UNIT VI
Respiratory Function

Chapter 20

Control of Respiratory Function

The respiratory system supplies the body with oxygen and rids the body of carbon dioxide. Respiration can be divided into three parts: ventilation, or the movement of air between the atmosphere and the respiratory portion of the lungs; perfusion, or the flow of blood through the lungs; and diffusion, or the transfer of gases between the air-filled spaces in the lungs and the blood. The nervous system controls the movement of the respiratory muscles and adjusts the rate of breathing so that it matches the needs of the body during various levels of activity. The content in this chapter focuses on the structure and function of the respiratory system as it relates to these aspects of respiration. The function of the red blood cell in the transport of oxygen is discussed in Chapter 11.

Structural Organization of the Respiratory System

The respiratory system consists of the air passages and the lungs. Functionally, the respiratory system can be divided into two parts: the *conducting airways,* through which air moves as it passes between the atmosphere and the lungs, and the *respiratory tissues* of the lungs, where gas exchange takes place. The process of moving air into and out of the lungs is referred to as *ventilation* and the process of gas exchange as *diffusion.*

THE CONDUCTING AIRWAYS

The conducting airways consist of the nasal passages, mouth and pharynx, larynx, trachea, bronchi, and bronchioles (Fig. 20-1). The air we breathe is warmed, filtered,

KEY CONCEPTS

Conducting and Respiratory Airways

- Respiration requires ventilation, or movement of gases into and out of the lungs; perfusion, or movement of blood through the lungs; and diffusion of gases between the lungs and the blood.
- Ventilation depends on conducting airways, including the nasopharynx and oropharynx, larynx, and tracheobronchial tree, which move air into and out of the lungs but do not participate in gas exchange.
- Gas exchange takes place in the respiratory airways of the lungs, where gases diffuse across the alveolar-capillary membrane as they are exchanged between the lungs and the blood that flows through the pulmonary capillaries.

and moistened as it moves through these structures. Heat is transferred to the air from the blood flowing through the walls of the respiratory passages; the mucociliary blanket removes foreign materials; and water from the mucous membranes is used to moisten the air.

The wall of conducting airways consists of three major components: a mucosal lining that is composed of epithelial and connective tissue, an underlying smooth muscle layer, and a supporting connective tissue layer (Fig. 20-2). The pseudostratified epithelial lining of the airways contains a mosaic of mucus-secreting gland cells, ciliated cells with hairlike projection, serous glands that secrete a watery fluid containing antibacterial enzymes, and the poorly differentiated basal cells (that possibly serve as stem cells for replacement of other cell types). In addition, some less common cell types are interspersed in different parts of the airways. The epithelial layer gradually becomes thinner as it moves from the pseudostratified epithelium of the bronchi to cuboidal epithelium of the bronchioles and then to squamous epithelium of the alveoli.

The mucus produced by the epithelial cells in the conducting airways forms a layer called the *mucociliary blanket* that protects the respiratory system by entrapping dust, bacteria, and other foreign particles that enter the airways. The cilia, which constantly are in motion, move the mucociliary blanket with its entrapped particles in an escalator-like fashion toward the oropharynx, from which it is expectorated or swallowed. The function of cilia in clearing the lower airways and alveoli is optimal at normal oxygen levels and is impaired in situations of low and high oxygen levels. It is also impaired by drying conditions, such as breathing heated but unhumidified indoor air during the winter months. Cigarette smoking slows down or paralyzes the motility of the cilia. This slowing allows the residue from tobacco smoke, dust, and other particles to accumulate in the lungs, decreasing the efficiency of this pulmonary defense system. As discussed in Chapter 22, these changes are thought to contribute to the development of chronic bronchitis and emphysema.

The air in the conducting airways is kept moist by water contained in the mucous layer. Moisture is added to the air as it moves through the conducting airways. (As water mixes with air, it is called *water vapor*.) The capacity of the air to contain water vapor without condensation increases as the temperature rises. Thus, the air in the alveoli, which is maintained at body temperature, usually contains considerably more water vapor than the atmospheric-temperature air that we breathe. The difference between the water vapor contained in the

