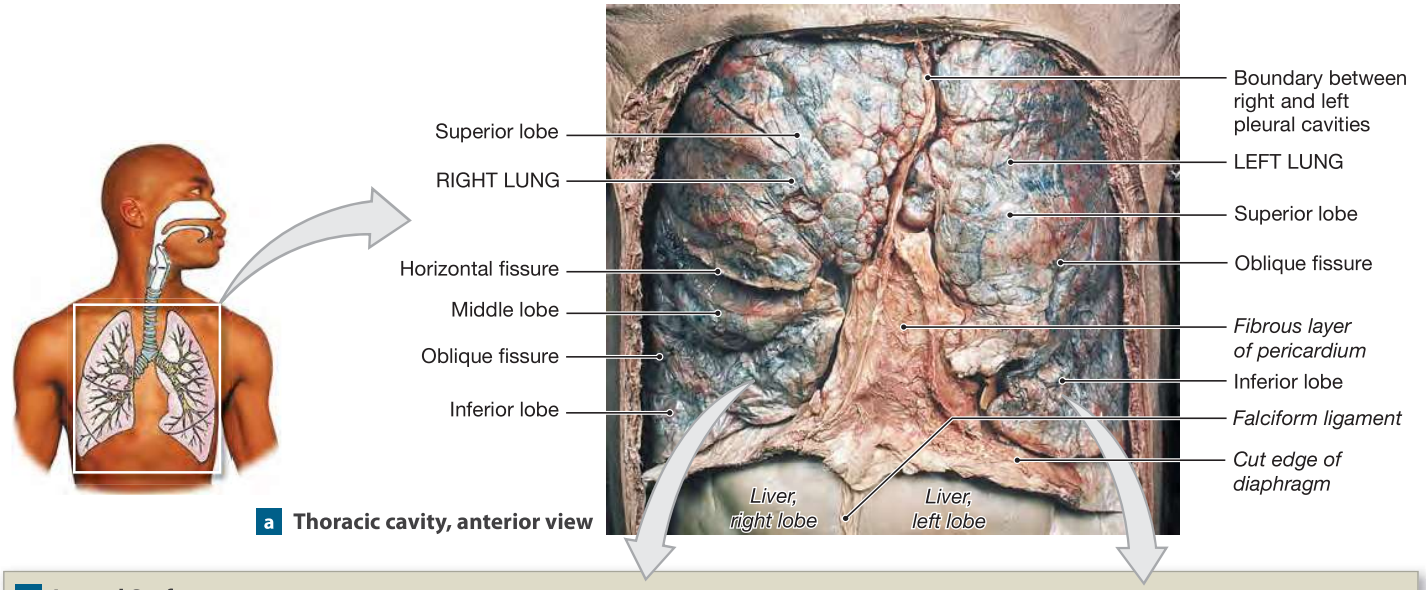
The Bronchi

The primary bronchi and their branches form the **bronchial tree.** Because the left and right primary bronchi are outside the lungs, they are called *extrapulmonary bronchi*. As the primary bronchi enter the lungs, they divide to form smaller passageways (**Figure 23–6a**). The branches within the lungs are collectively called the *intrapulmonary bronchi*.

Each primary bronchus divides to form **secondary bronchi,** also known as *lobar bronchi*. In each lung, one secondary bronchus goes to each lobe, so the right lung has three secondary bronchi, and the left lung has two.

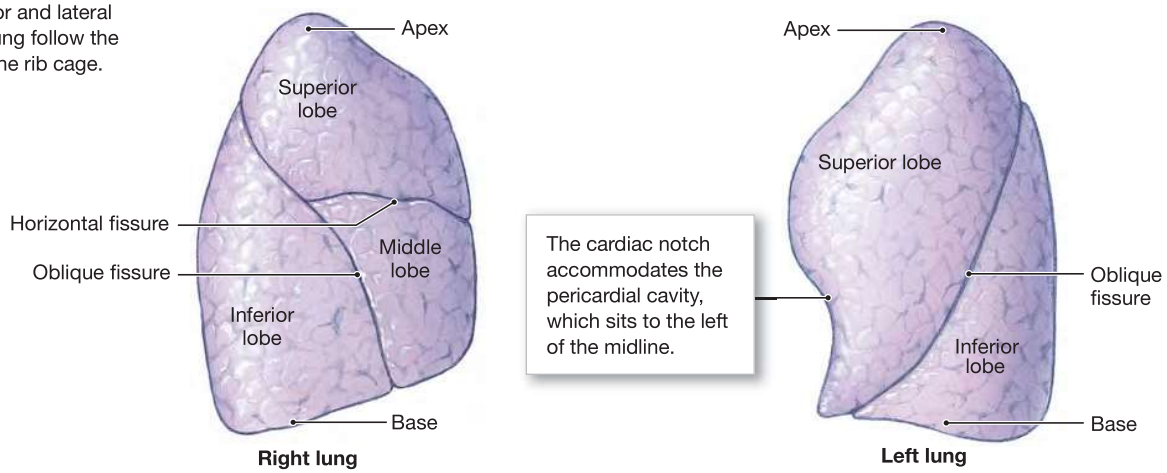
Figure 23–9 depicts the branching pattern of the left primary bronchus as it enters the lung. (The number of branches has been reduced for clarity.) In each lung, the secondary bronchi branch to form **tertiary bronchi,** or *segmental bronchi*. The branching pattern differs between the two lungs, but each tertiary bronchus ultimately supplies air to a single **bronchopulmonary segment,** a specific region of one lung (**Figure 23–9a**). The right lung has 10 bronchopulmonary segments. During development, the left lung also has 10 segments, but adjacent tertiary bronchi fuse, generally reducing the number to eight or nine.

Figure 23–7 The Gross Anatomy of the Lungs. ATLAS: Plates 42–47



b Lateral Surfaces

The curving anterior and lateral surfaces of each lung follow the inner contours of the rib cage.



c Medial Surfaces

The medial surfaces, which contain the hilum, have more irregular shapes. The medial surfaces of both lungs bear grooves that mark the positions of the great vessels and the heart.

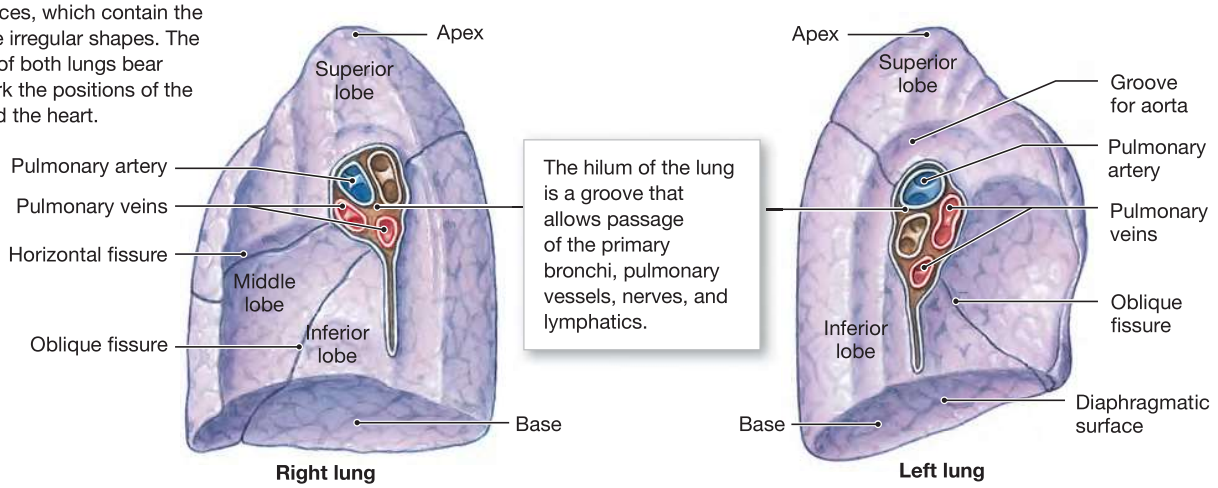
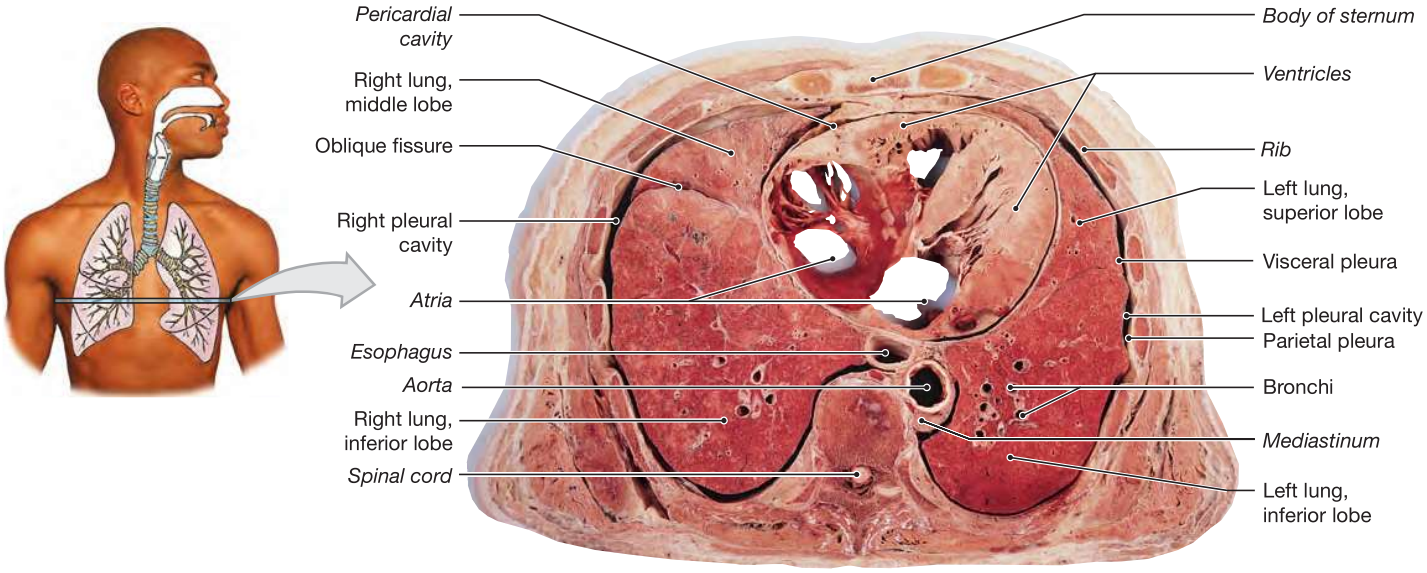


Figure 23–8 The Relationship between the Lungs and Heart. This transverse section was taken at the level of the cardiac notch.



The walls of the primary, secondary, and tertiary bronchi contain progressively less cartilage. In the secondary and tertiary bronchi, the cartilages form plates arranged around the lumen. These cartilages serve the same structural purpose as the rings of cartilage in the trachea and primary bronchi. As the amount of cartilage decreases, the amount of smooth muscle increases. With less cartilaginous support, the amount of tension in those smooth muscles has a greater effect on bronchial diameter and the resistance to airflow. During a respiratory infection, the bronchi and bronchioles can become inflamed and constricted, increasing resistance. In this condition, called **bronchitis,** the individual has difficulty breathing.

The Bronchioles

Each tertiary bronchus branches several times within a bronchopulmonary segment, forming many **bronchioles.** These bronchioles then branch into the finest conducting branches, called **terminal bronchioles.** Roughly 6500 terminal bronchioles arise from each tertiary bronchus. The lumen of each terminal bronchiole has a diameter of 0.3–0.5 mm.

The walls of bronchioles lack cartilage but are dominated by smooth muscle tissue (**Figure 23–9b**). In functional terms, bronchioles are to the respiratory system what arterioles are to the cardiovascular system. Changes in the diameter of the bronchioles control the resistance to airflow and the distribution of air in the lungs.

The autonomic nervous system controls the diameter of the bronchioles. It does so by regulating the activity in the smooth muscle layer. Sympathetic activation leads to **bronchodilation,** the enlargement of the diameter of the airway. Parasympathetic stimulation leads to **bronchoconstriction,** a reduction in the diameter of the airway. Bronchoconstriction also takes place during allergic reactions such as anaphylaxis, in response to histamine released by activated mast cells and basophils. ↩ p. 804

Bronchodilation and bronchoconstriction are ways of adjusting the resistance to airflow. These actions direct airflow toward or away from specific portions of the respiratory exchange surfaces. Tension in the smooth muscles commonly causes the bronchiole mucosa to form a series of folds that limits airflow. Excessive stimulation, as in **asthma** (AZ-muh), can almost completely prevent airflow along the terminal bronchioles.

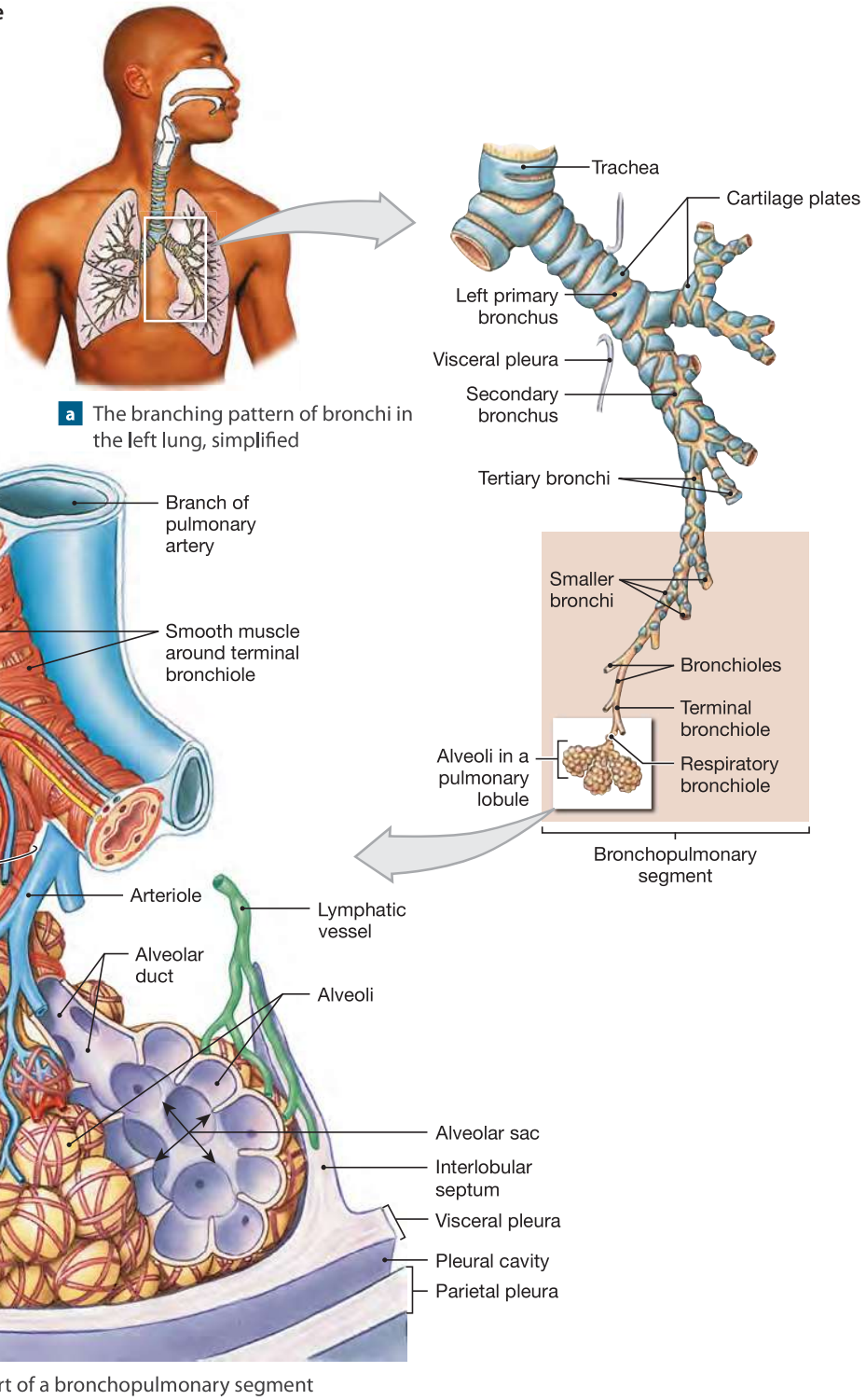
Pulmonary Lobules

The connective tissues of the root of each lung extend into the lung's *parenchyma*, or functional cells). These fibrous partitions, or *trabeculae*, contain elastic fibers, smooth muscles, and lymphatic vessels. The trabeculae branch repeatedly, dividing the lobes into ever-smaller compartments. The branches of the conducting passageways, pulmonary vessels, and nerves of the lungs follow these trabeculae.

The finest partitions, or **interlobular septa** (*septum*, a wall), divide the lung into **pulmonary lobules** (LOB-ūlz). Branches of the pulmonary arteries, pulmonary veins, and respiratory passageways supply each lobule (**Figure 23–9b**). The connective tissues of the septa are, in turn, continuous with those of the *visceral pleura*, the serous membrane covering the lungs.

Each terminal bronchiole delivers air to a single pulmonary lobule. Within the lobule, the terminal bronchiole branches to

Figure 23–9 The Bronchi and Lobules of the Lung. ATLAS: Plates 42b,c; 47b–d



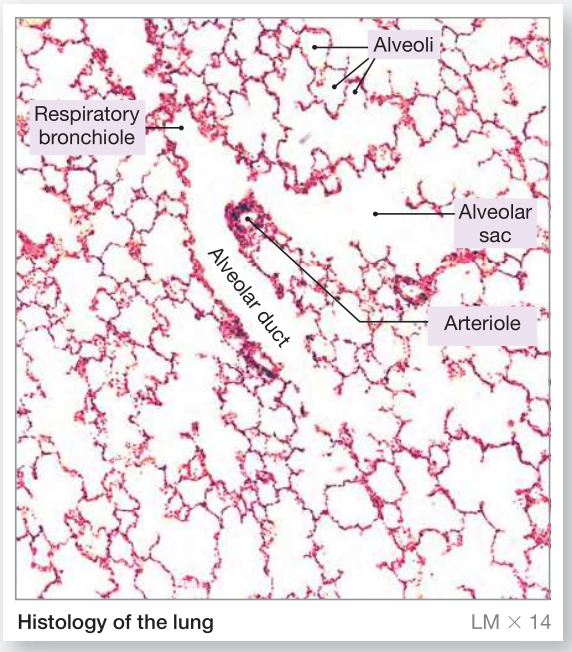
a The branching pattern of bronchi in the left lung, simplified

b The structure of a single pulmonary lobule, part of a bronchopulmonary segment

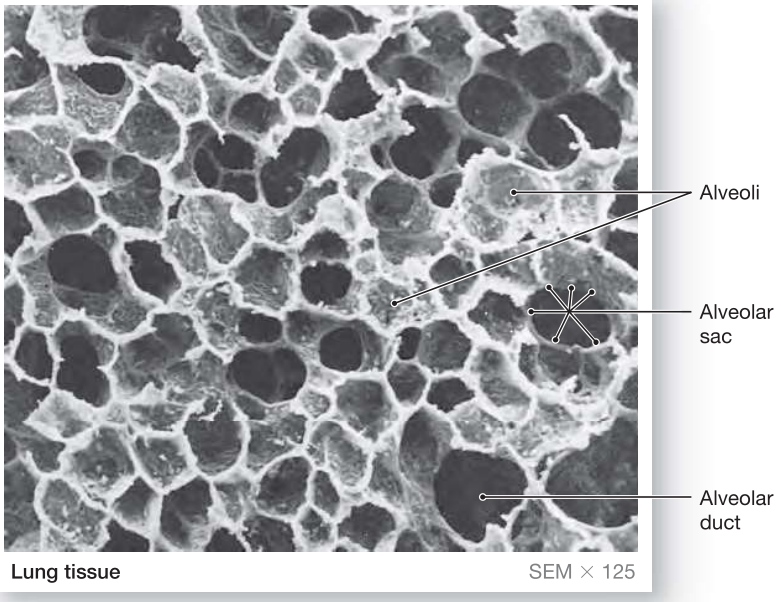
form several **respiratory bronchioles.** The respiratory bronchioles are the thinnest and most delicate branches of the bronchial tree. They deliver air to the gas exchange surfaces of the lungs.

Before incoming air moves beyond the terminal bronchioles, it has been filtered and humidified. A cuboidal epithelium lines the terminal bronchioles and respiratory bronchioles. There are only scattered cilia and no mucous cells or underlying mucous glands. If particulates or pathogens reach this part of the respiratory tract, there is little to prevent them from damaging the delicate exchange surfaces of the lungs.

Figure 23–10 Respiratory Tissue.



a Low power micrograph of lung tissue



b SEM of lung tissue showing the appearance and organization of the alveoli

Alveolar Ducts and Alveoli

Respiratory bronchioles are connected to individual alveoli and to multiple alveoli along regions called **alveolar ducts** (**Figures 23–9b** and **23–10**). Alveolar ducts end at **alveolar sacs,** common chambers connected to multiple individual alveoli. Each lung contains about 150 million alveoli. They give the lungs an open, spongy appearance.

Each alveolus is associated with an extensive network of capillaries (**Figure 23–11a**). A network of elastic fibers surrounds the capillaries. These fibers help maintain the relative positions of the alveoli and respiratory bronchioles. When these fibers recoil during exhalation, they reduce the size of the alveoli and help push air out of the lungs.

The alveolar epithelium consists mainly of simple squamous epithelium (**Figure 23–11b**). The squamous epithelial cells, called **pneumocytes type I,** are unusually thin and are the sites of gas diffusion. Roaming **alveolar macrophages,** or *dust cells,* patrol the epithelial surface. They phagocytize any particles that have eluded other defenses. Large **pneumocytes type II,** also called *septal cells,* are scattered among the squamous cells. The pneumocytes type II produce **surfactant** (sur-FAK-tant), an oily secretion containing phospholipids and proteins. They secrete surfactant onto the alveolar surfaces, where it forms a superficial coating over a thin layer of water.

Tips & Tricks

The term ***surfactant*** is derived from its purpose as a ***surf***ace **act**ive **ag**en***t***.

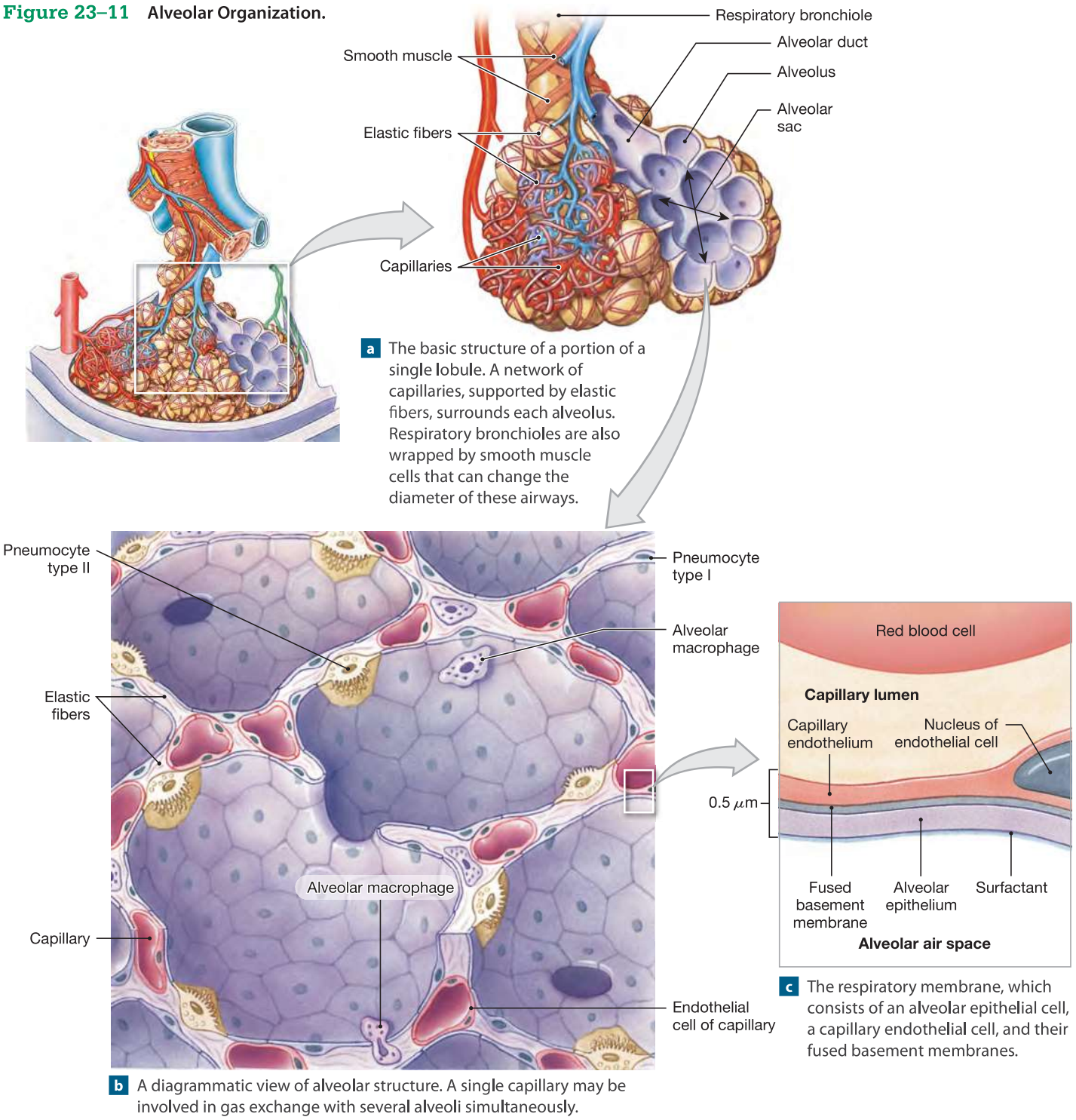
Surfactant plays a key role in keeping the alveoli open. It reduces surface tension in the liquid coating the alveolar surface. Recall from Chapter 2 that *surface tension* results from the attraction between water molecules at an air–water boundary. ↩ p. 33 Surface tension creates a barrier that keeps small objects from entering the water, but it also tends to collapse small air bubbles. Without surfactant, the surface tension would collapse the alveoli in much the same way. Surfactant forms a thin surface layer that interacts with the water molecules, reducing the surface tension and keeping the alveoli open.

If pneumocytes type II produce inadequate amounts of surfactant due to injury or genetic abnormalities, respiration becomes difficult. The alveoli collapse after each exhalation. With each breath, the inhalation must be forceful enough to pop open the alveoli. A person without enough surfactant is soon exhausted by the effort of inflating and deflating the lungs. This condition is called *respiratory distress syndrome*.

Gas exchange occurs across the **respiratory membrane** of the alveoli. The respiratory membrane has three layers (**Figure 23–11c**). It contains (1) the squamous epithelial cells lining the alveolus, (2) the endothelial cells lining an adjacent capillary, and (3) the fused basement membranes that lie between the alveolar and endothelial cells.

At the respiratory membrane, only a very short distance separates alveolar air from blood. The total distance can be as little as 0.1 μm, but averages about 0.5 μm. Diffusion proceeds very rapidly across the respiratory membrane because the distance is short and both oxygen and carbon dioxide are small,

Figure 23–11 **Alveolar Organization.**



a The basic structure of a portion of a single lobule. A network of capillaries, supported by elastic fibers, surrounds each alveolus. Respiratory bronchioles are also wrapped by smooth muscle cells that can change the diameter of these airways.

b A diagrammatic view of alveolar structure. A single capillary may be involved in gas exchange with several alveoli simultaneously.

c The respiratory membrane, which consists of an alveolar epithelial cell, a capillary endothelial cell, and their fused basement membranes.

lipid-soluble molecules. The plasma membranes of the epithelial and endothelial cells do not prevent oxygen and carbon dioxide from moving between blood and alveolar air.

Certain diseases can compromise the function of the respiratory membrane. **Pneumonia** (noo-MŌ-nē-uh) develops from an infection or any other stimulus that causes inflammation of the lobules of the lung. As inflammation occurs, fluids leak into the alveoli. The respiratory bronchioles swell, narrowing passageways and restricting the passage of air. Respiratory function deteriorates as a result. When bacteria are involved, they are generally types that normally inhabit the mouth and pharynx but have managed to evade the respiratory defenses.

Pneumonia becomes more likely when the respiratory defenses have already been compromised by other factors. Such factors include epithelial damage from smoking and the breakdown of the immune system in AIDS. The respiratory defenses of healthy individuals prevent infection and tissue damage, but the breakdown of those defenses in AIDS can lead to a massive, potentially fatal lung infection. The most common pneumonia that develops in individuals with AIDS results from infection by the fungus *Pneumocystis carinii*.

The Blood Supply to the Lungs

Two circuits nourish lung tissue. One supplies the *respiratory* portion of the lungs. The other perfuses the *conducting* portion.

The respiratory exchange surfaces receive blood from arteries of the pulmonary circuit. The pulmonary arteries carry deoxygenated blood. They enter the lungs at the hilum and branch with the bronchi as they approach the lobules. Each lobule receives an arteriole and a venule, and a network of capillaries surrounds each alveolus as part of the respiratory membrane. Oxygen-rich blood from the alveolar capillaries passes through the pulmonary venules and then enters the pulmonary veins, which deliver the blood to the left atrium.

In addition to providing for gas exchange, the endothelial cells of the alveolar capillaries are the primary source of *angiotensin-converting enzyme (ACE)*, which converts circulating angiotensin I to angiotensin II. This enzyme plays an important role in regulating blood volume and blood pressure. ↩ p. 731

The tissues of conducting passageways of your lungs receive oxygen and nutrients from capillaries supplied by the bronchial arteries, which branch from the thoracic aorta. The venous blood from these bronchial capillaries empties into bronchial veins or anastomoses and then into pulmonary veins. Blood flow outside the pulmonary veins bypasses the rest of the systemic circuit and dilutes the oxygenated blood leaving the alveoli.

Blood pressure in the pulmonary circuit is usually low. Systemic pressures in the pulmonary circuit are 30 mm Hg or less. With such pressures, pulmonary vessels can easily become blocked by small blood clots, fat masses, or air bubbles in the pulmonary arteries. Because the lungs receive the entire cardiac output, any such objects drifting in blood are likely to be trapped in the pulmonary arterial or capillary networks. Very small blood clots occasionally form in the venous system. These are usually trapped in the pulmonary capillary network, where they soon dissolve. Larger emboli are much more dangerous. The blockage of a branch of a pulmonary artery stops blood flow to a group of lobules or alveoli. This condition is called **pulmonary embolism.** If a pulmonary embolism is in place for several hours, the alveoli will permanently collapse. If the blockage occurs in a major pulmonary vessel rather than a minor branch, pulmonary resistance increases. The resistance places extra strain on the right ventricle, which may be unable to maintain cardiac output, and congestive heart failure can result.

The Pleural Cavities and Pleural Membranes

The thoracic cavity has the shape of a broad cone. Its walls are the rib cage, and the muscular diaphragm forms its floor. The two **pleural cavities** are separated by the mediastinum (**Figure 23–8**). Each lung is surrounded by a single pleural cavity, which is lined by a serous membrane called the **pleura** (PLOOR-uh; plural, *pleurae*). The pleura consists of two layers: the parietal pleura and the visceral pleura. The **parietal pleura** covers the inner surface of the thoracic wall and extends over the diaphragm and mediastinum. The **visceral pleura** covers the outer surfaces of the lungs, extending into the fissures between the lobes. Each pleural cavity actually represents a potential space rather than an open chamber, because the parietal and visceral pleurae are usually in close contact.

Both pleurae secrete a small amount of **pleural fluid.** Pleural fluid forms a moist, slippery coating that provides lubrication. It reduces friction between the parietal and visceral surfaces as you breathe. Samples of pleural fluid, obtained through a long needle inserted between the ribs, are sometimes needed for diagnostic purposes. This sampling procedure is called *thoracentesis* (thōr-a-sen-TĒ-sis; *thora-*, thoracic + *centesis*, puncture). The extracted fluid is examined for bacteria, blood cells, or other abnormal components.

In some diseases, the normal coating of pleural fluid does not prevent friction between the pleural surfaces. The result is pain and pleural inflammation, a condition called *pleurisy*. When pleurisy develops, the secretion of pleural fluid may be excessive, or the inflamed pleurae may adhere to one another, limiting movement. In either case, breathing becomes difficult, and prompt medical attention is required.

Checkpoint

13. **What would happen to the alveoli if surfactant were not produced?**
14. **Trace the path air takes in flowing from the glottis to the respiratory membrane.**
15. **Which arteries supply blood to the conducting portions and respiratory exchange surfaces of the lungs?**
16. **List the functions of the pleura.**

See the blue Answers tab at the back of the book.

23-6 External respiration and internal respiration allow gaseous exchange within the body

The general term *respiration* includes two integrated processes: *external respiration* and *internal respiration*. The definitions of these terms vary among references. In our discussion, **external respiration** includes all the processes involved in the exchange of oxygen and carbon dioxide between the body's interstitial fluids and the external environment. The purpose of external

respiration, and the primary function of the respiratory system, is to meet the respiratory demands of cells. **Internal respiration** is the absorption of oxygen and the release of carbon dioxide by those cells. We consider the biochemical pathways responsible for oxygen consumption and for the generation of carbon dioxide by mitochondria—pathways known collectively as *cellular respiration*—in Chapter 25.

Our discussion here focuses on three integrated steps in external respiration (**Figure 23–12**):

1. *Pulmonary ventilation*, or breathing, which physically moves air into and out of the lungs.
2. *Gas diffusion* across the respiratory membrane between alveolar air spaces and alveolar capillaries, and across capillary walls between blood and other tissues.
3. *Transport of oxygen and carbon dioxide* between alveolar capillaries and capillary beds in other tissues.

Abnormalities affecting any of the steps involved in external respiration ultimately affect the concentrations of gases in interstitial fluids, and thus cellular activities as well. If the oxygen level declines, the affected tissues will become starved for oxygen. **Hypoxia,** or low tissue oxygen levels, places severe limits on the metabolic activities of the affected area. For example, the effects of coronary ischemia result from chronic hypoxia affecting cardiac muscle cells. ↩ p. 682 If the oxygen supply is cut off completely, the condition called **anoxia** (an-OK-sē-uh; *a-*, without + *ox-*, oxygen) results. Anoxia kills cells very quickly. Much of the damage from strokes and heart attacks results from local anoxia.

In the sections that follow, we examine each of the processes involved in external respiration in greater detail.

Checkpoint

17. **Define external respiration and internal respiration.**
18. **Name the integrated steps involved in external respiration.**

See the blue Answers tab at the back of the book.

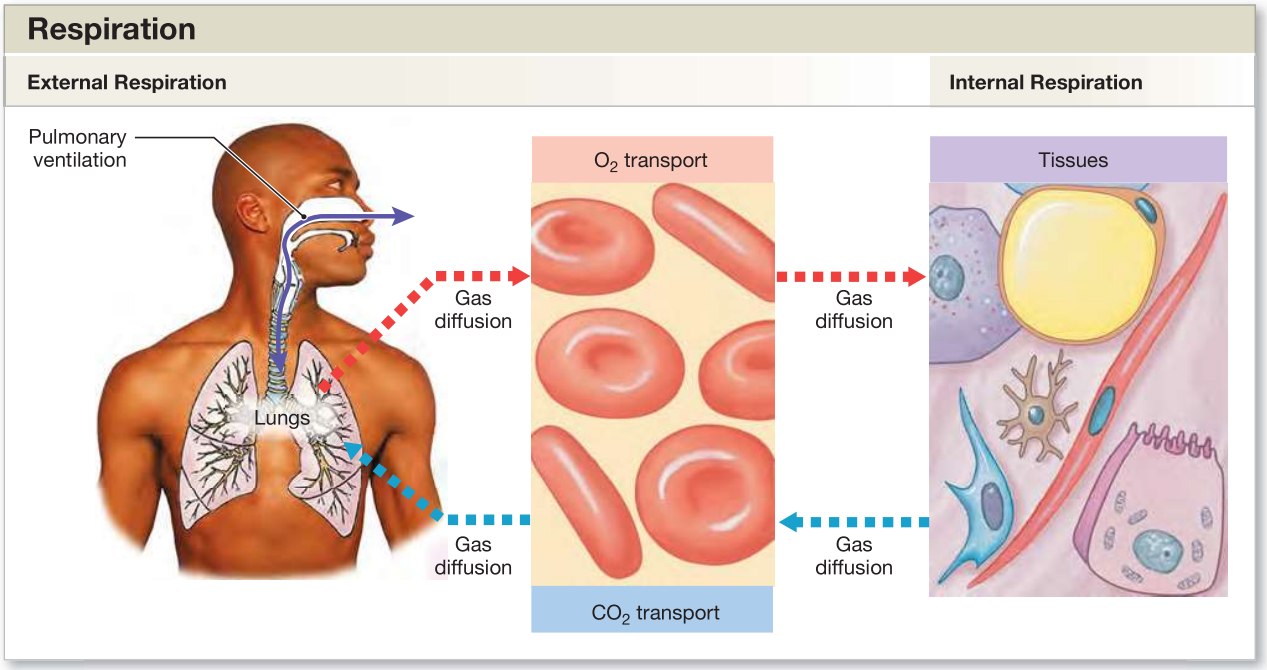
23-7 Pulmonary ventilation—the exchange of air between the atmosphere and the lungs—involves pressure changes, muscle movement, and respiratory rates and volumes

Pulmonary ventilation is the physical movement of air into and out of the respiratory tract. Its primary function is to maintain adequate *alveolar ventilation*—movement of air into and out of the alveoli. Alveolar ventilation prevents the buildup of carbon dioxide in the alveoli. It also ensures a continuous supply of oxygen that keeps pace with absorption by the bloodstream.

The Movement of Air

Some basic physical principles govern the movement of air. One of the most basic is that the weight of Earth's atmosphere

Figure 23–12 An Overview of the Key Steps in Respiration.



compresses our bodies and everything around us. This **atmospheric pressure** has several important physiological effects. For example, air moves into and out of the respiratory tract as the air pressure in the lungs cycles between below atmospheric pressure and above atmospheric pressure.

Gas Pressure and Volume (Boyle's Law)

The primary differences between liquids and gases reflect the interactions among individual molecules. The molecules in a liquid are in constant motion, but they are held closely together by weak interactions, such as the hydrogen bonding between adjacent water molecules. ↩ p. 33 Yet because the electrons of adjacent atoms tend to repel one another, liquids tend to resist compression. If you squeeze a balloon filled with water, it will distort into a different shape, but the volumes of the two shapes will be the same.

In a gas, such as air, the molecules bounce around as independent objects. At normal atmospheric pressures, gas molecules are much farther apart than the molecules in a liquid. The forces acting between gas molecules are minimal because the molecules are too far apart for weak interactions to take place, so an applied pressure can push them closer together. Consider a sealed container of air at atmospheric pressure. The pressure exerted by the gas inside results from gas molecules bumping into the walls of the container. The greater the number of collisions, the higher the pressure.

You can change the gas pressure within a sealed container by changing the volume of the container, giving the gas molecules more or less room in which to bounce around. If you decrease the volume of the container, pressure rises (**Figure 23–13a**). If you increase the volume of the container, pressure falls (**Figure 23–13b**).

For a gas in a closed container and at a constant temperature, pressure *(P)* is inversely proportional to volume *(V)*. That is, *if you decrease the volume of a gas, its pressure will rise. If you increase the volume of a gas, its pressure will fall*. In particular, the relationship between pressure and volume is reciprocal: If you double the external pressure on a flexible container, its volume will drop by half, and if you reduce the external pressure by half, the volume of the container will double. This relationship, $P = 1/V$, is called **Boyle's law** because it was first recognized by Robert Boyle in the 1600s.

Pressure and Airflow to the Lungs

Air flows from an area of higher pressure to an area of lower pressure. This tendency for directed airflow, plus the pressure–volume relationship of Boyle's law, provides the basis for pulmonary ventilation. A single respiratory cycle consists of an *inspiration*, or inhalation, and an *expiration*, or exhalation. Inhalation and exhalation involve changes in the volume of the lungs. These volume changes create pressure gradients that move air into or out of the respiratory tract.

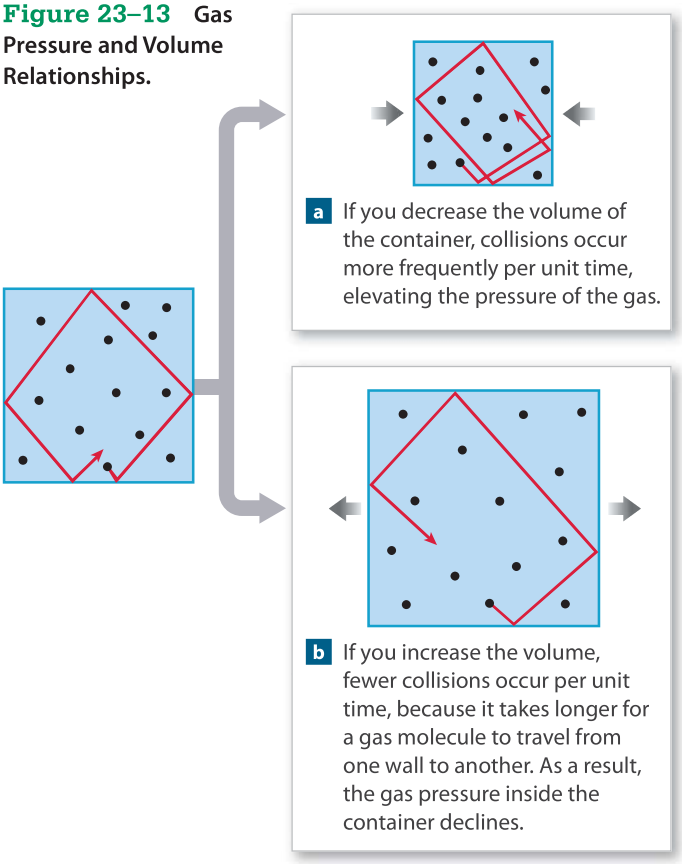


Figure 23–13 Gas Pressure and Volume Relationships.

Each lung is surrounded by a pleural cavity. The parietal and visceral pleurae are separated by only a thin film of pleural fluid. The two membranes can slide across one another, but they are held together by that fluid film. You can see the same principle when you set a wet glass on a smooth tabletop. You can slide the glass easily, but when you try to lift it, you feel considerable resistance. As you pull the glass away from the tabletop, you create a powerful suction. The only way to overcome it is to tilt the glass so that air is pulled between the glass and the table, breaking the fluid bond.

A comparable fluid bond exists between the parietal pleura and the visceral pleura covering the lungs. For this reason, the surface of each lung sticks to the inner wall of the chest and to the superior surface of the diaphragm. Movements of the diaphragm or rib cage that change the volume of the thoracic cavity also change the volume of the lungs (**Figure 23–14a**):

- The diaphragm forms the floor of the thoracic cavity. The relaxed diaphragm has the shape of a dome that projects superiorly into the thoracic cavity. When the diaphragm contracts, it tenses and moves inferiorly. This movement increases the volume of the thoracic cavity, reducing the pressure within it. When the diaphragm relaxes, it returns to its original position, and the volume of the thoracic cavity decreases.

- Due to the nature of the articulations between the ribs and the vertebrae, superior movement of the rib cage increases the depth and width of the thoracic cavity, increasing its volume. Inferior movement of the rib cage reverses the process, reducing the volume of the thoracic cavity.

At the start of a breath, pressures inside and outside the thoracic cavity are identical, and no air moves into or out of the lungs (**Figure 23–14b**). When the thoracic cavity enlarges, the lungs expand to fill the additional space (**Figure 23–14c**). This increase in volume lowers the pressure inside the lungs. Air then enters the respiratory passageways, because the pressure inside the lungs (P_{inside}) is lower than atmospheric pressure ($P_{outside}$). Air continues to enter the lungs until their volume stops increasing and the internal pressure is the same as that outside. When the thoracic cavity decreases in volume, pressures rise inside the lungs, forcing air out of the respiratory tract (**Figure 23–14d**).

Compliance

The **compliance** of the lungs is an indication of their expandability, or how easily the lungs expand. The lower the compliance, the greater the force required to fill the lungs. The greater the compliance, the easier it is to fill the lungs. Factors affecting compliance include the following:

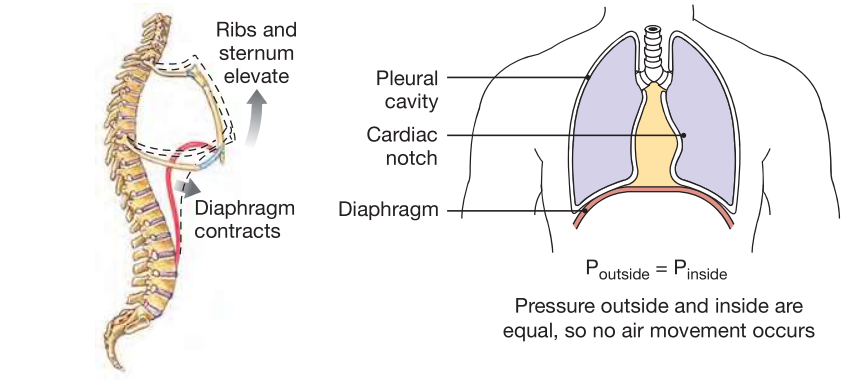
- *The Connective Tissue of the Lungs.* The loss of supporting tissues due to alveolar damage, as in *emphysema*, increases compliance.
- *The Level of Surfactant Production.* On exhalation, the collapse of alveoli due to inadequate surfactant, as in respiratory distress syndrome, reduces compliance.
- *The Mobility of the Thoracic Cage.* Arthritis or other skeletal disorders that affect the articulations of the ribs or spinal column also reduce compliance.

At rest, the muscular activity involved in pulmonary ventilation accounts for 3–5 percent of the resting energy demand. If compliance is reduced, that figure climbs dramatically. An individual may become exhausted simply trying to continue breathing.

Pressure Changes during Inhalation and Exhalation

To understand the mechanics of respiration and the principles of gas exchange, we must know the pressures inside and outside the respiratory tract. We can report pressure readings in several ways (**Table 23–1**). In this text, we use millimeters of mercury (mm Hg), as we did for blood pressure. Atmospheric pressure is also measured in *atmospheres*. One atmosphere of pressure (1 *atm*) is equivalent to 760 mm Hg.

Figure 23–14 Mechanisms of Pulmonary Ventilation.



a As the rib cage is elevated or the diaphragm is depressed, the volume of the thoracic cavity increases.

b At rest.

c **Inhalation.** Elevation of the rib cage and contraction of the diaphragm increase the size of the thoracic cavity. Pressure within the thoracic cavity decreases, and air flows into the lungs.

d **Exhalation.** When the rib cage returns to its original position and the diaphragm relaxes, the volume of the thoracic cavity decreases. Pressure rises, and air moves out of the lungs.

Table 23–1 The Four Most Common Methods of Reporting Gas Pressures

millimeters of mercury (mm Hg): This is the most common method of reporting blood pressure and gas pressures. Normal atmospheric pressure is approximately 760 mm Hg.
torr: This unit of measurement is preferred by many respiratory therapists; it is also commonly used in Europe and in some technical journals. One torr is equivalent to 1 mm Hg; in other words, normal atmospheric pressure is equal to 760 torr.
centimeters of water (cm H_2O): In a hospital setting, anesthetic gas pressures and oxygen pressures are commonly measured in centimeters of water. One cm H_2O is equivalent to 0.735 mm Hg; normal atmospheric pressure is 1033.6 cm H_2O.
pounds per square inch (psi): Pressures in compressed gas cylinders and other industrial applications are generally reported in psi. Normal atmospheric pressure at sea level is approximately 15 psi.