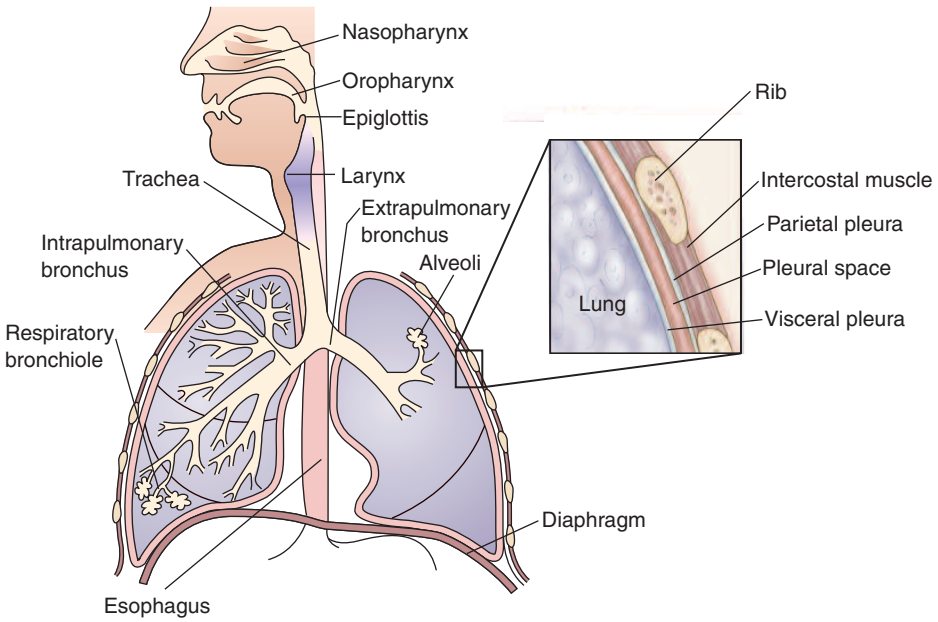


FIGURE 20-1 Structures of the respiratory system. The structures of the pleura are shown in the inset.

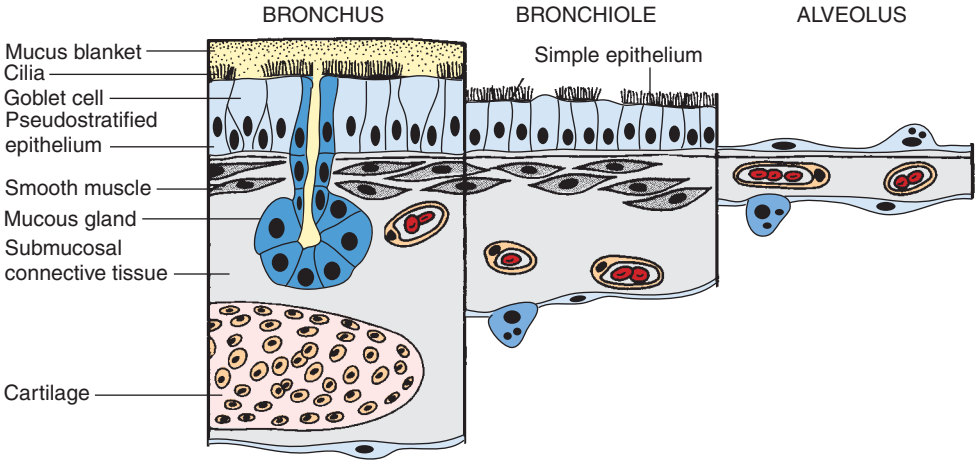


FIGURE 20-2 Airway wall structure: bronchus, bronchiole, and alveolus. The bronchial wall contains pseudostratified epithelium, smooth muscle cells, mucous glands, connective tissue, and cartilage. In smaller bronchioles, a simple epithelium is found, cartilage is absent, and the wall is thinner. The alveolar wall is designed for gas exchange, rather than structural support. (From Weibel E. R., Taylor R. C. [1988]. Design and structure of the human lung. In Fishman A. P. [ed.]. *Pulmonary diseases and disorders* [Vol. 1., p. 14]. New York: McGraw-Hill. Reproduced with permission of the McGraw-Hill Companies.)

air we breathe and that found in the alveoli is drawn from the moist surface of the mucous membranes that line the conducting airways and is a source of insensible water loss (see Chapter 6). Under normal conditions, approximately 1 pint of water is used each day to humidify the air we breathe. During fever, the water vapor in the lungs increases, causing more water to be lost through the respiratory tract. In addition, fever usually is accompanied by an increase in respiratory rate so that more air passes through the airways, withdrawing moisture from its mucosal surface. As a result, respiratory secretions thicken, preventing free movement of the cilia and impairing the protective function of the mucociliary defense system. This is particularly true in persons whose water intake is inadequate.

Nasopharyngeal Airways

The nose is the preferred route for the entrance of air into the respiratory tract during normal breathing. As air passes through the nasal passages, it is filtered, warmed, and humidified. The outer nasal passages are lined with coarse hairs, which filter and trap dust and other large particles from the air. The upper portion of the nasal cavity is lined with a mucous membrane that contains a rich network of small blood vessels; this portion of the nasal cavity supplies warmth and moisture to the air we breathe.