The Intrapulmonary Pressure

The direction of airflow is determined by the relationship between atmospheric pressure and intrapulmonary pressure. **Intrapulmonary** (in-tra-PUL-mo-nār-ē) **pressure,** or **intra-alveolar** (in-tra-al-VĒ-ō-lar) **pressure,** is the pressure inside the respiratory tract, at the alveoli.

When you are relaxed and breathing quietly, the difference between atmospheric pressure and intrapulmonary pressure is relatively small. On inhalation, your lungs expand, and the intrapulmonary pressure drops to about 759 mm Hg. Because the intrapulmonary pressure is 1 mm Hg below atmospheric pressure, it is generally reported as −1 mm Hg. On exhalation, your lungs recoil, and intrapulmonary pressure rises to 761 mm Hg, or +1 mm Hg (**Figure 23–15a**).

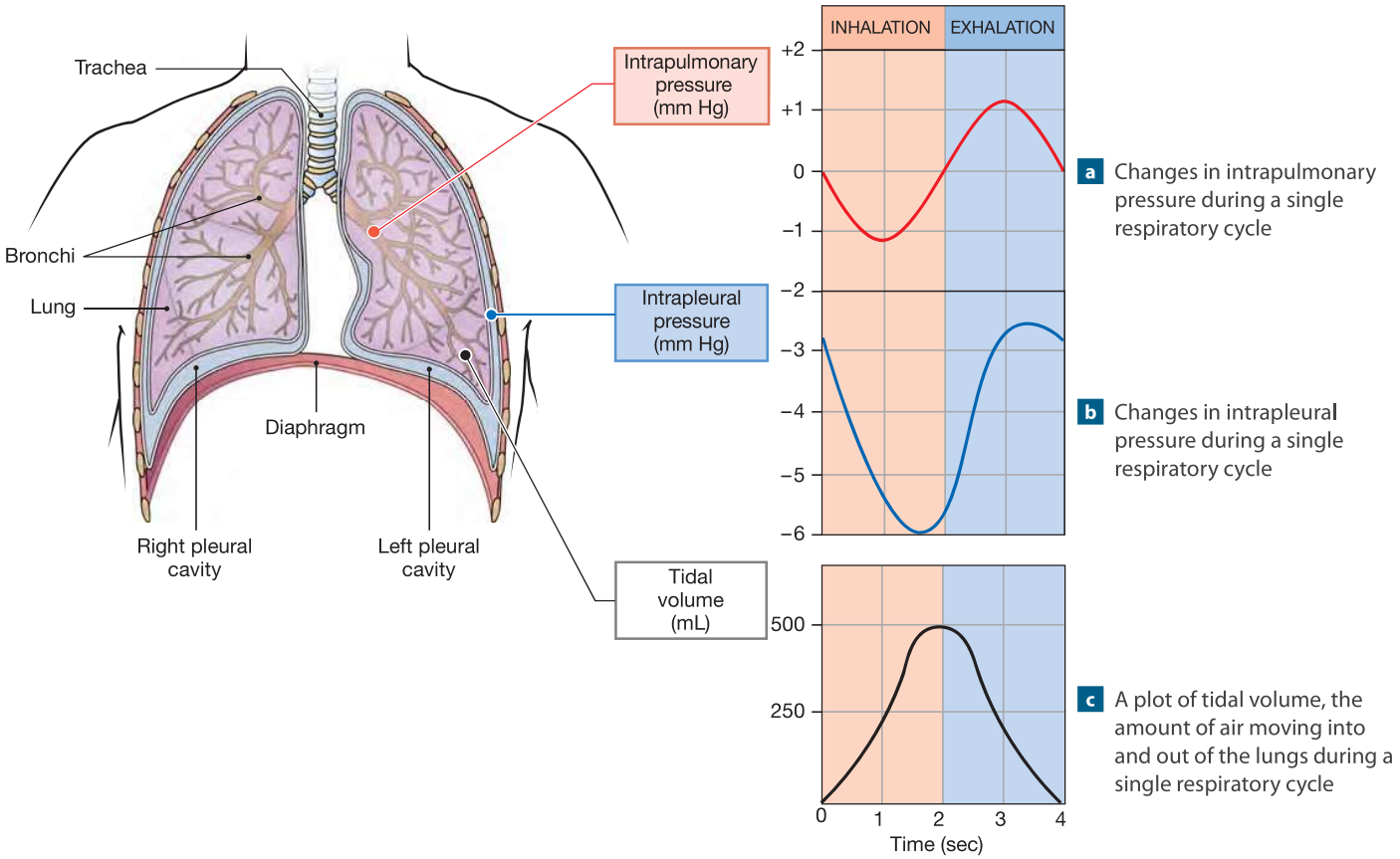
The size of the pressure gradient increases when you breathe heavily. When a trained athlete breathes at maximum capacity, the pressure differentials can reach −30 mm Hg during inhalation and +100 mm Hg if the individual is straining with the glottis kept closed. This is one reason you are told to exhale while lifting weights. Exhaling keeps your intrapulmonary pressures and peritoneal pressure from climbing so high that an alveolar rupture or hernia could occur.

The Intrapleural Pressure

Intrapleural pressure is the pressure in the pleural cavity, between the parietal and visceral pleurae. Intrapleural pressure averages about −4 mm Hg (**Figure 23–15b**). During a powerful inhalation, it can reach −18 mm Hg. This pressure is below atmospheric pressure, due to the relationship between the lungs and the body wall. Earlier, we noted that the lungs are highly elastic. In fact, they would collapse to about 5 percent of their normal resting volume if their elastic fibers could recoil completely. The elastic fibers cannot recoil so much, however. The reason is that they are not strong enough to overcome the fluid bond between the parietal and visceral pleurae.

The elastic fibers continuously oppose that fluid bond and pull the lungs away from the chest wall and diaphragm, lowering the intrapleural pressure slightly. The elastic fibers remain stretched even after a full exhalation. For this reason, intrapleural pressure remains below atmospheric pressure throughout normal cycles of inhalation and exhalation. The cyclical changes in the intrapleural pressure create the *respiratory pump* that assists the venous return to the heart.
↩ p. 722

Figure 23–15 Pressure and Volume Changes during Inhalation and Exhalation. One sequence of inhalation and exhalation constitutes a respiratory cycle.



The Respiratory Cycle

A **respiratory cycle** is a single cycle of inhalation and exhalation. The curves in **Figure 23–15a,b** show the intrapulmonary and intrapleural pressures during a single respiratory cycle of an individual at rest. The graph in **Figure 23–15c** plots the **tidal volume,** the amount of air you move into or out of your lungs during a single respiratory cycle.

Tips & Tricks

Tidal volume floods and ebbs like the ocean *tides*.

At the start of the respiratory cycle, the intrapulmonary and atmospheric pressures are equal, and no air is moving. Inhalation begins with the fall of intrapleural pressure that takes place when the thoracic cavity expands. This pressure gradually falls to approximately −6 mm Hg. Over the period, intrapulmonary pressure drops to just under −1 mm Hg. It then begins to rise as air flows into the lungs.

When exhalation begins, intrapleural and intrapulmonary pressures rise rapidly, forcing air out of the lungs. At the end of exhalation, air again stops moving when the difference between intrapulmonary and atmospheric pressures has been eliminated. The amount of air moved into the lungs during inhalation equals the amount moved out of the lungs during exhalation. That amount is the tidal volume.

The Mechanics of Breathing

As we have just seen, you move air into and out of the respiratory system by changing the volume of the lungs. Those changes alter the pressure relationships, producing air movement. The changes of volume in the lungs take place through the contraction of skeletal muscles—specifically, those that insert on the rib cage—and the *diaphragm*, which separates the thoracic and abdominopelvic cavities. Because of the nature of their articulations with the vertebrae, when the ribs are elevated they swing outward, increasing the depth of the thoracic cavity. ↩ p. 227 We can compare this movement to raising the handle of a bucket (**Figure 23–16a**).

Clinical Note

Pneumothorax Air can enter the pleural cavity due to an injury to the chest wall that penetrates the parietal pleura, or a rupture of the alveoli that breaks through the visceral pleura. This condition, called **pneumothorax** (noo-mō-THOR-aks; *pneumo-*, air), breaks the fluid bond between the pleurae and allows the elastic fibers to recoil, resulting in a "collapsed lung," or **atelectasis** (at-e-LEK-ta-sis; *atel-*, imperfect or incomplete + *ectasia*, distention). The opposite lung is not affected due to compartmentalization. The treatment for a collapsed lung involves removing as much of the air as possible from the affected pleural cavity and then sealing the opening. This treatment lowers the intrapleural pressure and reinflates the lung.

The Respiratory Muscles

We introduced the skeletal muscles involved in respiratory movements in Chapter 11. Of those muscles, the most important are the *diaphragm* and the *external intercostal muscles*. ↩ pp. 342–343, 345 These muscles are active during normal breathing at rest. The **accessory respiratory muscles** become active when the depth and frequency of respiration must be increased markedly. These muscles include the *internal intercostal*, *sternocleidomastoid*, *serratus anterior*, *pectoralis minor*, *scalene*, *transversus thoracis*, *transversus abdominis*, *external* and *internal oblique*, and *rectus abdominis muscles* (**Figure 23–16b–d**). ↩ pp. 337, 342, 348

Muscles Used in Inhalation. Inhalation is an active process. It involves one or more of the following actions:

- Contraction of the diaphragm flattens the floor of the thoracic cavity, increasing its volume and drawing air into the lungs. Contraction of the diaphragm brings about roughly 75 percent of the air movement in normal breathing at rest.
- Contraction of the external intercostal muscles assists in inhalation by raising the ribs. This action contributes roughly 25 percent of the volume of air in the lungs at rest.
- Contraction of accessory muscles, including the sternocleidomastoid, serratus anterior, pectoralis minor, and scalene muscles, can assist the external intercostal muscles in elevating the ribs. These muscles increase the speed and amount of rib movement.

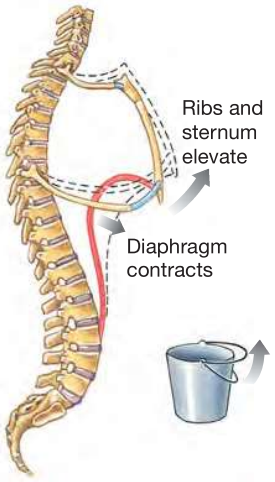
Muscles Used in Exhalation. Exhalation is either passive or active, depending on the level of respiratory activity. When exhalation is active, it may involve one or more of the following actions:

- The internal intercostal and transversus thoracic muscles depress the ribs. This action reduces the width and depth of the thoracic cavity.
- The abdominal muscles, including the external and internal oblique, transversus abdominis, and rectus abdominis muscles, can assist the internal intercostal muscles in exhalation by compressing the abdomen. This action forces the diaphragm upward.

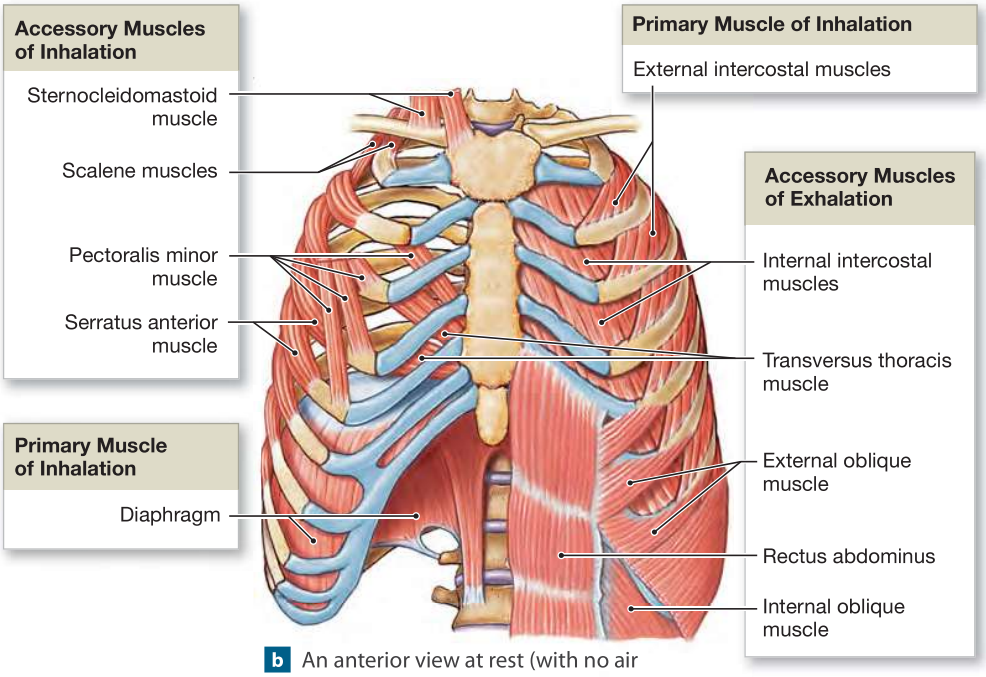
Modes of Breathing

We use the respiratory muscles in various combinations, depending on the volume of air that must be moved into or out of the system. We usually classify respiratory movements as *quiet breathing* or *forced breathing* according to the pattern of muscle activity during a single respiratory cycle.

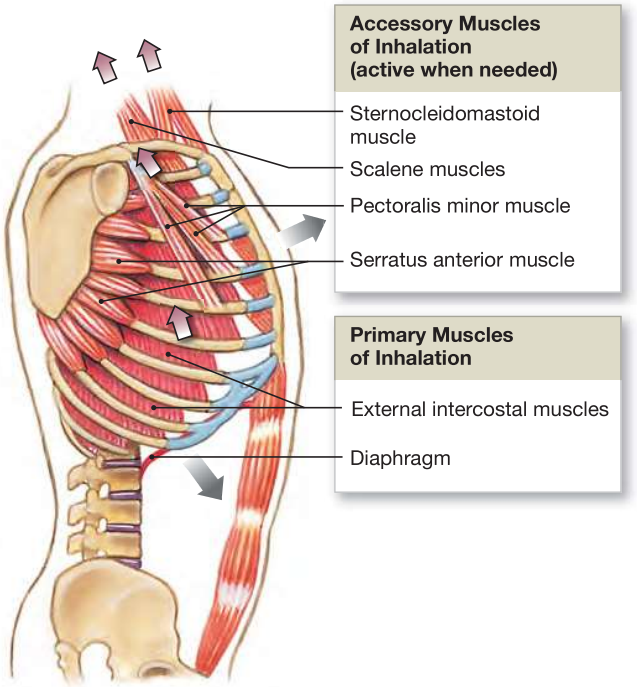
Figure 23–16 The Respiratory Muscles.



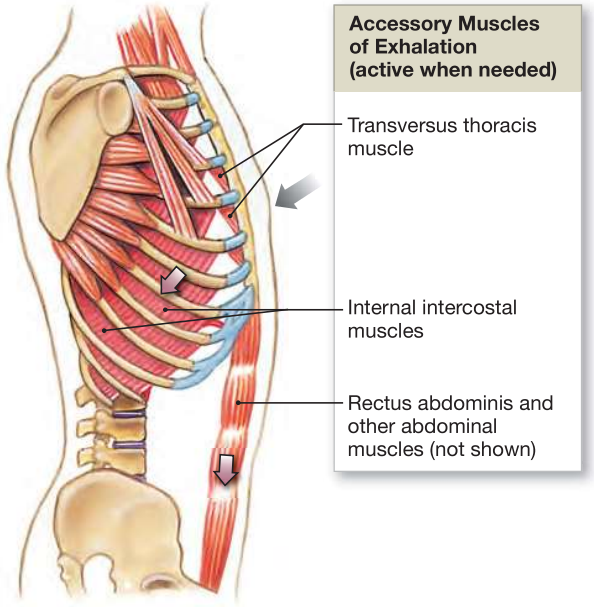
a Movements of the ribs and diaphragm that increase the volume of the thoracic cavity. Diaphragmatic movements were also illustrated in *Figure 23–14*.



b An anterior view at rest (with no air movement), showing the primary and accessory respiratory muscles.



c **Inhalation.** A lateral view during inhalation, showing the muscles that elevate the ribs.



d **Exhalation.** A lateral view during exhalation, showing the muscles that depress the ribs. The abdominal muscles that assist in exhalation are represented by a single muscle (the rectus abdominis).

Quiet Breathing. In **quiet breathing,** or **eupnea** (ŪP-nē-uh; *eu-*, true or normal + *-pnea*, respiration), inhalation involves muscular contractions, but exhalation is a passive process. Inhalation usually involves contracting both the diaphragm and the external intercostal muscles. The relative contributions of these muscles can vary:

- During **diaphragmatic breathing,** or **deep breathing,** contraction of the diaphragm provides the necessary change in thoracic volume. Air is drawn into the lungs as the diaphragm contracts. Air is exhaled passively when the diaphragm relaxes.
- In **costal breathing,** or **shallow breathing,** the thoracic volume changes because the rib cage alters its shape. Inhalation takes place when contractions of the external intercostal muscles raise the ribs and enlarge the thoracic cavity. Exhalation takes place passively when these muscles relax.

During quiet breathing, expansion of the lungs stretches their elastic fibers. In addition, elevation of the rib cage stretches opposing skeletal muscles and elastic fibers in the connective tissues of the body wall. When the muscles of inhalation relax, these elastic components recoil, returning the diaphragm, the rib cage, or both to their original positions. This action is called **elastic rebound.**

We typically use diaphragmatic breathing at minimal levels of activity. As we need increased volumes of air, our inspiratory movements become larger and the contribution of rib movement increases. Even when we are at rest, costal breathing can predominate when abdominal pressures, fluids, or masses restrict diaphragmatic movements. For example, pregnant women rely more and more on costal breathing as the enlarging uterus pushes the abdominal organs against the diaphragm.

Forced Breathing. **Forced breathing,** or **hyperpnea** (hī-PERP-nē-uh), involves active inspiratory and expiratory movements. In forced breathing, our accessory muscles assist with inhalation, and exhalation involves contraction of the internal intercostal muscles. At absolute maximum levels of forced breathing, our abdominal muscles take part in exhalation. Their contraction compresses the abdominal contents, pushing them up against the diaphragm. This action further reduces the volume of the thoracic cavity.

Respiratory Rates and Volumes

The respiratory system is extremely adaptable. You can be breathing slowly and quietly one moment, rapidly and deeply the next. The respiratory system adapts to meet the oxygen demands of the body by varying both the number of breaths per minute and the amount of air moved per breath. When you exercise at peak levels, the amount of air moving into and out of the respiratory tract can be 50 times the amount moved at rest.

Respiratory Rate

Your **respiratory rate** is the number of breaths you take each minute. As you read this, you are probably breathing quietly, with a low respiratory rate. The normal respiratory rate of a resting adult ranges from 12 to 18 breaths each minute, roughly one for every four heartbeats. Children breathe more rapidly, at rates of about 18–20 breaths per minute.

The Respiratory Minute Volume

We can calculate the amount of air moved each minute, symbolized $\dot{V}_E$, by multiplying the respiratory rate f by the tidal volume V_T. This value is called the **respiratory minute volume.** The respiratory rate at rest averages 12 breaths per minute, and the tidal volume at rest averages around 500 mL per breath. On that basis, we calculate the respiratory minute volume as follows:

$$\dot{V}_E = f \times V_T$$

$$\begin{pmatrix}\text{volume of air moved}\\ \text{each minute}\end{pmatrix} = \begin{pmatrix}\text{breaths per}\\ \text{minute}\end{pmatrix} \times \begin{pmatrix}\text{tidal}\\ \text{volume}\end{pmatrix}$$

$$= 12 \text{ per minute} \times 500 \text{ mL}$$

$$= 6000 \text{ mL per minute}$$

$$= 6.0 \text{ liters per minute}$$

In other words, the respiratory minute volume at rest is approximately 6 liters (1.6 gallons) per minute.

Alveolar Ventilation

The respiratory minute volume measures pulmonary ventilation. It provides an indication of how much air is moving into and out of the respiratory tract. However, only some of the inhaled air reaches the alveolar exchange surfaces. A typical inhalation pulls about 500 mL of air into the respiratory system. The first 350 mL of inhaled air travels along the conducting passageways and enters the alveolar spaces. The last 150 mL of inhaled air never gets that far. It stays in the conducting passageways and thus does not participate in gas exchange with blood. The volume of air in the conducting passages is known as the **anatomic dead space,** denoted V_D.

Alveolar ventilation, symbolized $\dot{V}_A$, is the amount of air reaching the alveoli each minute. The alveolar ventilation is less than the respiratory minute volume, because some of the air never reaches the alveoli, but instead remains in the dead space of the lungs. We can calculate alveolar ventilation by subtracting the dead space from the tidal volume:

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

$$\begin{pmatrix}\text{alveolar}\\ \text{ventilation}\end{pmatrix} = \begin{pmatrix}\text{breaths}\\ \text{per minute}\end{pmatrix} \times \begin{pmatrix}\text{tidal}\\ \text{volume}\end{pmatrix} - \begin{pmatrix}\text{anatomic}\\ \text{dead space}\end{pmatrix}$$

At rest, alveolar ventilation rates are approximately 4.2 liters per minute (12 per minute × 350 mL). However, the gas arriving in the alveoli is significantly different from the surrounding atmosphere. The reason is that inhaled air always mixes with

"used" air in the conducting passageways (the anatomic dead space) on its way in. The air in alveoli thus contains less oxygen and more carbon dioxide than does atmospheric air.

Relationships among V_T, $\dot{V}_E$, and $\dot{V}_A$

The respiratory minute volume can be increased by increasing either the tidal volume or the respiratory rate. In other words, you can breathe more deeply or more quickly or both. Under maximum stimulation, the tidal volume can increase to roughly 4.8 liters. At peak respiratory rates of 40–50 breaths per minute and maximum cycles of inhalation and exhalation, the respiratory minute volume can approach 200 liters (about 55 gal) per minute.

In functional terms, the alveolar ventilation rate is more important than the respiratory minute volume, because it determines the rate of delivery of oxygen to the alveoli. The respiratory rate and the tidal volume together determine the alveolar ventilation rate:

- For a given respiratory rate, increasing the tidal volume (breathing more deeply) increases the alveolar ventilation rate.
- For a given tidal volume, increasing the respiratory rate (breathing more quickly) increases the alveolar ventilation rate.

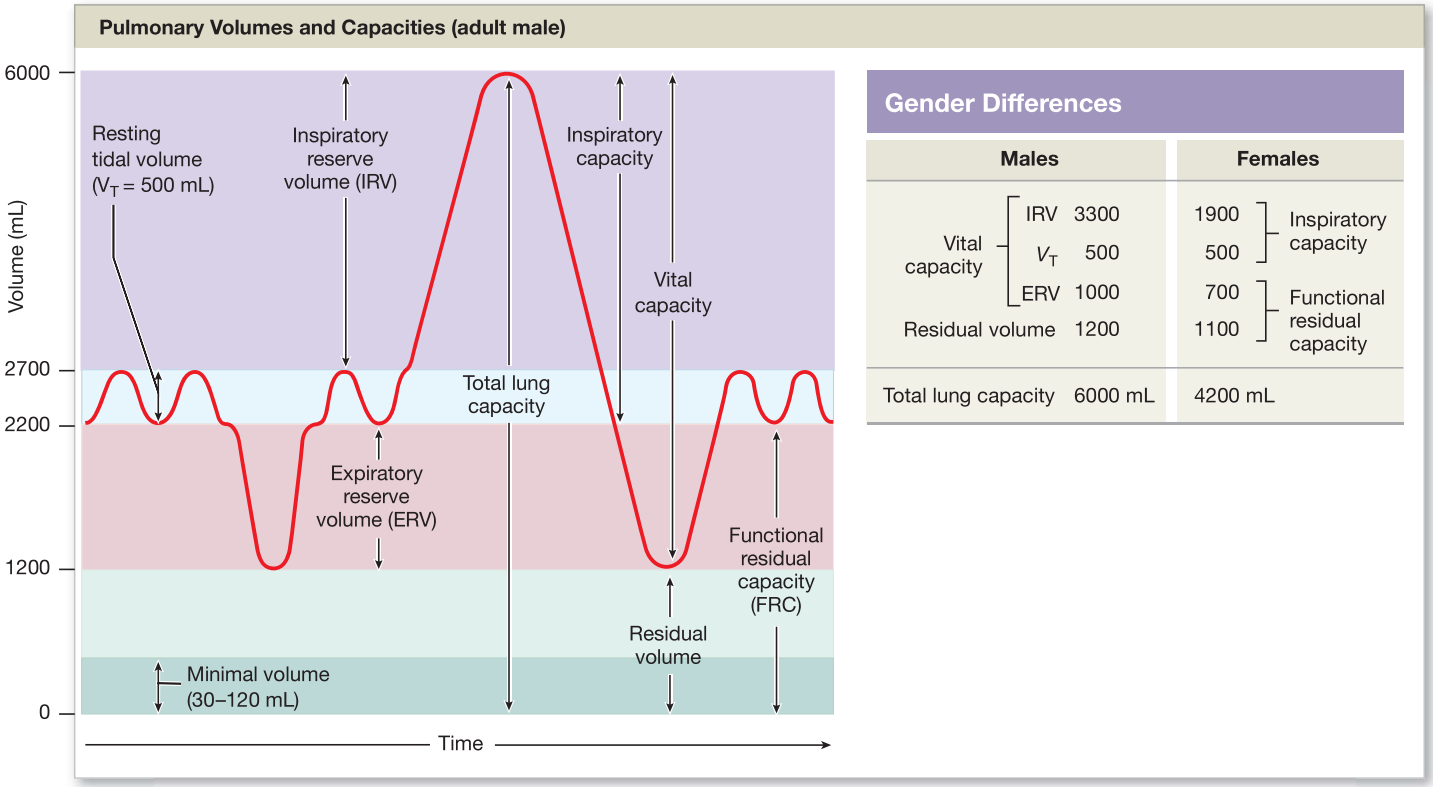
The alveolar ventilation rate can change independently of the respiratory minute volume. In our previous example, the respiratory minute volume at rest was 6 liters and the alveolar ventilation rate was 4.2 L/min. If the respiratory rate rises to 20 breaths per minute, but the tidal volume drops to 300 mL, the respiratory minute volume remains the same ($20 \times 300 = 6000$). However, the alveolar ventilation rate drops to only 3 L/min ($20 \times [300 - 150] = 3000$). For this reason, whenever the demand for oxygen increases, both the tidal volume *and* the respiratory rate must be regulated closely. (We focus on the mechanisms involved in a later section.)

Respiratory Performance and Volume Relationships

We exchange only a small proportion of the air in our lungs during a single quiet respiratory cycle. We can increase the tidal volume by inhaling more vigorously and exhaling more completely.

We can divide the total volume of the lungs into a series of *volumes* and *capacities* (each the sum of various volumes), as indicated in **Figure 23–17**. These measurements are obtained by an instrument called a **spirometer.** Spirometry values are useful in diagnosing problems with pulmonary ventilation. Adult females, on average, have smaller bodies and thus smaller lung volumes than do males. As a result, there are sex-related differences in respiratory volumes and capacities. The table in the figure shows representative values for both sexes.

Figure 23–17 **Pulmonary Volumes and Capacities.** The red line indicates the volume of air within the lung as respiratory movements are performed.



Pulmonary volumes include the following:

- The **resting tidal volume (V_t)** is the amount of air you move into or out of your lungs during a single respiratory cycle under resting conditions. The resting tidal volume averages about 500 mL in both males and females.
- The **expiratory reserve volume (ERV)** is the amount of air that you can voluntarily expel after you have completed a normal, quiet respiratory cycle. As an example, with maximum use of the accessory muscles, males can expel an additional 1000 mL of air, on average. Female expiratory reserve volume averages 700 mL.
- The **residual volume** is the amount of air that remains in your lungs even after a maximal exhalation—typically about 1200 mL in males and 1100 mL in females. The **minimal volume,** a component of the residual volume, is the amount of air that would remain in your lungs if they were allowed to collapse. The minimal volume ranges from 30 to 120 mL. Unlike other volumes, it cannot be measured in a healthy person. The minimal volume and the residual volume are very different, because the fluid bond between the lungs and the chest wall normally prevents the recoil of the elastic fibers in the lungs. Some air remains in the lungs, even at minimal volume, because the surfactant coating the alveolar surfaces prevents their collapse.
- The **inspiratory reserve volume (IRV)** is the amount of air that you can take in over and above the tidal volume. On average, the lungs of males are larger than those of females. For this reason, the inspiratory reserve volume of males averages 3300 mL, compared with 1900 mL in females.

We can calculate respiratory capacities by adding the values of various volumes. Examples include the following:

- The **inspiratory capacity** is the amount of air that you can draw into your lungs after you have completed a quiet respiratory cycle. The inspiratory capacity is the sum of the tidal volume and the inspiratory reserve volume.
- The **functional residual capacity (FRC)** is the amount of air remaining in your lungs after you have completed a quiet respiratory cycle. The FRC is the sum of the expiratory reserve volume and the residual volume.
- The **vital capacity** is the maximum amount of air that you can move into or out of your lungs in a single respiratory cycle. The vital capacity is the sum of the expiratory reserve volume, the tidal volume, and the inspiratory reserve volume. It averages around 4800 mL in males and 3400 mL in females.
- The **total lung capacity** is the total volume of your lungs. We calculate it by adding the vital capacity and the residual volume. The total lung capacity averages around 6000 mL in males and 4200 mL in females.

Pulmonary function tests monitor several aspects of respiratory function by measuring rates and volumes of air movement.

Checkpoint

19. **Define compliance and identify the factors that affect it.**
20. **Name the various measurable pulmonary volumes.**
21. **Mark breaks a rib that punctures the chest wall on his left side. What do you expect will happen to his left lung as a result?**
22. **In pneumonia, fluid accumulates in the alveoli of the lungs. How would this accumulation affect vital capacity?**

See the blue Answers tab at the back of the book.

23-8 Gas exchange depends on the partial pressures of gases and the diffusion of molecules

Pulmonary ventilation ensures both that your alveoli are supplied with oxygen and that the carbon dioxide arriving from your bloodstream is removed. The actual process of gas exchange takes place between blood and alveolar air across the respiratory membrane. To understand these events, let's first consider (1) the *partial pressures* of the gases involved and (2) the diffusion of molecules between a gas and a liquid. Then we can discuss the movement of oxygen and carbon dioxide across the respiratory membrane.

The Gas Laws

Gases are exchanged between the alveolar air and the blood through diffusion, which takes place in response to concentration gradients. As we saw in Chapter 3, the rate of diffusion varies in response to a variety of factors, including the size of the concentration gradient and the temperature. ↩ p. 87 The principles that govern the movement and diffusion of gas molecules, such as those in the atmosphere, are relatively straightforward. These principles, known as *gas laws*, have been understood for about 250 years. You have already heard about Boyle's law, which determines the direction of air movement in pulmonary ventilation. In this section, you will learn about gas laws and other factors that determine the rate of oxygen and carbon dioxide diffusion across the respiratory membrane.

Dalton's Law and Partial Pressures

The air we breathe is a mixture of gases. Nitrogen molecules (N_2) are the most abundant, accounting for about 78.6 percent of atmospheric gas molecules. Oxygen molecules (O_2), the second most abundant, make up roughly 20.9 percent of air. Most of the remaining 0.5 percent consists of water molecules, with carbon dioxide (CO_2) contributing a mere 0.04 percent.

Atmospheric pressure, 760 mm Hg, represents the combined effects of collisions involving each type of molecule in air. At any moment, 78.6 percent of those collisions involve nitrogen molecules, 20.9 percent oxygen molecules, and so on. Thus, each of the gases contributes to the total pressure in proportion to its relative abundance. This relationship is known as **Dalton's law.**

The **partial pressure** of a gas is the pressure contributed by a single gas in a mixture of gases. The partial pressure is abbreviated by the symbol P or p. A subscript shows the gas in question. For example, the partial pressure of oxygen is abbreviated P_{O_2}.

All the partial pressures added together equal the total pressure exerted by a gas mixture. For the atmosphere, this relationship can be summarized as follows:

$$P_{N_2} + P_{O_2} + P_{H_2O} + P_{CO_2} = 760 \text{ mm Hg}$$

We can easily calculate the partial pressure of each gas because we know the individual percentages of each gas in air. For example, the partial pressure of oxygen, P_{O_2} is 20.9 percent of 760 mm Hg, or roughly 159 mm Hg. Table 23–2 includes the partial pressures of other atmospheric gases.

Diffusion between Liquids and Gases (Henry's Law)

Differences in pressure, which move gas molecules from one place to another, also affect the movement of gas molecules into and out of solution. At a given temperature, the amount of a particular gas in solution is directly proportional to the partial pressure of that gas. This principle is known as **Henry's law.**

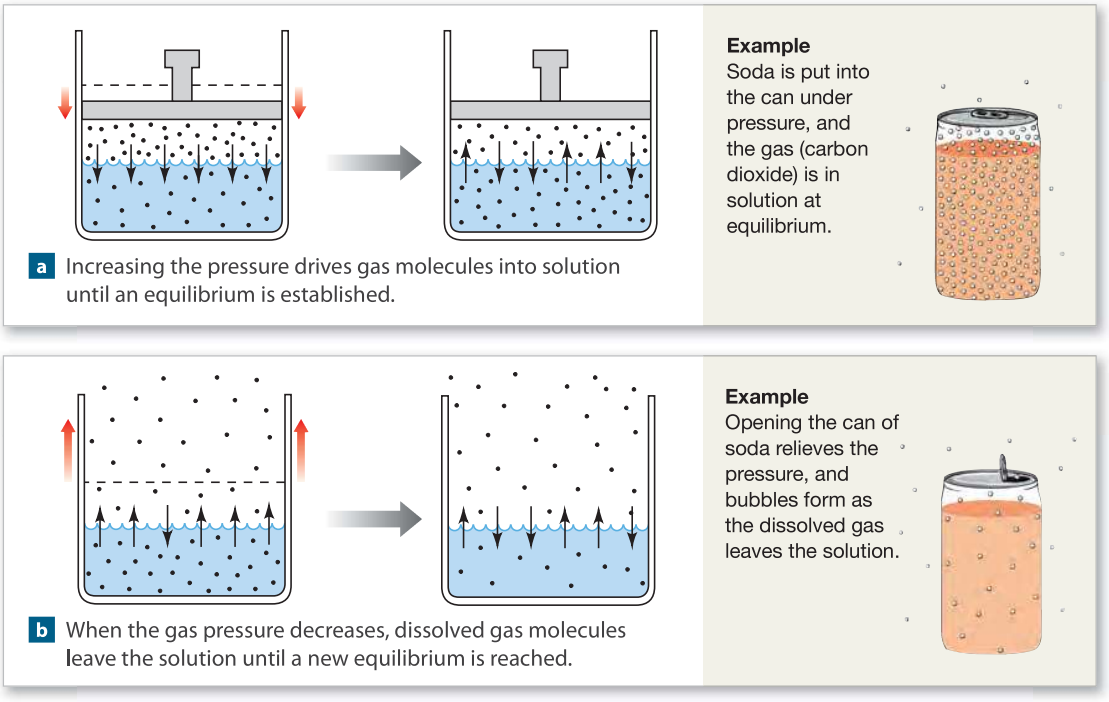
When a gas under pressure contacts a liquid, the pressure tends to force gas molecules into solution. At a given pressure, the number of dissolved gas molecules rises until an equilibrium is established. At equilibrium, gas molecules diffuse out of the liquid as quickly as they enter it, so the total number of gas molecules in solution remains constant. If the partial pressure goes up, more gas molecules go into solution. If the partial pressure goes down, gas molecules come out of solution.

You see Henry's law in action whenever you open a can of soda. The soda was put into the can under pressure, and the gas (carbon dioxide) is in solution (Figure 23–18a). When you

Table 23–2 Partial Pressures (mm Hg) and Normal Gas Concentrations (%) in Air

Source of Sample	Nitrogen (N_2)	Oxygen (O_2)	Carbon Dioxide (CO_2)	Water Vapor (H_2O)
Inhaled air (dry)	597 (78.6%)	159 (20.9%)	0.3 (0.04%)	3.7 (0.5%)
Alveolar air (saturated)	573 (75.4%)	100 (13.2%)	40 (5.2%)	47 (6.2%)
Exhaled air (saturated)	569 (74.8%)	116 (15.3%)	28 (3.7%)	47 (6.2%)

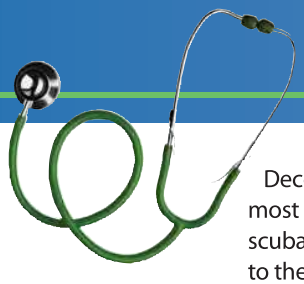
Figure 23–18 Henry's Law and the Relationship between Solubility and Pressure.



Clinical Note

Decompression Sickness

Doubling over in pain



Decompression sickness is a painful condition that develops when a person is exposed to a sudden drop in atmospheric pressure. Nitrogen is the gas responsible for the problems experienced, due to its high partial pressure in air. When the pressure drops, nitrogen comes out of solution, forming bubbles like those in a shaken can of soda. The bubbles may form in joint cavities, in the bloodstream, and in the cerebrospinal fluid. Individuals with decompression sickness typically curl up from the pain in affected joints. This reaction accounts for the condition's common name: *the bends*.

Decompression sickness most commonly affects scuba divers who return to the surface too quickly after breathing air under greater-than-normal pressure while submerged. It can also develop in airline passengers subject to sudden losses of cabin pressure.

open the can, the pressure falls and the gas molecules begin coming out of solution (**Figure 23–18b**). Theoretically, the process will continue until an equilibrium develops between the surrounding air and the gas in solution. In fact, the volume of the can is so small, and the volume of the atmosphere so great, that within a half hour or so virtually all the carbon dioxide comes out of solution. You are left with "flat" soda.

The actual *amount* of a gas in solution at a given partial pressure and temperature depends on the solubility of the gas in that particular liquid. In body fluids, carbon dioxide is highly soluble, and oxygen is somewhat less soluble. Nitrogen has very limited solubility. The dissolved gas content is usually reported in milliliters of gas per 100 mL (1 dL) of solution. To see the differences in relative solubility of these three gases, we can compare the gas content of blood in the pulmonary veins with the partial pressure of each gas in the alveoli. In a pulmonary vein, plasma generally contains 2.62 mL/dL of dissolved CO_2 (P_{CO_2} = 40 mm Hg), 0.29 mL/dL of dissolved O_2 (P_{O_2} = 100 mm Hg), and 1.25 mL/dL of dissolved N_2 (P_{N_2} = 573 mm Hg). Thus even though the partial pressure of carbon dioxide is less than one-tenth the partial pressure of nitrogen, the plasma contains more than twice as much carbon dioxide as nitrogen in solution.

Diffusion and Respiratory Function

The gas laws apply to the diffusion of oxygen, carbon dioxide, and nitrogen between a gas and a liquid. We will now consider how differing partial pressures and solubilities determine the direction and rate of diffusion across the respiratory membrane that separates the air within the alveoli from the blood in alveolar capillaries.

The Composition of Alveolar Air

As soon as air enters the respiratory tract, its characteristics begin to change. In passing through the nasal cavity, inhaled air becomes warmer, and the amount of water vapor increases. Humidification and filtration continue as the air travels through the pharynx, trachea, and bronchial passageways. On reaching the alveoli, the incoming air mixes with air remaining in the alveoli from the previous respiratory cycle. For this reason, alveolar air contains more carbon dioxide and less oxygen than does atmospheric air.

The last 150 mL of inhaled air never gets farther than the conducting passageways. It remains in the anatomic dead space of the lungs. During the next exhalation, the departing alveolar air mixes with air in the dead space, producing yet another mixture that differs from both atmospheric and alveolar samples. The differences in composition between atmospheric (inhaled) and alveolar air are given in **Table 23–2**.

Efficiency of Diffusion at the Respiratory Membrane

Gas exchange at the respiratory membrane is efficient for the following five reasons:

1. *The differences in partial pressure across the respiratory membrane are substantial.* This fact is important, because the greater the difference in partial pressure, the faster the rate of gas diffusion. Conversely, if P_{O_2} in alveoli decreases, the rate of oxygen diffusion into blood drops. This is why many people feel light-headed at altitudes of 3000 m or more. The partial pressure of oxygen in their alveoli has dropped so low that the rate of oxygen absorption is significantly reduced.

2. *The distances involved in gas exchange are short.* The fusion of capillary and alveolar basement membranes reduces the distance for gas exchange to an average of 0.5μm. Inflammation of the lung tissue or a buildup of fluid in alveoli increases the diffusion distance and impairs alveolar gas exchange.
3. *The gases are lipid soluble.* Both oxygen and carbon dioxide diffuse readily through the surfactant layer and the alveolar and endothelial plasma membranes.
4. *The total surface area is large.* The combined alveolar surface area at peak inhalation may approach 140 m^2 (1506 ft^2). This area is slightly bigger than half of a tennis court. Damage to alveolar surfaces, which occurs in emphysema, reduces the available surface area and the efficiency of gas transfer.
5. *Blood flow and airflow are coordinated.* This close coordination makes both pulmonary ventilation and pulmonary circulation more efficient. For example, blood flow is greatest around alveoli with the highest P_{O_2} values, where oxygen uptake can proceed with maximum efficiency. If the normal blood flow is impaired (as it is in *pulmonary embolism*), or if the normal airflow is interrupted (as it is in various forms of *pulmonary obstruction*), this coordination is lost and respiratory efficiency decreases.

Partial Pressures in Alveolar Air and Alveolar Capillaries

Figure 23–19 illustrates the partial pressures of oxygen and carbon dioxide in the pulmonary and systemic circuits. Notice that blood arriving from the pulmonary arteries has a lower P_{O_2} and a higher P_{CO_2} than does alveolar air (**Figure 23–19a**). Diffusion between the alveolar gas mixture and the alveolar capillaries then raises the P_{O_2} of blood and lowers its P_{CO_2}. By the time the blood enters the pulmonary venules, it has reached equilibrium with the alveolar air. Blood departs the alveoli with a P_{O_2} of about 100 mm Hg and a P_{CO_2} of roughly 40 mm Hg.

Diffusion between alveolar air and blood in the alveolar capillaries occurs very rapidly. When you are at rest, a red blood cell moves through one of your alveolar capillaries in about 0.75 second. When you exercise, the passage takes less than 0.3 second. This amount of time is usually sufficient to reach an equilibrium between the alveolar air and the blood.

Partial Pressures in the Systemic Circuit

Oxygenated blood leaves the alveolar capillaries to return to the heart, to be pumped into the systemic circuit. As this blood enters the pulmonary veins, it mixes with blood that flowed through capillaries around conducting passageways. Because gas exchange in the lungs occurs only at alveoli, the blood leaving the conducting passageways carries relatively little oxygen. The partial pressure of oxygen in the pulmonary veins therefore drops to about 95 mm Hg. This is the P_{O_2} in the blood that enters the systemic circuit. No further changes in partial pressure occur until the blood reaches the systemic capillaries (**Figure 23–19b**).

Normal interstitial fluid has a P_{O_2} of 40 mm Hg. As a result, oxygen diffuses out of the capillaries until the capillary partial pressure is the same as that in the adjacent tissues. Inactive peripheral tissues normally have a P_{CO_2} of about 45 mm Hg, whereas blood entering peripheral capillaries normally has a P_{CO_2} of 40 mm Hg. As a result, carbon dioxide diffuses into the blood as oxygen diffuses out (**Figure 23–19b**).

Clinical Note

Blood Gas Analysis Blood samples can be analyzed to determine their concentrations of dissolved gases. The usual tests include the determination of pH, P_{CO_2}, and P_{O_2} in an arterial sample. Such samples provide information about the degree of oxygenation in peripheral tissues. For example, if the arterial P_{CO_2} is very high and the P_{O_2} is very low, tissues are not receiving adequate oxygen. This problem may be solved by providing the patient with a gas mixture that has a high P_{O_2} (or even pure oxygen, with a P_{O_2} of 760 mm Hg).

Blood gas measurements also provide information on the efficiency of gas exchange at the lungs. If the arterial P_{O_2} remains low despite the administration of oxygen, or if the P_{CO_2} is very high, pulmonary exchange problems, such as pulmonary edema, asthma, or pneumonia, may exist.

Checkpoint

23. **Define Dalton's law.**
24. **Define Henry's law.**

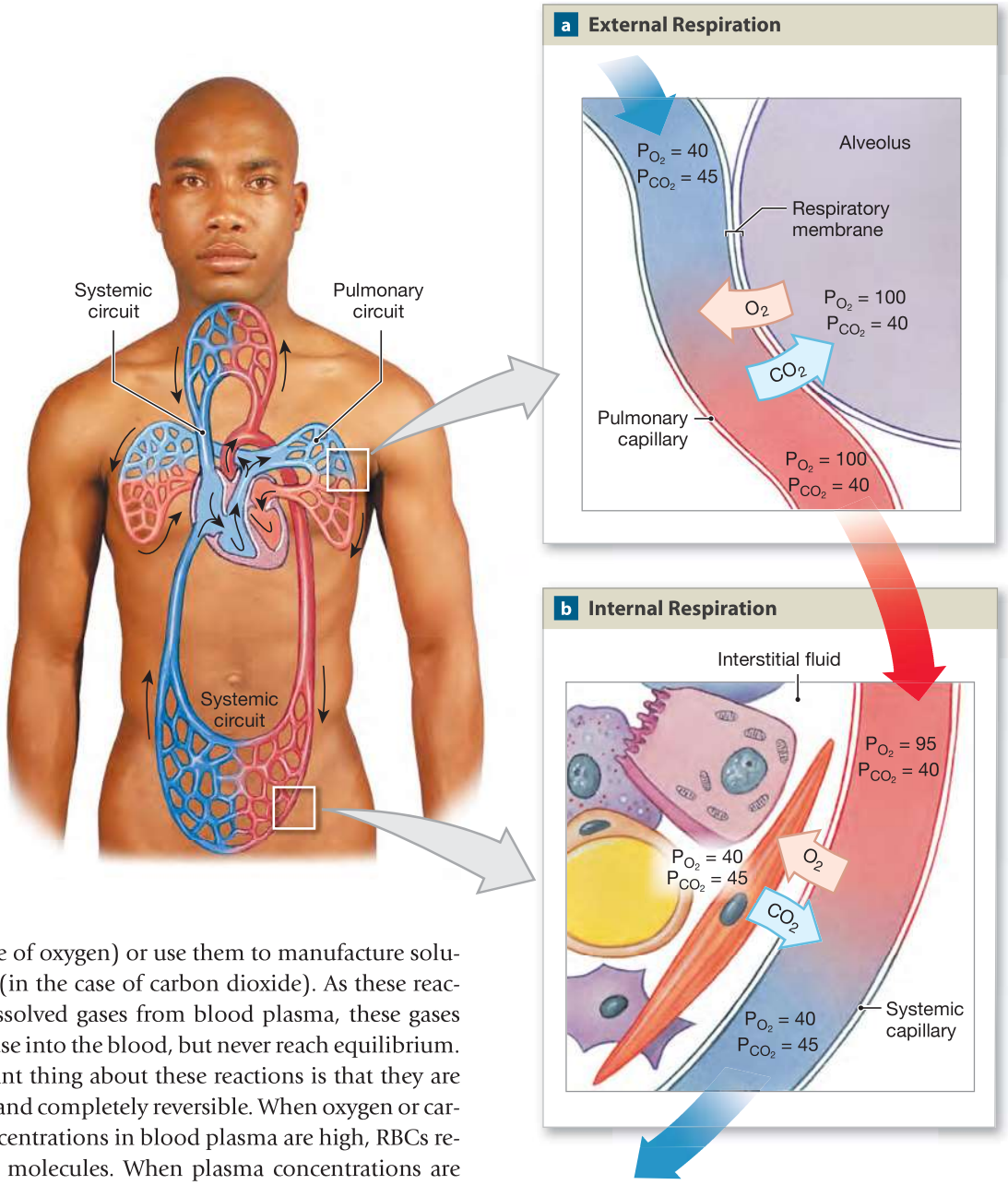
See the blue Answers tab at the back of the book.

23-9 Most oxygen is transported bound to hemoglobin; and carbon dioxide is transported in three ways: as carbonic acid, bound to hemoglobin, or dissolved in plasma

Oxygen and carbon dioxide have limited solubilities in blood plasma. For example, at the normal P_{O_2} of alveoli, 100 mL of plasma absorbs only about 0.3 mL of oxygen. The limited solubilities of these gases are a problem. The peripheral tissues need more oxygen and generate more carbon dioxide than the plasma alone can absorb and transport.

Red blood cells (RBCs) solve this problem. They remove dissolved oxygen and CO_2 molecules from plasma and bind

Figure 23–19 An Overview of Respiratory Processes and Partial Pressures in Respiration.



them (in the case of oxygen) or use them to manufacture soluble compounds (in the case of carbon dioxide). As these reactions remove dissolved gases from blood plasma, these gases continue to diffuse into the blood, but never reach equilibrium.

The important thing about these reactions is that they are both temporary and completely reversible. When oxygen or carbon dioxide concentrations in blood plasma are high, RBCs remove the excess molecules. When plasma concentrations are falling, the RBCs release their stored reserves.

Oxygen Transport

Each 100 mL of blood leaving the alveolar capillaries carries away about 20 mL of oxygen. Only 1.5 percent (about 0.3 mL) of this amount is oxygen molecules in solution. The rest of the oxygen molecules are bound to *hemoglobin (Hb) molecules.* Recall that the hemoglobin molecule consists of four globular protein subunits, each containing a heme unit. The oxygen molecules bind to the iron ions in the center of heme units. ↩ p. 645 Thus, each hemoglobin molecule can bind four molecules of oxygen, forming **oxyhemoglobin (HbO_2).** This reaction is reversible. We can summarize it as

$$Hb + O_2 \rightleftharpoons HbO_2.$$

This reversible reaction allows hemoglobin to pick up oxygen in the lungs and then release it to body tissues elsewhere.

Each red blood cell has approximately 280 million molecules of hemoglobin. With four heme units per hemoglobin molecule, each RBC potentially can carry more than a billion molecules of oxygen.

The percentage of heme units containing bound oxygen at any given moment is called the **hemoglobin saturation.** If all the Hb molecules in the blood are fully loaded with oxygen, saturation is 100 percent. If, on average, each Hb molecule carries two O_2 molecules, saturation is 50 percent.

In Chapter 2, we saw that the shape and functional properties of a protein change in response to changes in its environment. ↩ p. 50 Hemoglobin is no exception. Any changes in shape can affect oxygen binding. Under normal conditions, the most important environmental factors affecting hemoglobin are (1) the P_{O_2} of blood, (2) blood pH, (3) temperature, and (4) ongoing metabolic activity within RBCs.

Hemoglobin and P_{O_2}

Hemoglobin in RBCs carries most of the oxygen in the bloodstream and releases it in response to changes in the partial pressure of oxygen in the surrounding plasma. If the P_{O_2} increases, hemoglobin binds oxygen. If the P_{O_2} decreases, hemoglobin releases oxygen.

An **oxygen–hemoglobin saturation curve,** or *oxygen–hemoglobin dissociation curve*, is a graph that relates the hemoglobin saturation to the partial pressure of oxygen (**Figure 23–20**). The binding and dissociation, or release, of oxygen to hemoglobin is a typical reversible reaction. At equilibrium, oxygen molecules bind to heme at the same rate that other oxygen molecules are being released. If the P_{O_2} increases, then more oxygen molecules bind to hemoglobin, and fewer are released. Referring to the equation given in the previous section, we say that the reaction shifts to the right. If the P_{O_2} decreases, more oxygen molecules are released from hemoglobin, while fewer oxygen molecules bind. In this case, we say that the reaction shifts to the left.

Notice that the graph of this relationship between P_{O_2} and hemoglobin saturation is a curve rather than a straight line. It is a curve because the shape of the hemoglobin molecule changes slightly each time it binds an oxygen molecule. This change in shape enhances the ability of hemoglobin to bind *another* oxygen molecule. In other words, the binding of the first oxygen molecule makes it easier to bind the second; binding the second promotes binding of the third; and binding the third enhances binding of the fourth.

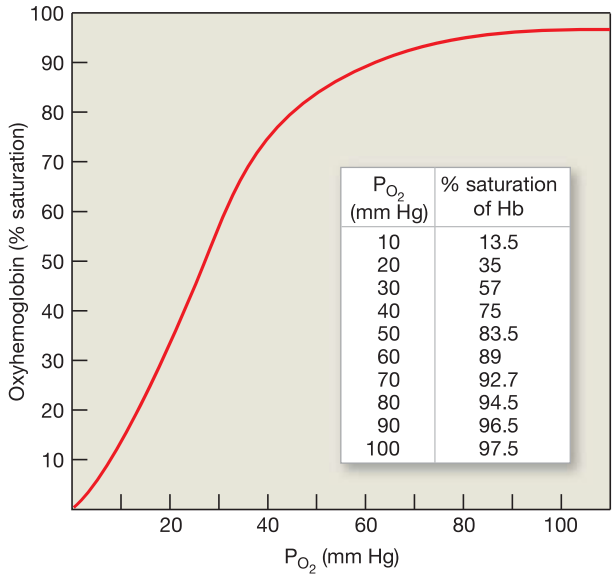
Because each arriving oxygen molecule makes it easier for hemoglobin to bind the *next* oxygen molecule, the saturation curve takes the form shown in **Figure 23–20**. Once the first oxygen molecule binds to the hemoglobin, the slope rises rapidly until it levels off near 100 percent saturation. While the slope is steep, a very small change in plasma P_{O_2} results in a large change in the amount of oxygen bound to Hb or released from HbO_2. Notice that hemoglobin will be more than 90 percent saturated if exposed to an alveolar P_{O_2} above 60 mm Hg. Thus, near-normal oxygen transport can continue even when the oxygen content of alveolar air decreases below normal, or P_{O_2} = 100 mm Hg. Without this ability, you could not survive at high altitudes. Conditions that significantly reduce pulmonary ventilation would be immediately fatal.

At normal alveolar pressures (P_{O_2} = 100 mm Hg) the hemoglobin saturation is very high (97.5 percent), but complete saturation does not occur until the P_{O_2} reaches excessively high levels (about 250 mm Hg). In functional terms, the maximum saturation is not as important as the ability of hemoglobin to provide oxygen over the normal P_{O_2} range in body tissues. Over that range—from 100 mm Hg at the alveoli to perhaps 15 mm Hg in active tissues—the saturation drops from 97.5 percent to less than 20 percent, and a small change in P_{O_2} makes a big difference in terms of the amount of oxygen bound to hemoglobin.

Note that the relationship between P_{O_2} and hemoglobin saturation remains valid whether the P_{O_2} is rising or falling. If the P_{O_2} increases, the saturation goes up and hemoglobin stores oxygen. If the P_{O_2} decreases, hemoglobin releases oxygen into its surroundings. When oxygenated blood arrives in the peripheral capillaries, the blood P_{O_2} declines rapidly due to gas exchange with the interstitial fluid. As the P_{O_2} falls, hemoglobin gives up its oxygen.

The relationship between the P_{O_2} and hemoglobin saturation provides a mechanism for automatic regulation of oxygen delivery. Inactive tissues have little demand for oxygen, and the local P_{O_2} is usually about 40 mm Hg. Under these conditions, hemoglobin does not release much oxygen. As it passes through the capillaries, it goes from 97 percent saturation (P_{O_2} = 95 mm Hg) to 75 percent saturation (P_{O_2} = 40 mm Hg). Because hemoglobin

Figure 23–20 An Oxygen–Hemoglobin Saturation Curve.
The saturation characteristics of hemoglobin at various partial pressures of oxygen under normal conditions (body temperature of 37°C and blood pH of 7.4).



P_{O_2} (mm Hg)	% saturation of Hb
10	13.5
20	35
30	57
40	75
50	83.5
60	89
70	92.7
80	94.5
90	96.5
100	97.5

still retains three-quarters of its oxygen, venous blood has a relatively large oxygen reserve. This reserve is important, because it can be mobilized if tissue oxygen demands increase.

Active tissues use oxygen at an accelerated rate, so their P_{O_2} may drop to 15–20 mm Hg. Hemoglobin passing through these capillaries goes from 97 percent saturation to about 20 percent saturation. In practical terms, this means that as blood circulates through peripheral capillaries, active tissues receive 3.5 times as much oxygen as do inactive tissues.

Hemoglobin and pH

At a given P_{O_2}, hemoglobin releases additional oxygen if the pH decreases. The oxygen–hemoglobin saturation curve in **Figure 23–20** was determined in normal blood, with a pH of 7.4 and a temperature of 37°C. In addition to consuming oxygen, active tissues generate acids that lower the pH of the interstitial fluid. When the pH drops, the shape of hemoglobin molecules changes. As a result of this change, the molecules release their oxygen reserves more readily, so the slope of the hemoglobin saturation curve changes (**Figure 23–21a**). In other words, as pH drops, the saturation declines. At a tissue P_{O_2} of 40 mm Hg, for example, you can see in **Figure 23–21a** that a pH drop from 7.4 to 7.2 changes hemoglobin saturation from 75 percent to 60 percent. This means that hemoglobin molecules release 20 percent more oxygen in peripheral tissues at a pH of 7.2 than they do at a pH of 7.4. This effect of pH on the hemoglobin saturation curve is called the **Bohr effect.**

Carbon dioxide is the primary compound responsible for the Bohr effect. When CO_2 diffuses into the blood, it rapidly diffuses into red blood cells. There, an enzyme called **carbonic anhydrase** catalyzes the reaction of CO_2 with water molecules:

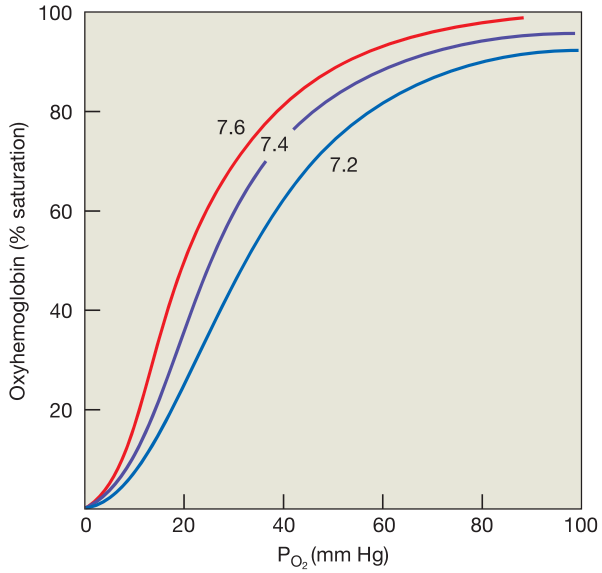
$$CO_2 + H_2O \overset{\text{carbonic anhydrase}}{\rightleftharpoons} H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

The product of this enzymatic reaction, H_2CO_3, is called *carbonic acid*, because it dissociates into a hydrogen ion (H^+) and a bicarbonate ion (HCO_3^-). The rate of carbonic acid formation depends on the amount of carbon dioxide in solution, which, as noted earlier, depends on the P_{CO_2}. When the P_{CO_2} rises, the rate of carbonic acid formation accelerates and the reaction proceeds from left to right. The hydrogen ions that are generated diffuse out of the RBCs, and the pH of the plasma drops. When the P_{CO_2} declines, hydrogen ions diffuse out of the plasma and into the RBCs. As a result, the pH of the plasma rises as the reaction proceeds from right to left.

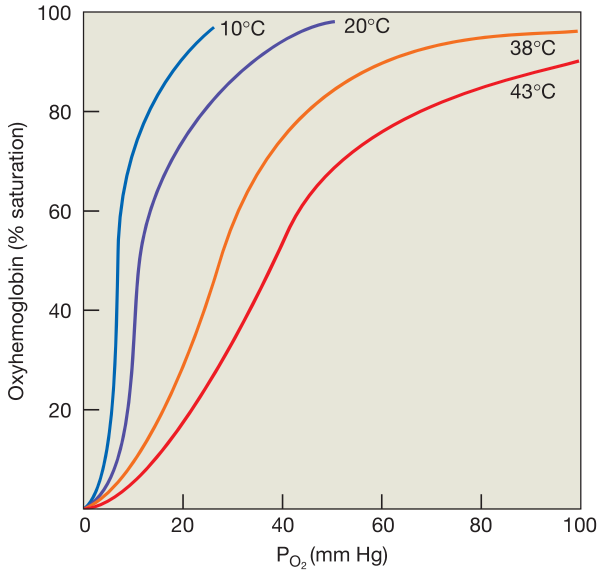
Hemoglobin and Temperature

At a given P_{O_2}, hemoglobin releases additional oxygen if the temperature increases. Changes in temperature affect the slope of the hemoglobin saturation curve (**Figure 23–21b**). As the temperature rises, hemoglobin releases more oxygen. As the temperature declines, hemoglobin holds oxygen more tightly. Temperature effects are significant only in active tissues that are generating large amounts of heat. For example, active skeletal muscles generate heat, and the heat warms blood that flows

Figure 23–21 The Effects of pH and Temperature on Hemoglobin Saturation.



a **Effect of pH.** When the pH drops below normal levels, more oxygen is released; the oxygen–hemoglobin saturation curve shifts to the right. When the pH increases, less oxygen is released; the curve shifts to the left.



b **Effect of temperature.** When the temperature rises, more oxygen is released; the oxygen–hemoglobin saturation curve shifts to the right.

Clinical Note

Carbon Monoxide Poisoning The exhaust of automobiles and other petroleum-burning engines, of oil lamps, and of fuel-fired space heaters contains *carbon monoxide* (CO). Each winter entire families die from **carbon monoxide poisoning.** Carbon monoxide competes with oxygen molecules for the binding sites on heme units. Unfortunately, the carbon monoxide usually wins the competition, because at very low partial pressures it has a much stronger affinity for hemoglobin than does oxygen. The bond formed between CO and heme is extremely durable, so the attachment of a CO molecule essentially makes that heme unit inactive for respiratory purposes.

If CO molecules make up just 0.1 percent of inhaled air, enough hemoglobin is affected that human survival becomes impossible without medical assistance. Treatment includes: (1) preventing further CO exposure, (2) administering pure oxygen, because at sufficiently high partial pressures, the oxygen molecules gradually replace CO at the hemoglobin molecules; and, if necessary, (3) transfusing compatible red blood cells.

through these organs. As the blood warms, the Hb molecules release more oxygen than can be used by the active muscle fibers.

Hemoglobin and BPG

Red blood cells lack mitochondria. These cells produce ATP only by glycolysis. As a result, lactic acid is formed, as we saw in Chapter 10. ↩ p. 307 The metabolic pathways involved in glycolysis in a RBC also generate the compound **2,3-bisphosphoglycerate** (biz-fos-fō-GLIS-er-āt), or **BPG.** This compound has a direct effect on oxygen binding and release. For any partial pressure of oxygen, the higher the concentration of BPG, the greater the release of oxygen by Hb molecules. Normal RBCs always contain BPG.

Both BPG synthesis and the Bohr effect improve oxygen delivery when the pH changes: BPG levels rise when the pH increases, and the Bohr effect appears when the pH decreases. The concentration of BPG can be increased by high blood pH, thyroid hormones, growth hormone, epinephrine, and androgens. When plasma P_{O_2} levels are low for an extended time, red blood cells generate more BPG. These factors improve oxygen delivery to the tissues, because when BPG levels are elevated, hemoglobin releases about 10 percent more oxygen at a given P_{O_2} than it would do otherwise.

The production of BPG decreases as RBCs age. For this reason, the level of BPG can determine how long a blood bank can store fresh whole blood. When BPG levels get too low, hemoglobin becomes firmly bound to the available oxygen. The blood is then useless for transfusions, because the RBCs will no longer release oxygen to peripheral tissues, even at a disastrously low P_{O_2}.

Fetal Hemoglobin

The RBCs of a developing fetus contain **fetal hemoglobin.** The structure of fetal hemoglobin differs from that of adult hemoglobin, giving it a much higher affinity for oxygen. At the same P_{O_2}, fetal hemoglobin binds more oxygen than does adult hemoglobin (**Figure 23–22**). This trait is key to transferring oxygen across the placenta.

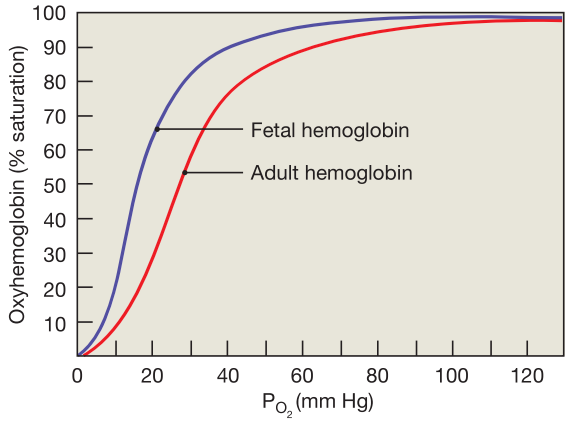
A fetus obtains oxygen from the maternal bloodstream. At the placenta, maternal blood has a relatively low P_{O_2}, ranging from 35 to 50 mm Hg. If maternal blood arrives at the placenta with a P_{O_2} of 40 mm Hg, hemoglobin saturation is roughly 75 percent. The fetal blood arriving at the placenta has a P_{O_2} close to 20 mm Hg. However, because fetal hemoglobin has a higher affinity for oxygen, it is still 58 percent saturated.

As diffusion takes place between fetal blood and maternal blood, oxygen enters the fetal bloodstream until the P_{O_2} reaches equilibrium at 30 mm Hg. At this P_{O_2}, the maternal hemoglobin is less than 60 percent saturated, but the fetal hemoglobin is over 80 percent saturated, as you can see on **Figure 23–22**. The steep slope of the saturation curve for fetal hemoglobin means that when fetal RBCs reach peripheral tissues of the fetus, the Hb molecules release a large amount of oxygen in response to a very small change in P_{O_2}.

Carbon Dioxide Transport

Carbon dioxide is generated by aerobic metabolism in peripheral tissues. Carbon dioxide travels in the bloodstream in three different ways. After entering the blood, a CO_2 molecule either (1) is converted to a molecule of carbonic acid, (2) binds to hemoglobin within red blood cells, or (3) dis-

Figure 23–22 **A Functional Comparison of Fetal and Adult Hemoglobin.**



solves in plasma. All three reactions are completely reversible, allowing carbon dioxide to be picked up from body tissues and then delivered to the alveoli. Let's consider the events that take place as blood enters peripheral tissues in which the P_{CO_2} is 45 mm Hg.

Carbonic Acid Formation

Roughly 70 percent of the carbon dioxide absorbed by blood is transported as molecules of carbonic acid. Carbon dioxide is converted to carbonic acid through the activity of the enzyme carbonic anhydrase in RBCs. The carbonic acid molecules immediately dissociate into a hydrogen ion and a bicarbonate ion, as described earlier (p. 844). We can ignore the intermediate steps in this sequence and summarize the reaction as

$$CO_2 + H_2O \overset{\text{carbonic anhydrase}}{\rightleftharpoons} H^+ + HCO_3^-$$

This reaction is completely reversible. In peripheral capillaries, it proceeds vigorously, tying up large numbers of CO_2 molecules. The reaction continues as carbon dioxide diffuses out of the interstitial fluids.

The hydrogen ions and bicarbonate ions have different fates. Most of the hydrogen ions bind to hemoglobin molecules, forming HbH^+. The Hb molecules function as pH buffers, tying up the released hydrogen ions before the ions can leave the RBCs and lower the pH of the plasma. The bicarbonate ions move into the plasma with the aid of a countertransport mechanism that exchanges intracellular bicarbonate ions (HCO_3^-) for extracellular chloride ions (Cl^-). This exchange trades one anion for another and does not require ATP. The result is a mass movement of chloride ions into the RBCs, an event known as the **chloride shift.**

CO_2 Binding to Hemoglobin

About 23 percent of the carbon dioxide carried by blood is bound to the protein portions of Hb molecules inside RBCs. These CO_2 molecules are attached to exposed amino groups ($—NH_2$) of the Hb molecules. The resulting compound is called **carbaminohemoglobin** (kar-BAM-i-nō-hē-mō-glō-bin), $HbCO_2$. We can summarize the reversible reaction as follows:

$$CO_2 + HbNH_2 \rightleftharpoons HbNHCOOH$$

We can abbreviate this reaction without the amino groups as

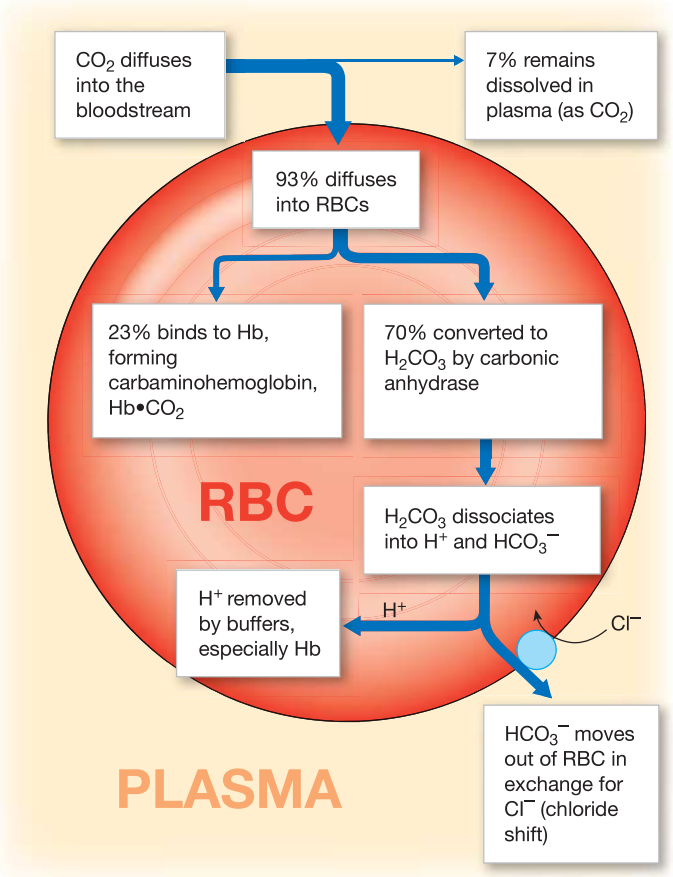
$$CO_2 + Hb \rightleftharpoons HbCO_2$$

Transport in Plasma

Plasma becomes saturated with carbon dioxide quite rapidly. Only about 7 percent of the carbon dioxide absorbed at peripheral capillaries is transported as dissolved gas molecules. RBCs absorb the rest and convert it using carbonic anhydrase or store it as carbaminohemoglobin.

Figure 23–23 summarizes carbon dioxide transport.

Figure 23–23 Carbon Dioxide Transport in Blood.



Summary: Gas Transport

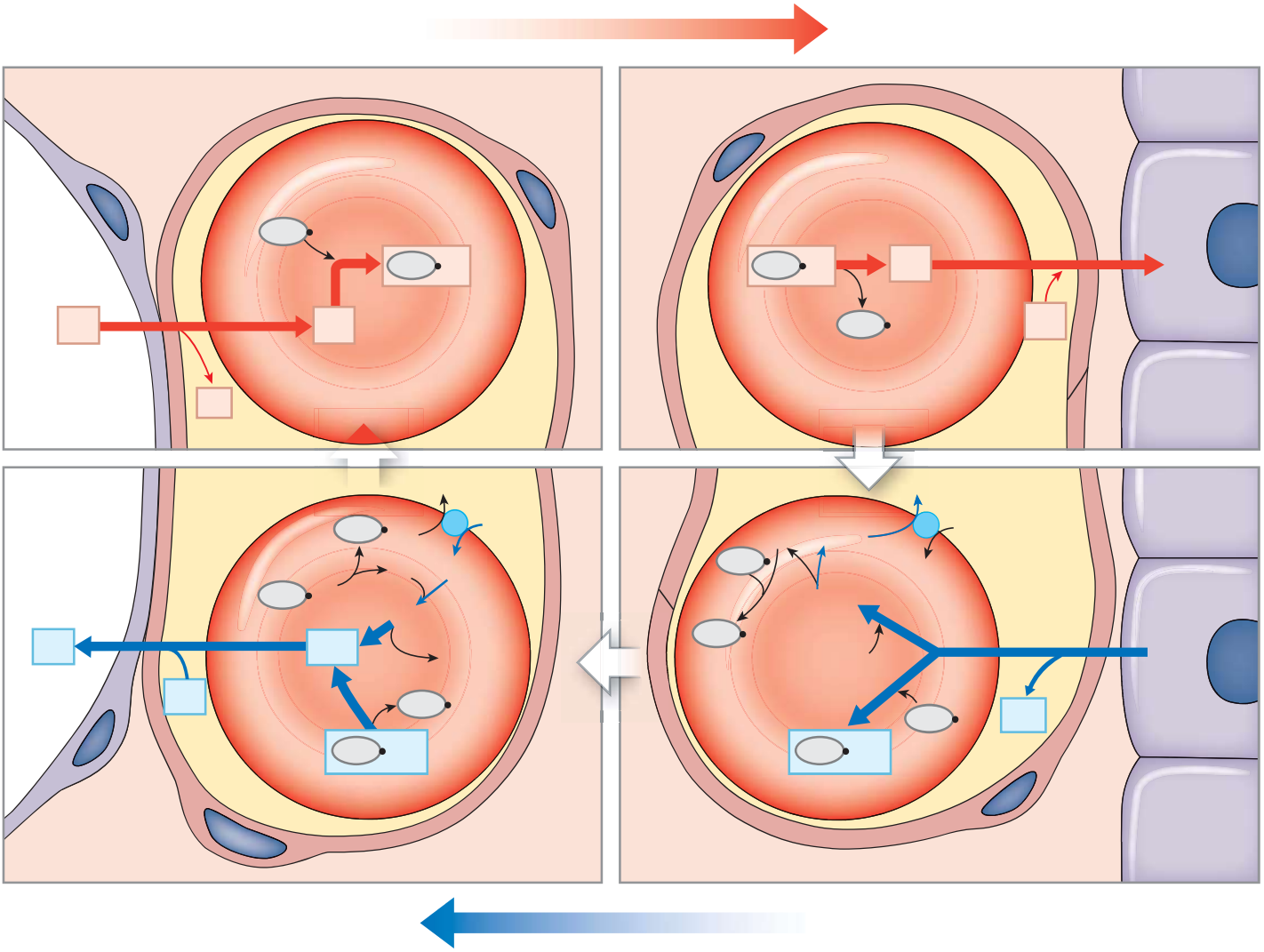
Figure 23–24 summarizes the transport of oxygen and carbon dioxide in the respiratory and cardiovascular systems. Note that the bottom portion of the figure shows the carbon dioxide being delivered to the alveoli. The reactions we have just discussed then proceed in the reverse direction.

Gas transport is a dynamic process. It is capable of varying its responses to meet changing circumstances. Some of the responses are automatic and result from the basic chemistry of the transport mechanisms. Other responses require coordinated adjustments in the activities of the cardiovascular and respiratory systems. We consider those levels of control and regulation next.

Checkpoint

25. **Identify the three ways that carbon dioxide is transported in the bloodstream.**
26. **As you exercise, hemoglobin releases more oxygen to active skeletal muscles than it does when those muscles are at rest. Why?**
27. **How would blockage of the trachea affect blood pH?**

See the blue Answers tab at the back of the book.



At the lungs, local factors coordinate (1) *lung perfusion*, or blood flow to the alveoli, with (2) *alveolar ventilation*, or airflow. This local coordination takes place over a wide range of conditions and activity levels. As blood flows toward the alveolar capillaries, it is directed toward lobules with a relatively high P_{O_2}. This movement takes place because alveolar capillaries constrict when the local P_{O_2} is low. (This response is the opposite of that seen in peripheral tissues, as we noted in Chapter 21. ↩ p. 736)

Also in the lungs, smooth muscles in the walls of bronchioles are sensitive to the P_{CO_2} of the air they contain. When the P_{CO_2} goes up, the bronchioles increase in diameter (bronchodilation). When the P_{CO_2} declines, the bronchioles constrict (bronchoconstriction). Airflow is therefore directed to lobules with a high P_{CO_2}. These lobules get their carbon dioxide from blood and are actively engaged in gas exchange. The response of the bronchioles to P_{CO_2} is especially important, because improvements in airflow to functional alveoli can at least partially compensate for damage to pulmonary lobules.

Local adjustments improve the efficiency of gas transport by directing blood flow to alveoli with low CO_2 levels and increasing airflow to alveoli with high CO_2 levels. These adjustments in alveolar blood flow and bronchiole diameter take place automatically. When activity levels increase and the demand for oxygen rises, the cardiac output and respiratory rates increase under neural control.

The Respiratory Centers of the Brain

Respiratory control has both involuntary and voluntary components. Your brain's involuntary centers regulate the activities of the respiratory muscles. These centers control the respiratory minute volume by adjusting the frequency and depth of pulmonary ventilation. They make these adjustments in response to sensory information arriving from your lungs and other parts of the respiratory tract, as well as from a variety of other sites.

The voluntary control of respiration reflects activity in the cerebral cortex. This activity affects the output of either the respiratory centers in the medulla oblongata and pons or motor neurons in the spinal cord that control respiratory muscles. The **respiratory centers** are three pairs of nuclei in the reticular formation of the medulla oblongata and pons. The motor neurons in the spinal cord are generally controlled by *respiratory reflexes*, but they can also be controlled voluntarily through commands delivered by the corticospinal pathway. ↩ p. 509

Respiratory Centers in the Medulla Oblongata

We introduced the *respiratory rhythmicity centers* of the medulla oblongata in Chapter 14. ↩ p. 458 These paired centers set the pace of respiration. Each center can be subdivided into a *dorsal respiratory group (DRG)* and a *ventral respiratory group (VRG)*.

The DRG functions in every respiratory cycle, whether quiet or forced. The DRG's *inspiratory center* contains neurons that control lower motor neurons innervating the external intercostal muscles and the diaphragm.

The VRG functions only during forced breathing. It has an *expiratory center* consisting of neurons that innervate lower motor neurons controlling accessory respiratory muscles involved in active exhalation. Its *inspiratory center* contains neurons involved in maximal inhalation.

Reciprocal inhibition takes place between the neurons involved with inhalation and exhalation. ↩ p. 440 When the inspiratory neurons are active, the expiratory neurons are inhibited, and vice versa. The pattern of interaction between these groups differs between quiet breathing and forced breathing. During quiet breathing (**Figure 23–25a**):

- Activity in the DRG increases over a period of about 2 seconds, stimulating the inspiratory muscles. Over this period, inhalation takes place.
- After 2 seconds, the DRG neurons become inactive. They remain quiet for the next 3 seconds and allow the inspiratory muscles to relax. Over this period, passive exhalation takes place.

During forced breathing (**Figure 23–25b**):

- Increases in the level of activity in the DRG stimulate neurons of the VRG that activate the accessory muscles involved in inhalation.
- After each inhalation, active exhalation takes place as the neurons of the expiratory center stimulate the appropriate accessory muscles.

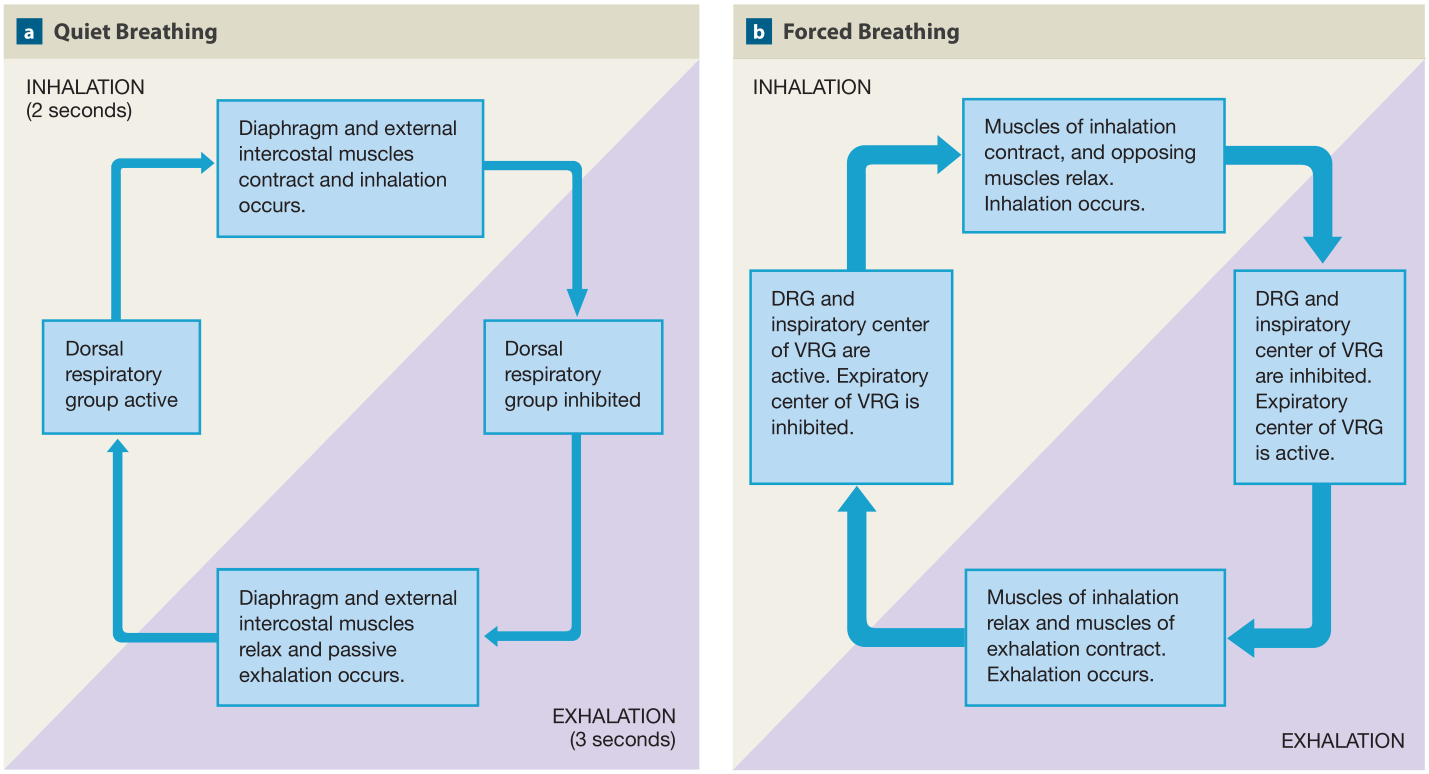
The basic pattern of respiration thus reflects a cyclic interaction between the DRG and the VRG. The pace of this interaction is thought to be established by pacemaker cells that spontaneously undergo rhythmic patterns of activity. Attempts to locate the pacemaker, however, have been unsuccessful.

Central nervous system stimulants, such as amphetamines or even caffeine, increase the respiratory rate by facilitating the respiratory centers. These actions are opposed by CNS depressants, such as barbiturates or opiates.

The Apneustic and Pneumotaxic Centers of the Pons

The apneustic centers and pneumotaxic centers of the pons regulate the depth and rate of respiration in response to sensory stimuli or input from other centers in the brain. Each apneustic center provides continuous stimulation to the DRG on that side of the brain stem. During quiet breathing, stimulation from the apneustic center helps increase the intensity of inhalation over the next 2 seconds. Under normal conditions, after 2 seconds the apneustic center is inhibited by signals from the pneumotaxic center on that side. During forced breathing, the apneustic

Figure 23–25 Basic Regulatory Patterns of Respiration.



centers also respond to sensory input from the vagus nerves regarding the amount of lung inflation.

The pneumotaxic centers inhibit the apneustic centers and promote passive or active exhalation. Centers in the hypothalamus and cerebrum can alter the activity of the pneumotaxic centers, as well as the respiratory rate and depth. However, essentially normal respiratory cycles continue even if the brain stem superior to the pons has been severely damaged.

In some cases, the inhibitory output of the pneumotaxic centers is cut off by a stroke or other damage to the brain stem, and sensory innervation from the lungs is eliminated due to damage to the vagus nerves. In these cases, the person inhales to maximum capacity and maintains that state for 10–20 seconds at a time. Intervening exhalations are brief, and little pulmonary ventilation occurs.

The CNS regions involved with respiratory control are diagrammed in **Spotlight Figure 23–26**. Interactions between the DRG and the VRG establish the basic pace and depth of respiration. The pneumotaxic centers modify that pace: An increase in pneumotaxic output quickens the pace of respiration by shortening the duration of each inhalation. A decrease in pneumotaxic output slows the respiratory pace, but increases the depth of respiration, because the apneustic centers are more active.

Sudden infant death syndrome (SIDS), also known as *crib death*, kills an estimated 10,000 infants each year in the United States alone. Most crib deaths occur between midnight and 9:00 A.M., in the late fall or winter, and involve infants 2 to 4 months old. Eyewitness accounts indicate that the sleeping infant suddenly stops breathing, turns blue, and relaxes. Genetic factors appear to be involved, but controversy remains as to the relative importance of other factors. The age at the time of death corresponds with a period when the pacemaker complex and respiratory centers are establishing connections with other portions of the brain. It has been suggested that SIDS results from a problem in the interconnection process that disrupts the reflexive respiratory pattern.

Respiratory Reflexes

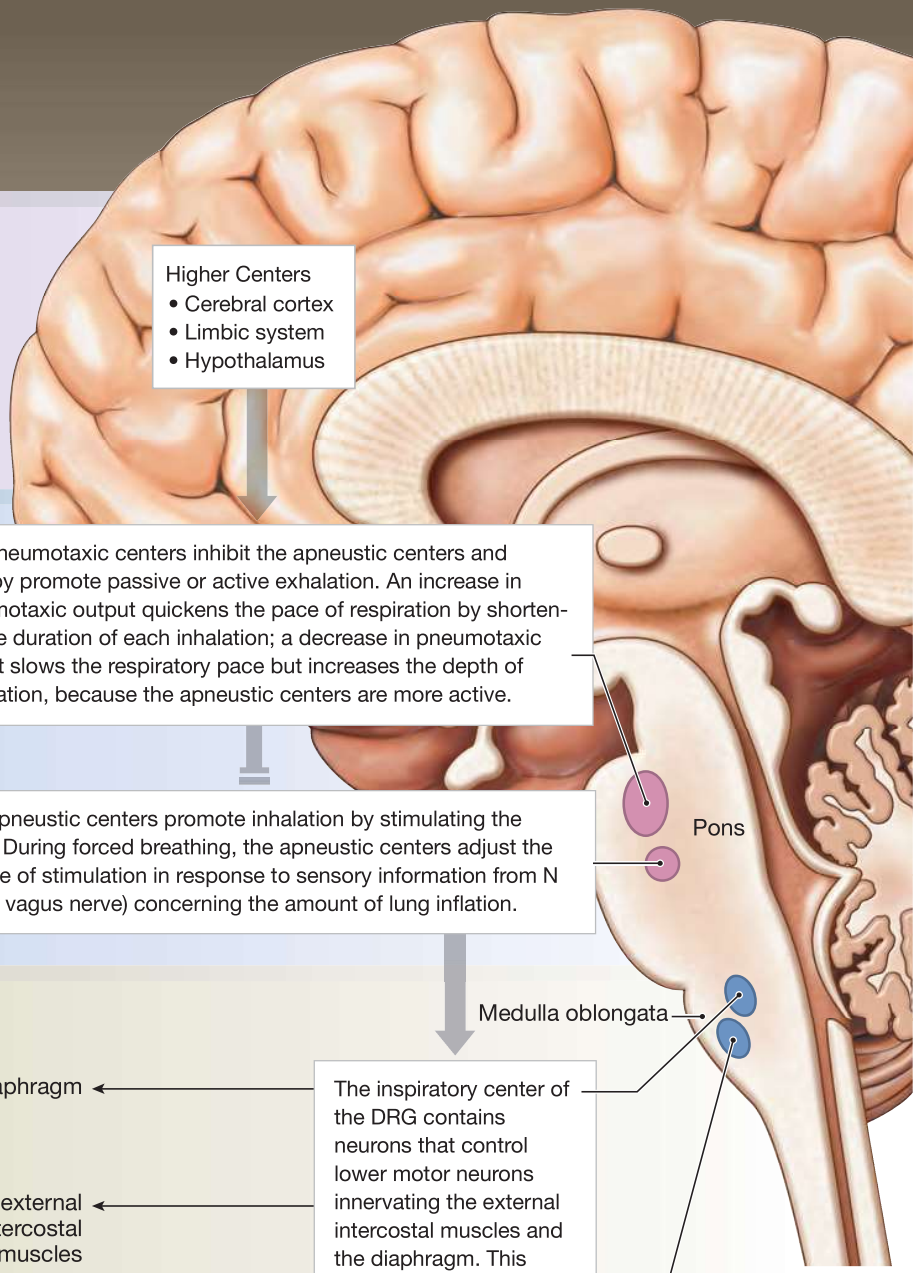
The activities of the respiratory centers are modified by sensory information from several sources:

- Chemoreceptors sensitive to the P_{CO_2}, pH, or P_{O_2} of the blood or cerebrospinal fluid.
- Baroreceptors in the aortic or carotid sinuses sensitive to changes in blood pressure.
- Stretch receptors that respond to changes in the volume of the lungs.
- Irritating physical or chemical stimuli in the nasal cavity, larynx, or bronchial tree.
- Other sensations, including pain, changes in body temperature, and abnormal visceral sensations.

Spotlight

Figure 23–26
Control of Respiration

Respiratory control involves multiple levels of regulation. Most of the regulatory activities occur outside of our awareness.



LEVEL 3 — Higher Centers

Higher centers in the hypothalamus, limbic system, and cerebral cortex can alter the activity of the pneumotaxic centers, but essentially normal respiratory cycles continue even if the brain stem superior to the pons has been severely damaged.

LEVEL 2 — Apneustic and Pneumotaxic Centers

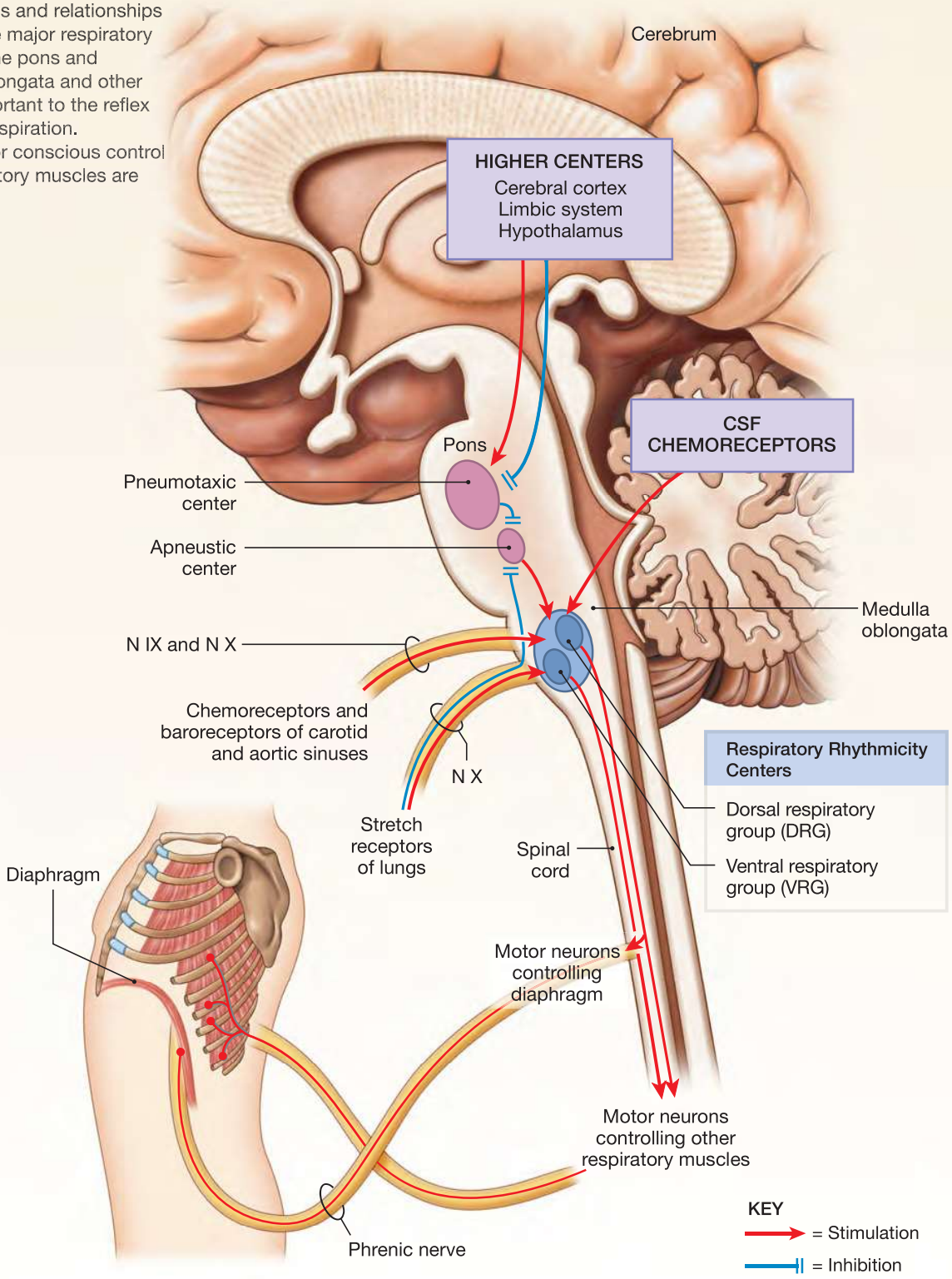
The **apneustic** (ap-NOO-stik) centers and the **pneumotaxic** (noo-mō-TAKS-ik) centers of the pons are paired nuclei that adjust the output of the respiratory rhythmicity centers.

LEVEL 1 — Respiratory Rhythmicity Centers

The most basic level of respiratory control involves pacemaker cells in the medulla oblongata. These neurons generate cycles of contraction and relaxation in the diaphragm. The respiratory rhythmicity centers set the pace of respiration by adjusting the activities of these pacemakers and coordinating the activities of additional respiratory muscles. Each rhythmicity center can be subdivided into a dorsal respiratory group (DRG) and a ventral respiratory group (VRG). The DRG modifies its activities in response to input from chemoreceptors and baroreceptors that monitor O_2, CO_2, and pH in the blood and CSF and from stretch receptors that monitor the degree of stretching in the walls of the lungs.

Respiratory Centers and Reflex Controls

The locations and relationships between the major respiratory centers in the pons and medulla oblongata and other factors important to the reflex control of respiration. Pathways for conscious control over respiratory muscles are not shown.



Information from these receptors alters the pattern of respiration. The induced changes have been called *respiratory reflexes*.

The Chemoreceptor Reflexes

The respiratory centers are strongly influenced by chemoreceptor inputs from cranial nerves IX and X, and from receptors that monitor the composition of the cerebrospinal fluid (CSF):

- The glossopharyngeal nerves (N IX) carry chemoreceptive information from the carotid bodies, adjacent to the carotid sinus. ↩ pp. 502, 740 The carotid bodies are stimulated by a decrease in the pH or P_{O_2} of blood. Because changes in P_{CO_2} affect pH, a rise in the P_{CO_2} indirectly stimulates these receptors.
- The vagus nerves (N X) monitor chemoreceptors in the aortic bodies, near the aortic arch. ↩ pp. 502, 740 These receptors are sensitive to the same stimuli as the carotid bodies. Carotid and aortic body receptors are often called *peripheral chemoreceptors*.
- Chemoreceptors are located on the ventrolateral surface of the medulla oblongata in a region known as the *chemosensitive area*. The neurons in that area respond only to the P_{CO_2} and pH of the CSF. They are often called *central chemoreceptors*.

We discussed chemoreceptors and their effects on cardiovascular function in Chapters 15 and 21. ↩ pp. 502, 729–730 Stimulation of these chemoreceptors leads to an increase in the depth and rate of respiration. Under normal conditions, a drop in arterial P_{O_2} has little effect on the respiratory centers, until the arterial P_{O_2} drops by about 40 percent, to below 60 mm Hg. If the P_{O_2} of arterial blood drops to 40 mm Hg (the level in peripheral tissues), the respiratory rate increases by only 50–70 percent. In contrast, a rise of just 10 percent in the arterial P_{CO_2} causes the respiratory rate to double, even if the P_{O_2} remains completely normal. Carbon dioxide levels are therefore responsible for regulating respiratory activity under normal conditions.

Although the receptors monitoring CO_2 levels are more sensitive, oxygen and carbon dioxide receptors work together in a crisis. Carbon dioxide is generated during oxygen consumption, so when oxygen concentrations are falling rapidly, CO_2 levels are usually increasing. This cooperation breaks down only under unusual circumstances. For example, you can hold your breath longer than normal by taking deep, full breaths, but the practice is very dangerous. The danger lies in the fact that the increased ability is due not to extra oxygen, but to less carbon dioxide. If the P_{CO_2} is driven down far enough, your ability to hold your breath can increase to the point at which you become unconscious from oxygen starvation in the brain without ever feeling the urge to breathe.

The chemoreceptors are subject to adaptation—a decrease in sensitivity after chronic stimulation—if the P_{O_2} or P_{CO_2} remains abnormal for an extended period. This adaptation can complicate the treatment of chronic respiratory disorders. For example, if the P_{O_2} remains low for an extended period while the P_{CO_2} remains chronically elevated, the chemoreceptors will reset to those values. They will then oppose any attempts to return the partial pressures to the proper range.

Any condition altering the pH of blood or CSF affects respiratory performance because the chemoreceptors monitoring CO_2 levels are also sensitive to pH. The rise in lactic acid levels after exercise, for example, causes a drop in pH that helps stimulate respiratory activity.

Hypercapnia and Hypocapnia. **Hypercapnia** is an increase in the P_{CO_2} of arterial blood. **Figure 23–27a** diagrams the central response to hypercapnia. Stimulation of chemoreceptors in the carotid and aortic bodies triggers this response. It is reinforced by the stimulation of CNS chemoreceptors. Carbon dioxide crosses the blood–brain barrier quite rapidly. For this reason, a rise in arterial P_{CO_2} almost immediately raises CO_2 levels in the CSF, lowering the pH of the CSF and stimulating the chemoreceptive neurons of the medulla oblongata.

These chemoreceptors stimulate the respiratory centers to increase the rate and depth of respiration. Your breathing becomes more rapid, and more air moves into and out of your lungs with each breath. Because more air moves into and out of the alveoli each minute, alveolar concentrations of carbon dioxide decline, accelerating the diffusion of carbon dioxide out of alveolar capillaries. In this way, homeostasis is restored.

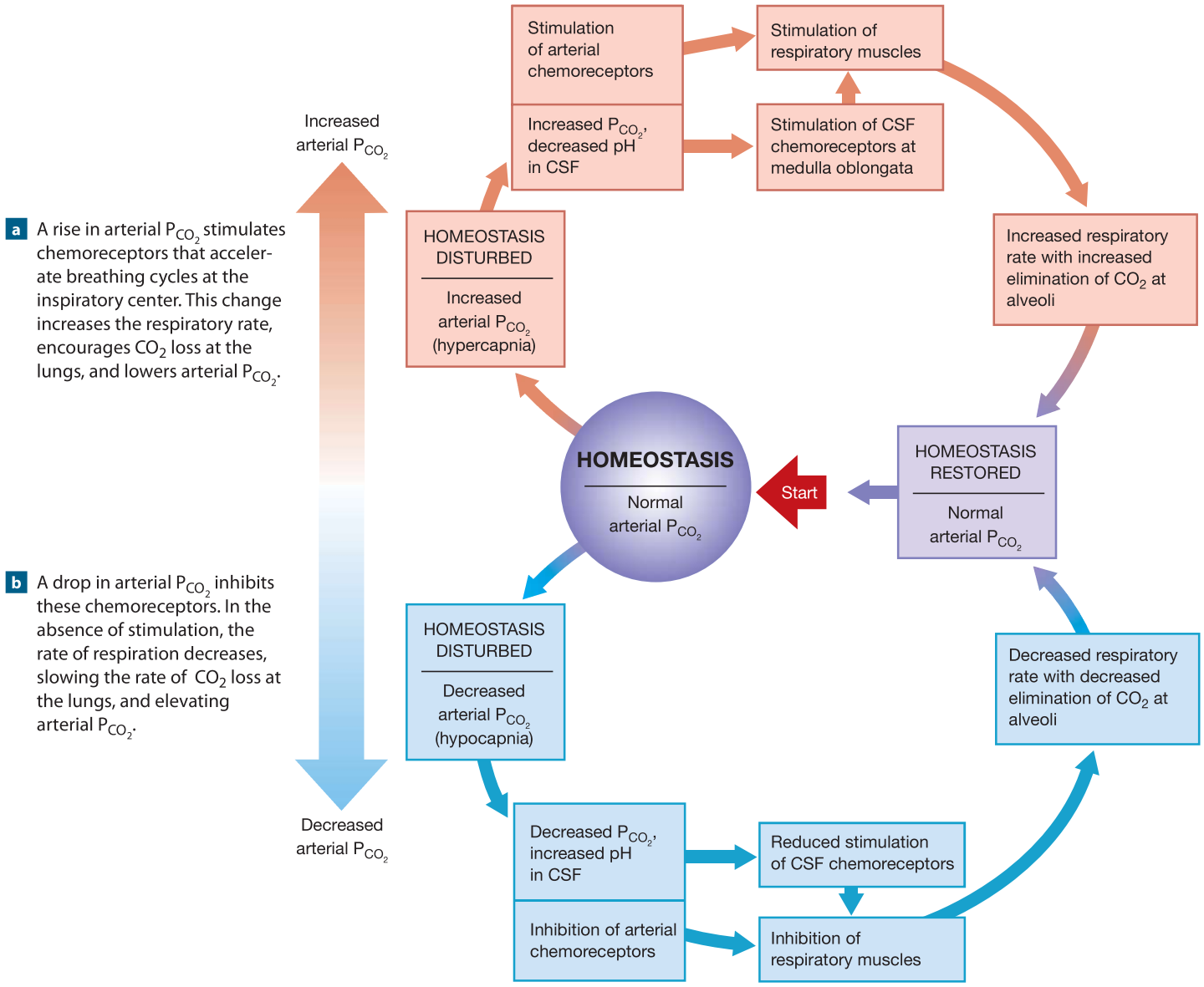
The most common cause of hypercapnia is hypoventilation. In **hypoventilation,** the respiratory rate remains abnormally low and cannot meet the demands for normal oxygen delivery and carbon dioxide removal. Carbon dioxide then accumulates in the blood.

If the rate and depth of respiration exceed the demands for oxygen delivery and carbon dioxide removal, the condition called **hyperventilation** exists. Hyperventilation gradually leads to **hypocapnia,** an abnormally low P_{CO_2}. If the arterial P_{CO_2} drops below normal levels, chemoreceptor activity decreases and the respiratory rate falls (**Figure 23–27b**). This situation continues until the P_{CO_2} returns to normal and homeostasis is restored.

The Baroreceptor Reflexes

We described the effects of carotid and aortic baroreceptor stimulation on systemic blood pressure in Chapter 21. ↩ p. 728 The output from these baroreceptors also affects the respiratory centers. When blood pressure falls, the respiratory rate increases. When blood pressure rises, the respiratory rate declines. These adjustments result from the stimulation or inhibition of the respiratory centers by sensory fibers in the glossopharyngeal (N IX) and vagus (N X) nerves.

Figure 23–27 The Chemoreceptor Response to Changes in P_{CO_2}.



The Hering–Breuer Reflexes

The **Hering–Breuer reflexes** are named after the physiologists who described them in 1865. The sensory information from these reflexes goes to the apneustic centers and the ventral respiratory group. The Hering–Breuer reflexes are not involved in normal quiet breathing (eupnea) or in tidal volumes under 1000 mL. There are two such reflexes:

1. The **inflation reflex** prevents overexpansion of the lungs during forced breathing. Lung expansion stimulates stretch receptors in the smooth muscle tissue around bronchioles. Sensory fibers from the stretch receptors of each lung reach the respiratory rhythmicity center on the same side via the vagus nerve. As lung volume increases, the dorsal respiratory group is gradually inhibited, and the expiratory center of the VRG is stimulated. Inhalation stops as the lungs near maximum volume. Active exhalation then begins.
2. The **deflation reflex** normally functions only during forced exhalation, when both the inspiratory and expiratory centers are active. This reflex inhibits the expiratory centers and stimulates the inspiratory centers when the lungs are deflating. These receptors are distinct from those of the inflation reflex. They are located in the alveolar wall near the alveolar capillary network. The smaller the volume of the lungs, the greater the degree of inhibition. Finally, exhalation stops and inhalation begins.

Protective Reflexes

Protective reflexes operate when you are exposed to toxic vapors, chemical irritants, or mechanical stimulation of the respiratory tract. The receptors involved are located in the epithelium of the respiratory tract. Examples of protective reflexes include sneezing, coughing, and laryngeal spasms.

Sneezing is triggered by an irritation of the nasal cavity wall. Coughing is triggered by an irritation of the larynx, trachea, or bronchi. Both reflexes involve **apnea** (AP-nē-uh), a period in which respiration is suspended. A forceful expulsion of air usually follows to remove the offending stimulus. The glottis is forcibly closed while the lungs are still relatively full. The abdominal and internal intercostal muscles then contract suddenly, creating pressures that blast air out of the respiratory passageways when the glottis reopens. Air leaving the larynx can travel at 160 kph (99 mph), carrying mucus, foreign particles, and irritating gases out of the respiratory tract via the nose or mouth.

Laryngeal spasms result when chemical irritants, foreign objects, or fluids enter the area around the glottis. This reflex generally closes the airway temporarily. A very strong stimulus, such as a toxic gas, could close the glottis so powerfully that you could lose consciousness and die without taking another breath. Fine chicken bones or fish bones that pierce the laryngeal walls can also stimulate laryngeal spasms, swelling, or both, restricting the airway.

Voluntary Control of Respiration

Activity of the cerebral cortex has an indirect effect on the respiratory centers, as the following examples show:

- Conscious thought processes tied to strong emotions, such as rage or fear, affect the respiratory rate by stimulating centers in the hypothalamus.
- Emotional states can affect respiration by activating the sympathetic or parasympathetic division of the autonomic nervous system. Sympathetic activation causes bronchodilation and increases the respiratory rate. Parasympathetic stimulation has the opposite effect.
- An anticipation of strenuous exercise can trigger an automatic increase in the respiratory rate, along with increased cardiac output, by sympathetic stimulation.

Conscious control over respiratory activities may bypass the respiratory centers completely, using pyramidal fibers that innervate the same lower motor neurons that are controlled by the DRG and VRG. This control mechanism is an essential part of speaking, singing, and swimming, when respiratory activities must be precisely timed. Higher centers can also have an inhibitory effect on the apneustic centers and on the DRG and VRG. This effect is important when you hold your breath.

Your abilities to override the respiratory centers have limits, however. The chemoreceptor reflexes are extremely powerful in stimulating respiration, and you cannot consciously suppress them. For example, you cannot kill yourself by holding your breath "till you turn blue." Once the P_{CO_2} rises to critical levels, you are forced to take a breath.

Changes in the Respiratory System at Birth

The respiratory systems of fetuses and newborns differ in several important ways. Before delivery, pulmonary arterial resistance is high, because the pulmonary vessels are collapsed. The rib cage is compressed, and the lungs and conducting passageways contain only small amounts of fluid and no air. During delivery, the lungs are compressed further. As the placental connection is lost, blood oxygen levels fall and carbon dioxide levels climb rapidly.

At birth, the newborn infant takes a truly heroic first breath through powerful contractions of the diaphragmatic and external intercostal muscles. The inhaled air must enter the respiratory passageways with enough force to overcome surface tension and inflate the bronchial tree and most of the alveoli. The same drop in pressure that pulls air into the lungs also pulls blood into the pulmonary circulation. The changes in blood flow and rise in oxygen levels lead to the closure of the *foramen ovale*, an interatrial connection, and the *ductus arteriosus*, the fetal connection between the pulmonary trunk and the aorta. ↩ pp. 755–756 ATLAS: Embryology Summary 18: The Development of the Respiratory System

The exhalation that follows does not empty the lungs completely, because the rib cage does not return to its former, fully compressed state. Cartilages and connective tissues keep the conducting passageways open, and surfactant covering the alveolar surfaces prevents their collapse. The next breaths complete the inflation of the alveoli.

Pathologists sometimes use these physical changes to determine whether a newborn infant died before delivery or shortly thereafter. Before the first breath, the lungs are completely filled with amniotic fluid, and extracted lungs will sink if placed in water. After the infant's first breath, even the collapsed lungs contain enough air to keep them afloat.

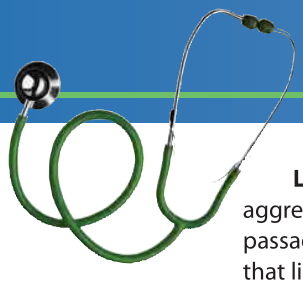
Checkpoint

28. **What effect does exciting the pneumotaxic centers have on respiration?**
29. **Are peripheral chemoreceptors as sensitive to levels of carbon dioxide as they are to levels of oxygen?**
30. **Little Johnny is angry with his mother, so he tells her that he will hold his breath until he turns blue and dies. Should Johnny's mother worry?**

See the blue Answers tab at the back of the book.

Clinical Note

Emphysema and Lung Cancer



Where there's **smoking,** there's **disease**

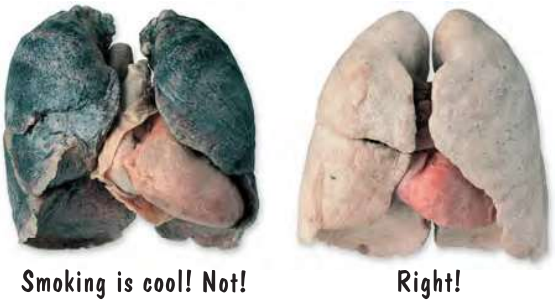
Emphysema and lung cancer are two relatively common disorders that are often associated with cigarette smoking.

Emphysema (em-fi-ZĒ-muh) is a chronic, progressive condition characterized by shortness of breath and an inability to tolerate physical exertion. The underlying problem is the destruction of alveolar surfaces and inadequate surface area for oxygen and carbon dioxide exchange. In essence, respiratory bronchioles and alveoli are functionally eliminated. The alveoli gradually expand, and adjacent alveoli merge to form larger air spaces supported by fibrous tissue without alveolar capillary networks. As connective tissues are eliminated, compliance increases, so air moves into and out of the lungs more easily than before. However, the loss of respiratory surface area restricts oxygen absorption, so the individual becomes short of breath.

Emphysema has been linked to breathing air that contains fine particles or toxic vapors, such as those in cigarette smoke. Genetic factors also predispose individuals to the condition. Some degree of emphysema is a normal consequence of aging, however. An estimated 66 percent of adult males and 25 percent of adult females have detectable areas of emphysema in their lungs.

Lung cancer, or *bronchopulmonary carcinoma*, is an aggressive class of malignancies originating in the bronchial passageways or alveoli. These cancers affect the epithelial cells that line conducting passageways, mucous glands, or alveoli. Signs and symptoms generally do not appear until tumors restrict airflow or compress adjacent structures. Chest pain, shortness of breath, a cough or a wheeze, and weight loss commonly occur. Treatment programs vary with the cellular organization of the tumor and whether metastasis (cancer cell migration) has occurred. Surgery, radiation therapy, or chemotherapy may be involved.

According to the CDC, more people die from lung cancer than any other type of cancer. Lung cancer affects an estimated 106,374 men and 90,080 women in the United States.

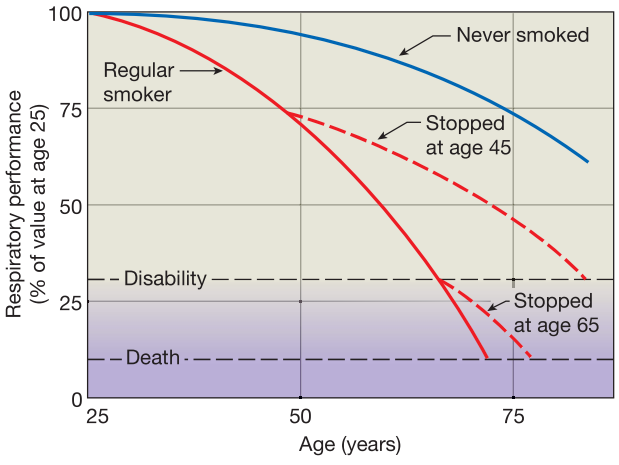


23-11 Respiratory performance declines with age

Many factors interact to reduce the efficiency of the respiratory system in elderly individuals. Here are three examples:

1. With age, elastic tissue deteriorates throughout the body. These changes reduce the compliance of the lungs and lower vital capacity.
2. Chest movements are restricted by arthritic changes in the rib articulations and by decreased flexibility at the costal cartilages. Along with the changes in item 1, the stiffening and reduction in chest movement effectively limit the respiratory minute volume. This restriction contributes to the reduction in exercise performance and capabilities with increasing age.
3. Some degree of emphysema is normal in individuals over age 50. However, the extent varies widely with the lifetime exposure to cigarette smoke and other respiratory irritants. **Figure 23–28** compares the respiratory performance of individuals who have never smoked with individuals who have smoked for various periods of time. The message is quite clear: Some decrease in respiratory performance is inevitable, but you can prevent serious respiratory deterioration by stopping smoking or never starting.

Figure 23–28 Decline in Respiratory Performance with Age and Smoking. The relative respiratory performances of individuals who have never smoked, individuals who quit smoking at age 45, individuals who quit smoking at age 65, and lifelong smokers.



Checkpoint

31. **Name several age-related factors that affect the respiratory system.**

See the blue Answers tab at the back of the book.

23-12 The respiratory system provides oxygen to, and eliminates carbon dioxide from, other organ systems

The goal of respiratory activity is to maintain homeostatic oxygen and carbon dioxide levels in peripheral tissues. Changes in respiratory activity alone are seldom enough to accomplish this. Coordinated changes in cardiovascular activity must also take place.

Consider these examples of the integration between the respiratory and cardiovascular systems:

- At the local level, changes in lung perfusion in response to changes in alveolar P_{O_2} improve the efficiency of gas exchange within or among lobules.
- Chemoreceptor stimulation not only increases the respiratory drive, but it also causes blood pressure to rise and cardiac output to increase.
- The stimulation of baroreceptors in the lungs has secondary effects on cardiovascular function. For example, the stimulation of airway stretch receptors not only triggers the inflation reflex, but also increases heart rate. Thus, as the lungs fill, cardiac output rises and more blood flows through the alveolar capillaries.

The adaptations that take place at high altitudes are an excellent example of the functional interplay between the respiratory and cardiovascular systems. Atmospheric pressure decreases with increasing altitude, and so do the partial pressures of the component gases, including oxygen. People living in Denver or Mexico City function normally with alveolar oxygen pressures in the 80–90 mm Hg range. At higher elevations, alveolar P_{O_2} is even lower. At 3300 meters (10,826 ft), an altitude many hikers and skiers have experienced, alveolar P_{O_2} is about 60 mm Hg.

Despite the low alveolar P_{O_2}, millions of people live and work at altitudes this high or higher. Important physiological adjustments include increased respiratory rate, increased heart rate, increased BPG levels, and elevated hematocrit. Thus, even though the hemoglobin is not fully saturated, the bloodstream holds more of it, and the round trip between the lungs and the peripheral tissues takes less time. However, most of these adaptations take days to weeks to develop. As a result, athletes planning to compete in events at high altitude must begin training under such conditions well in advance.

The respiratory system is functionally linked to all other body systems as well. **Figure 23–29** illustrates these interrelationships with the systems studied so far.

Checkpoint

32. **Identify the functional relationship between the respiratory system and all other organ systems.**
33. **Describe the functional relationship between the respiratory system and the lymphatic system.**

See the blue Answers tab at the back of the book.

Related Clinical Terms

asbestosis: Pneumoconiosis, disease of the lungs, caused by the inhalation of asbestos particles over time.
asphyxia: Impaired oxygen–carbon dioxide exchange that results in suffocation.
aspirate: Drawing fluid from the body by suction; foreign material accidentally sucked into the lungs.
bronchography: A procedure in which radiopaque materials are introduced into the airways to improve x-ray imaging of the bronchial tree.
bronchoscope: A fiber-optic bundle small enough to be inserted into the trachea and finer airways; the procedure is called *bronchoscopy*.
cardiopulmonary resuscitation (CPR): The application of cycles of compression to the rib cage and mouth-to-mouth breathing to restore cardiovascular and respiratory function.
Cheyne-Stokes breathing: Hyperpnea (deep, fast breathing) alternating with apnea (absence of breathing).
chronic obstructive pulmonary disease (COPD): A general term describing temporary or permanent lung disease of the bronchial tree.
dyspnea: The condition of labored breathing.
endotracheal tube: Tube that is passed through the mouth or nose to the trachea.
Heimlich maneuver, or *abdominal thrust*: Sudden compression applied to the abdomen just inferior to the diaphragm, to force air out of the lungs to clear a blocked trachea or larynx.
hemoptysis: Coughing up blood or bloody mucus.
hemothorax: The condition of having blood in the pleural cavity.
hyperbaric oxygenation: Therapy to force more oxygen into the blood by use of a pressure chamber.
nasal polyps: Benign growths on the mucous lining of the nasal cavity.
orthopnea: Condition in which one has breathing difficulty except when in an upright position.

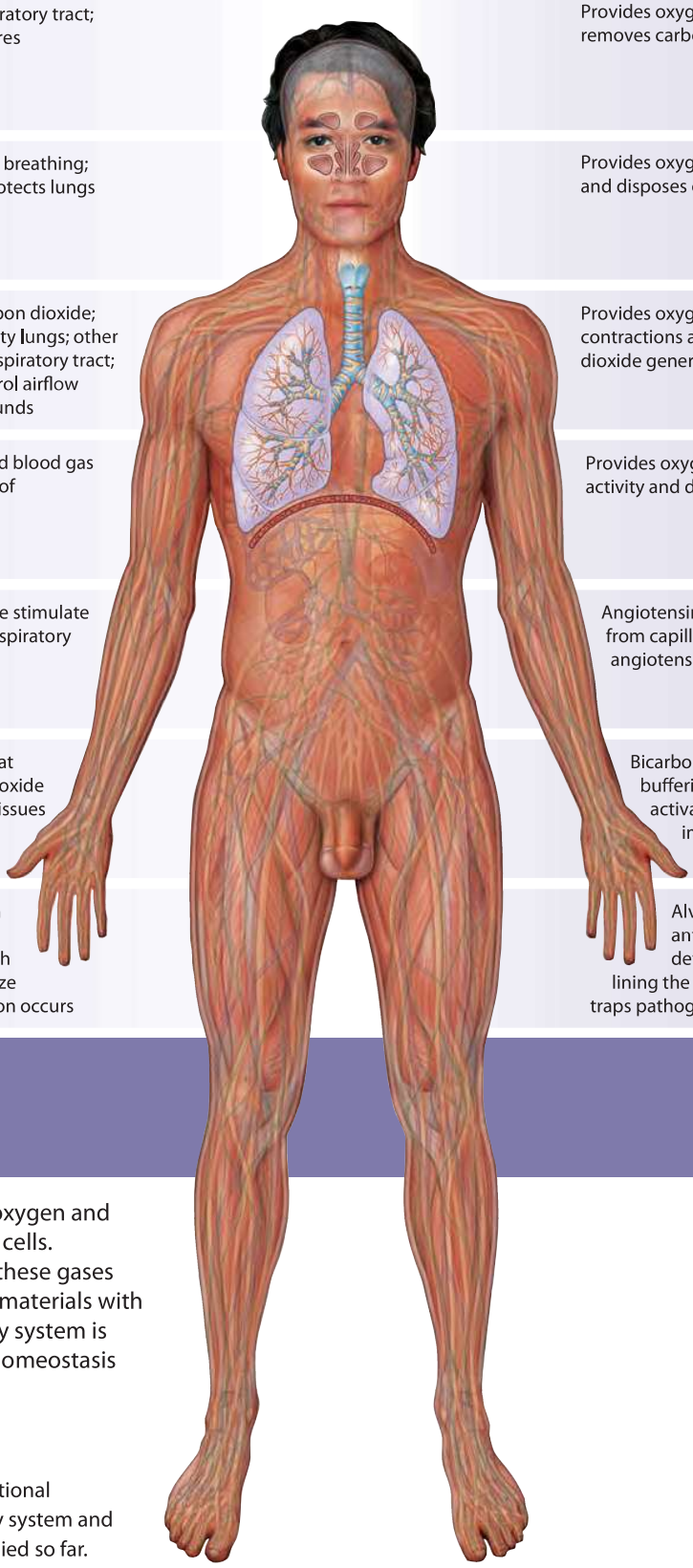
SYSTEM INTEGRATOR

Body System → Respiratory System

Body System	Respiratory System
Integumentary	Protects portions of upper respiratory tract; hairs guard entry to external nares
Skeletal	Movements of ribs important in breathing; axial skeleton surrounds and protects lungs
Muscular	Muscular activity generates carbon dioxide; respiratory muscles fill and empty lungs; other muscles control entrances to respiratory tract; intrinsic laryngeal muscles control airflow through larynx and produce sounds
Nervous	Monitors respiratory volume and blood gas levels; controls pace and depth of respiration
Endocrine	Epinephrine and norepinephrine stimulate respiratory activity and dilate respiratory passageways
Cardiovascular	Circulates the red blood cells that transport oxygen and carbon dioxide between lungs and peripheral tissues
Lymphatic	Tonsils protect against infection at entrance to respiratory tract; lymphatic vessels monitor lymph drainage from lungs and mobilize adaptive defenses when infection occurs

Respiratory System → Body System

Respiratory System	Body System
Provides oxygen to nourish tissues and removes carbon dioxide	Integumentary Page 165
Provides oxygen to skeletal structures and disposes of carbon dioxide	Skeletal Page 275
Provides oxygen needed for muscle contractions and disposes of carbon dioxide generated by active muscles	Muscular Page 369
Provides oxygen needed for neural activity and disposes of carbon dioxide	Nervous Page 543
Angiotensin-converting enzyme (ACE) from capillaries of lungs converts angiotensin I to angiotensin II	Endocrine Page 632
Bicarbonate ions contribute to buffering capability of blood; activation of angiotensin II by ACE important in regulation of blood pressure and volume	Cardiovascular Page 759
Alveolar phagocytes present antigens to trigger specific defenses; mucous membrane lining the nasal cavity and upper pharynx traps pathogens, protects deeper tissues	Lymphatic Page 807



The RESPIRATORY System

The respiratory system provides oxygen and eliminates carbon dioxide for our cells. Stabilizing the concentrations of these gases involves a continual exchange of materials with the outside world. The respiratory system is therefore crucial to maintaining homeostasis for all body systems.

Figure 23–29 diagrams the functional relationships between the respiratory system and the other body systems we have studied so far.

Digestive Page 910

Urinary Page 992

Reproductive Page 1072

otorhinolaryngology: Branch of medicine dealing with disease and treatment of the ear, nose, and throat.
rales: Abnormal hissing or other respiratory sounds.
rhinitis: Inflammation of the nasal cavity.
rhinoplasty: Plastic surgery of the nose.
severe acute respiratory syndrome (SARS): A harsh viral respiratory illness caused by a coronavirus that typically progresses to pneumonia.
sputum: A mixture of saliva and mucus coughed up from the respiratory tract, often as the result of an infection.
stridor: Harsh vibrating breathing sound caused by an obstruction in the windpipe or larynx.
stuttering: To speak with a continued involuntary repetition of sounds.
tachypnea: Rapid rate of breathing.
tussis: A cough.
wheeze: An audible whistling sound when breathing.

Chapter Review

Study Outline

An introduction to the respiratory system p. 814

1. Body cells must obtain oxygen and eliminate carbon dioxide. Gas exchange takes place at respiratory surfaces inside the lungs.

23-1 The respiratory system, organized into an upper respiratory system and a lower respiratory system, has several basic functions p. 814

2. The functions of the **respiratory system** include (1) providing an area for gas exchange between air and circulating blood; (2) moving air to and from exchange surfaces; (3) protecting respiratory surfaces from environmental variations and defending the respiratory system and other tissues from invasion by pathogens; (4) producing sounds; and (5) facilitating the detection of olfactory stimuli.
3. The respiratory system includes the **upper respiratory system,** composed of the nose, nasal cavity, paranasal sinuses, and pharynx, and the **lower respiratory system,** which includes the larynx, trachea, bronchi, bronchioles, and alveoli of the lungs. *(Figure 23–1)*
4. The **respiratory tract** consists of the conducting airways that carry air to and from the **alveoli.** The passageways of the upper respiratory tract filter and humidify incoming air. The lower respiratory tract includes delicate conduction passages and the exchange surfaces of the alveoli.
5. The **respiratory mucosa** (respiratory epithelium and underlying connective tissue) lines the conducting portion of the respiratory tract.
6. The respiratory epithelium changes in structure along the respiratory tract. It is supported by the **lamina propria,** a layer of areolar tissue. *(Figure 23–2)*
7. Contamination of the respiratory system is prevented by the mucus and cilia of the **respiratory defense system.** *(Figure 23–2)*

23-2 Located outside the thoracic cavity, the upper respiratory system consists of the nose, nasal cavity, paranasal sinuses, and pharynx p. 817

8. The upper respiratory system consists of the nose, nasal cavity, paranasal sinuses, and pharynx. *(Figures 23–1, 23–3)*
9. Air normally enters the respiratory system through the **external nares,** which open into the *nasal cavity*. The **nasal vestibule** (entryway) is guarded by hairs that screen out large particles. *(Figure 23–3)*
10. Incoming air flows through the **superior, middle,** and **inferior meatuses** (narrow grooves) and bounces off the conchal surfaces. *(Figure 23–3)*
11. The **hard palate** separates the oral and nasal cavities. The **soft palate** separates the superior nasopharynx from the rest of the pharynx. The connections between the nasal cavity and nasopharynx are the **internal nares.**
12. The nasal mucosa traps particles, warms and humidifies incoming air, and cools and dehumidifies outgoing air.
13. The **pharynx,** or throat, is a chamber shared by the digestive and respiratory systems. The **nasopharynx** is the superior part of the pharynx. The **oropharynx** is continuous with the oral cavity. The **laryngopharynx** includes the narrow zone between the hyoid bone and the entrance to the esophagus. *(Figure 23–3)*

23-3 Composed of cartilages, ligaments, and muscles, the larynx produces sound p. 819

14. Inhaled air passes through the **glottis** en route to the lungs; the **larynx** surrounds and protects the glottis. *(Figure 23–4)*
15. The cylindrical larynx is composed of three large cartilages (the **thyroid cartilage, cricoid cartilage,** and **epiglottis**) and three smaller pairs of cartilages (the **arytenoid, corniculate,** and **cuneiform cartilages**). The epiglottis projects into the pharynx. *(Figures 23–4, 23–5)*
16. Two pairs of folds span the glottis: the inelastic **vestibular folds** and the more delicate **vocal folds.** *(Figure 23–5)*
17. Air passing through the glottis vibrates the vocal folds, producing sound. The pitch of the sound depends on the diameter, length, and tension of the vocal folds.
18. The muscles of the neck and pharynx position and stabilize the larynx. The smaller intrinsic muscles regulate tension in the vocal folds or open and close the glottis. During swallowing, both sets of muscles help prevent particles from entering the glottis.

23-4 The trachea and primary bronchi convey air to and from the lungs p. 822

19. The **trachea** extends from the sixth cervical vertebra to the fifth thoracic vertebra. The **submucosa** contains C-shaped **tracheal cartilages,** which stiffen the tracheal walls and protect the airway. The posterior tracheal wall can distort to permit large masses of food to pass through the esophagus. *(Figure 23–6)*
20. The trachea branches within the mediastinum to form the **right** and **left primary bronchi.** Each bronchus enters a lung at the **hilum** (a groove). The **root** is a connective tissue mass that includes the bronchus, pulmonary vessels, and nerves. *(Figures 23–6, 23–7)*

23-5 Enclosed by a pleural membrane, the lungs are paired organs containing alveoli, which permit gaseous exchange p. 822

21. The **lobes** of the lungs are separated by fissures. The right lung has three lobes, the left lung two. *(Figure 23–7)*
22. The anterior and lateral surfaces of the lungs follow the inner contours of the rib cage. The concavity of the medial surface of the left lung is the **cardiac notch,** which conforms to the shape of the pericardium. *(Figures 23–7, 23–8)*
23. The primary bronchi and their branches form the **bronchial tree.** The **secondary** and **tertiary bronchi** are branches within the lungs. As they branch, the amount of cartilage in their walls decreases and the amount of smooth muscle increases. *(Figure 23–9)*
24. Each tertiary bronchus supplies air to a single **bronchopulmonary segment.** *(Figure 23–9)*
25. **Bronchioles** within the bronchopulmonary segments ultimately branch into **terminal bronchioles.** Each terminal bronchiole delivers air to a single **pulmonary lobule** in which the terminal bronchiole branches into **respiratory bronchioles.** The connective tissues of the root of the lung extend into the parenchyma of the lung as a series of *trabeculae* (partitions) that branch to form **interlobular septa,** which divide the lung into lobules. *(Figure 23–9)*
26. The respiratory bronchioles open into **alveolar ducts,** where many alveoli are interconnected. The respiratory exchange surfaces are extensively connected to the circulatory system via the capillaries of the pulmonary circuit. *(Figure 23–10)*
27. The **respiratory membrane** consists of a simple squamous epithelium, the endothelial cell lining an adjacent capillary, and their fused basement membranes. **Pneumocytes type II** (septal cells) scattered in the respiratory membrane produce **surfactant** that reduces surface tension and keeps the alveoli from collapsing. **Alveolar macrophages** patrol the epithelium and engulf foreign particles. *(Figure 23–11)*
28. The conducting portions of the respiratory tract receive blood from the external carotid arteries, the thyrocervical trunks, and the bronchial arteries. Venous blood flows into the pulmonary veins, bypassing the rest of the systemic circuit and diluting the oxygenated blood leaving the alveoli.
29. Each lung is surrounded by a single **pleural cavity** lined by a **pleura** (serous membrane). The two types of pleurae are the **parietal pleura,** covering the inner surface of the thoracic wall, and the **visceral pleura,** covering the lungs.

23-6 External respiration and internal respiration allow gaseous exchange within the body p. 829

30. Respiratory physiology focuses on a series of integrated processes. **External respiration** is the exchange of oxygen and carbon dioxide between interstitial fluid and the external environment and includes **pulmonary ventilation** (breathing). **Internal respiration** is the exchange of oxygen and carbon dioxide between interstitial fluid and cells. If the oxygen content declines, the affected tissues suffer from **hypoxia;** if the oxygen supply is completely shut off, **anoxia** and tissue death result. *(Figure 23–12)*

23-7 Pulmonary ventilation—the exchange of air between the atmosphere and the lungs—involves pressure changes, muscle movement, and respiratory rates and volumes p. 830

31. **Pulmonary ventilation** is the physical movement of air into and out of the respiratory tract.
32. As pressure on a gas decreases, its volume expands; as pressure increases, gas volume contracts. This inverse relationship is **Boyle's law.** *(Figure 23–13; Table 23–1)*
33. Movement of the diaphragm and ribs changes lung volume.
34. The relationship between **intrapulmonary pressure** (the pressure inside the respiratory tract) and **atmospheric pressure (atm)** determines the direction of airflow. **Intrapleural pressure** is the pressure in the potential space between the parietal and visceral pleurae. *(Figures 23–14, 23–15)*
35. A **respiratory cycle** is a single cycle of inhalation and exhalation. The amount of air moved in one respiratory cycle is the **tidal volume.** A **spirometer** is an instrument used to measure the capacity of the lungs. *(Figure 23–15)*
36. The diaphragm and the external and internal intercostal muscles are involved in normal **quiet breathing,** or **eupnea.** Accessory muscles become active during the active inspiratory and expiratory movements of **forced breathing,** or **hyperpnea.** *(Figure 23–16)*
37. **Alveolar ventilation** is the amount of air reaching the alveoli each minute. The **vital capacity** includes the **tidal volume** plus the **expiratory** and **inspiratory reserve volumes.** The air left in the lungs at the end of maximum exhalation is the **residual volume.** *(Figure 23–17)*

23-8 Gas exchange depends on the partial pressures of gases and the diffusion of molecules p. 838

38. In a mixed gas, the individual gases exert a pressure proportional to their abundance in the mixture **(Dalton's law).** The pressure contributed by a single gas is its **partial pressure.** (Table 23–2)
39. The amount of a gas in solution is directly proportional to the partial pressure of that gas **(Henry's law).** *(Figure 23–18)*
40. Alveolar air and atmospheric air differ in composition. Gas exchange across the respiratory membrane is efficient due to differences in partial pressures, the short diffusion distance, lipid-soluble gases, the large surface area of all the alveoli combined, and the coordination of blood flow and airflow. *(Figure 23–19)*

23-9 Most oxygen is transported bound to hemoglobin; and carbon dioxide is transported in three ways: as carbonic acid, bound to hemoglobin, or dissolved in plasma p. 841

41. Blood entering peripheral capillaries delivers oxygen and absorbs carbon dioxide. The transport of oxygen and carbon dioxide in blood involves reactions that are completely reversible.
42. Oxygen is carried mainly by RBCs, reversibly bound to hemoglobin. At alveolar P_{O_2} hemoglobin is almost fully saturated; at the P_{O_2} of peripheral tissues, it releases oxygen but still retains a substantial oxygen reserve. The effect of pH on the hemoglobin saturation curve is called the **Bohr effect.** When low plasma P_{O_2} continues for extended periods, red blood cells generate more **2,3-bisphosphoglycerate (BPG),** which reduces hemoglobin's affinity for oxygen. *(Figures 23–20, 23–21)*
43. **Fetal hemoglobin** has a stronger affinity for oxygen than does adult hemoglobin, aiding the removal of oxygen from maternal blood. *(Figure 23–22)*
44. Aerobic metabolism in peripheral tissues generates CO_2. About 7 percent of the CO_2 transported in blood is dissolved in the plasma, 23 percent is bound as **carbaminohemoglobin,** and 70 percent is converted to carbonic acid, which dissociates into H^+ and HCO_3^-. *(Figure 23–23)*
45. Driven by differences in partial pressure, oxygen enters the blood at the lungs and leaves it in peripheral tissues; similar

forces drive carbon dioxide into the blood at the tissues and into the alveoli at the lungs. *(Figure 23–24)*

23-10 Neurons in the medulla oblongata and pons, along with respiratory reflexes, control respiration p. 847

46. Normally, the cellular rates of gas absorption and generation are matched by the capillary rates of delivery and removal and are identical to the rates of oxygen absorption and carbon dioxide removal at the lungs. When these rates are unbalanced, homeostatic mechanisms restore equilibrium.
47. Local factors regulate alveolar blood flow *(lung perfusion)* and airflow *(alveolar ventilation)*. Alveolar capillaries constrict under conditions of low oxygen, and bronchioles dilate under conditions of high carbon dioxide.
48. The **respiratory centers** include three pairs of nuclei in the reticular formation of the pons and medulla oblongata. The *respiratory rhythmicity centers* set the pace for respiration; the **apneustic centers** cause strong, sustained inspiratory movements; and the **pneumotaxic centers** inhibit the apneustic centers and promote exhalation. *(Figure 23–25, Spotlight Figure 23–26)*
49. Stimulation of the chemoreceptor reflexes is based on the level of carbon dioxide in the blood and CSF. *(Spotlight Figure 23–26, Figure 23–27)*
50. The **inflation reflex** prevents overexpansion of the lungs during forced breathing. The **deflation reflex** stimulates inhalation when the lungs are collapsing.
51. Conscious and unconscious thought processes can affect respiration by affecting the respiratory centers.
52. Before delivery, the fetal lungs are filled with body fluids and collapsed. At the first breath, the lungs inflate and do not collapse completely thereafter.

23-11 Respiratory performance declines with age p. 855

53. The respiratory system is generally less efficient in the elderly because (1) elastic tissue deteriorates, lowering compliance and the vital capacity of the lungs; (2) movements of the chest are restricted by arthritic changes and decreased flexibility of costal cartilages; and (3) some degree of emphysema is generally present. *(Figure 23–28)*

23-12 The respiratory system provides oxygen to, and eliminates carbon dioxide from, other organ systems p. 856

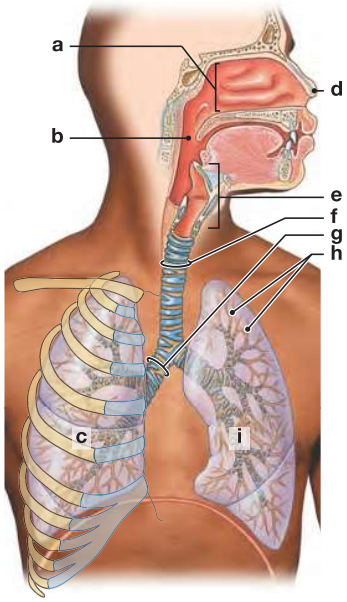
54. The respiratory system has extensive anatomical and physiological connections to the cardiovascular system. *(Figure 23–29)*

Review Questions

See the blue Answers tab at the back of the book.

LEVEL 1 Reviewing Facts and Terms

1. Identify the structures of the respiratory system in the following figure:
   (a) _____
   (b) _____
   (c) _____
   (d) _____
   (e) _____
   (f) _____
   (g) _____
   (h) _____
   (i) _____



2. Surfactant
   (a) protects the surface of the lungs.
   (b) phagocytizes small particulates.
   (c) replaces mucus in the alveoli.
   (d) helps prevent the alveoli from collapsing.
   (e) is not found in healthy lung tissue.
3. The hard palate separates the
   (a) nasal cavity from the larynx.
   (b) left and right sides of the nasal cavity.
   (c) nasal cavity and the oral cavity.
   (d) external nares from the internal nares.
   (e) soft palate from the nasal cavity.
4. Air moves into the lungs because
   (a) the gas pressure in the lungs is less than atmospheric pressure.
   (b) the volume of the lungs decreases with inspiration.
   (c) the thorax is muscular.
   (d) contraction of the diaphragm decreases the volume of the thoracic cavity.
   (e) the respiratory control center initiates active expansion of the thorax.
5. The glottis closes partway through an exhalation. The abdominal and internal intercostal muscles then contract suddenly, creating pressure that blasts the air out of the respiratory passages. This describes a
   (a) sneeze. (b) hiccough.
   (c) cough. (d) laryngeal spasm.
   (e) gag.
6. When the diaphragm and external intercostal muscles contract,
   (a) exhalation occurs.
   (b) intrapulmonary pressure increases.
   (c) intrapleural pressure decreases.
   (d) the volume of the lungs decreases.
   (e) the size of the thoracic cavity increases.

7. During the winter, Brad sleeps in a dorm room that lacks any humidifier for the heated air. In the mornings he notices that his nose is "stuffy" similar to when he has a cold, but after showering and drinking some water, the stuffiness disappears until the next morning. What might be the cause of Brad's nasal condition?
8. Distinguish the structures of the upper respiratory system from those of the lower respiratory system.
9. Name the three regions of the pharynx. Where is each region located?
10. List the cartilages of the larynx. What are the functions of each?
11. What three integrated steps are involved in external respiration?
12. What important physiological differences exist between fetal hemoglobin and maternal hemoglobin?
13. By what three ways is carbon dioxide transported in the bloodstream?

LEVEL 2 Reviewing Concepts

14. Which of the following does *not* occur in internal respiration?
    (a) Oxygen diffuses from the blood to the interstitial spaces.
    (b) Carbon dioxide diffuses from the interstitial spaces to the blood.
    (c) Hemoglobin binds more oxygen.
    (d) Bicarbonate ions are formed in red blood cells.
    (e) Chloride ions diffuse into red blood cells as bicarbonate ions diffuse out.
15. Gas exchange at the respiratory membrane is efficient because
    (a) the differences in partial pressure are substantial.
    (b) the gases are lipid soluble.
    (c) the total surface area is large.
    (d) of a, b, and c.
16. For any partial pressure of oxygen, if the concentration of 2,3-bisphosphoglycerate (BPG) increases,
    (a) the amount of oxygen released by hemoglobin will decrease.
    (b) the oxygen levels in hemoglobin will be unaffected.
    (c) the amount of oxygen released by hemoglobin will increase.
    (d) the amount of carbon dioxide carried by hemoglobin will increase.
17. An increase in the partial pressure of carbon dioxide in arterial blood causes chemoreceptors to stimulate the respiratory centers, resulting in
    (a) a decreased respiratory rate.
    (b) an increased respiratory rate.
    (c) hypocapnia.
    (d) hypercapnia.
18. Why is breathing through the nasal cavity more desirable than breathing through the mouth?
19. How would you justify the statement "The bronchioles are to the respiratory system what the arterioles are to the cardiovascular system"?
20. How are pneumocytes type II involved with keeping the alveoli from collapsing?
21. How does pulmonary ventilation differ from alveolar ventilation, and what is the function of each type of ventilation?
22. What is the significance of (a) Boyle's law, (b) Dalton's law, and (c) Henry's law to the process of respiration?
23. What happens to the process of respiration when a person is sneezing or coughing?
24. What are the differences between pulmonary volumes and respiratory capacities? How are pulmonary volumes and respiratory capacities determined?
25. What is the functional difference between the dorsal respiratory group (DRG) and the ventral respiratory group (VRG) of the medulla oblongata?

LEVEL 3 Critical Thinking and Clinical Applications

26. Billy's normal alveolar ventilation rate (AVR) during mild exercise is 6.0 L/min. While at the beach on a warm summer day, he goes snorkeling. The snorkel has a volume of 50 mL. Assuming that the water is not too cold and that snorkeling is mild exercise for Billy, what would his respiratory rate have to be for him to maintain an AVR of 6.0 L/min while snorkeling? (Assume a constant tidal volume of 500 mL and an anatomic dead space of 150 mL.)
27. Mr. B. has had chronic advanced emphysema for 15 years. While hospitalized with a respiratory infection, he goes into respiratory distress. Without thinking, his nurse immediately administers pure oxygen, which causes Mr. B. to stop breathing. Why?
28. Cary hyperventilates for several minutes before diving into a swimming pool. After he enters and begins swimming underwater, he blacks out and almost drowns. What caused this to happen?
29. Why do individuals who are anemic generally not exhibit an increase in respiratory rate or tidal volume, even though their blood is not carrying enough oxygen?
30. Doris has an obstruction of her right primary bronchus. As a result, how would you expect the oxygen–hemoglobin saturation curve for her right lung to compare with that for her left?