The mouth serves as an alternative airway when the nasal passages are plugged or when there is a need for the exchange of large amounts of air, as occurs during exercise. The oropharynx extends posteriorly from the soft palate to the epiglottis. The oropharynx is the only opening between the nose and mouth and the lungs. Both swallowed food on its way to the esophagus and air on its way to the larynx pass through it. Obstruction of the oropharynx leads to immediate cessation of ventilation. Neural control of the tongue and pharyngeal muscles may be impaired in coma and certain types of neurologic disease. In these conditions, the tongue falls back into the pharynx and obstructs the airway, particularly if the person is lying on his or her back. Swelling of the pharyngeal structures caused by injury, infection, or severe allergic reaction also predisposes a person to airway obstruction, as does the presence of a foreign body.

Laryngotracheal Airways

The larynx connects the oropharynx with the trachea. The walls of the larynx are supported by rigid cartilaginous structures that prevent collapse during inspiration. The functions of the larynx can be divided into two categories: those associated with speech and those associated with protecting the lungs from substances other than air. The larynx is located in a strategic position between the upper airways and the lungs and sometimes is referred to as the "watchdog of the lungs."

The cavity of the larynx is divided into two pairs of two-by-two folds of mucous membrane stretching from front to back with an opening in the midline (Fig. 20-3). The upper pair of folds, called the *vestibular folds*, has a protective function. The lower pair of folds has cord-like margins; they are termed the *vocal folds* because their vibrations are required for making vocal sounds. The true vocal folds and the elongated opening between them is called the *glottis*. A complex set of muscles controls the opening and closing of the glottis. Speech involves the intermittent release of expired air and opening and closing of the glottis. The epiglottis, which is located above the vocal folds, is a large, leaf-shaped piece of cartilage that is covered with epithelium. During swallowing, the free

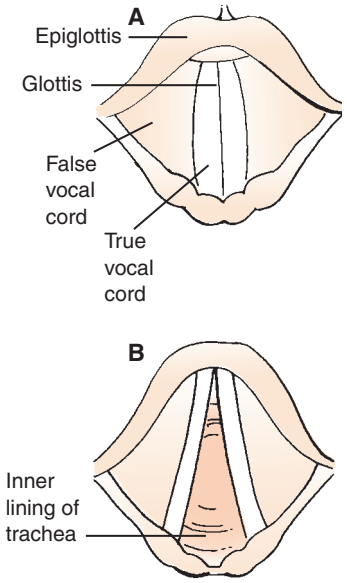


FIGURE 20-3 Epiglottis and vocal cords viewed from above with (**A**) glottis closed and (**B**) glottis open.

edges of the epiglottis move downward to cover the larynx, thus routing liquids and foods into the esophagus.

In addition to opening and closing the glottis for speech, the vocal folds of the larynx can perform a sphincter function in closing off the airways. When confronted with substances other than air, the laryngeal muscles contract and close off the airway. At the same time, the cough reflex is initiated as a means of removing a foreign substance from the airway. If the swallowing mechanism is partially or totally paralyzed, food and fluids can enter the airways instead of the esophagus when a person attempts to swallow. These substances are not easily removed; and when they are pulled into the lungs, they can cause a serious inflammatory condition called *aspiration pneumonia*.

Tracheobronchial Tree

The tracheobronchial tree, which consists of the trachea, bronchi, and bronchioles, can be viewed as a system of branching tubes (Fig. 20-4). It is similar to a tree whose branches become smaller and more numerous as they divide. There are approximately 23 levels of branching, beginning with the conducting airways and ending with the respiratory airways, where gas exchange takes place (Fig. 20-5). The walls of the tracheobronchial tree are composed of several layers: an inner mucosal layer, a submucosal layer, and an outer adventitial layer. These layers vary at different levels of the tracheobronchial tree.

The trachea, or windpipe, is a continuous tube that connects the larynx and the major bronchi of the lungs (see Fig. 20-4). The walls of the trachea are supported by horseshoe- or C-shaped rings of hyaline cartilage, which prevent it from collapsing when the pressure in the thorax becomes negative. The open part of the C-shaped ring, which abuts the esophagus, is connected by smooth muscle. Since this portion of the trachea is not rigid, the esophagus can expand anteriorly as swallowed food passes through it.

The trachea divides into two branches, forming the right and left main or primary bronchi. Between the main bronchi is a keel-like ridge called the *carina*. The mucosa of the carina is highly sensitive; violent coughing is initiated when a foreign object (*e.g.*, suction catheter) makes contact with it. The structure of the primary bronchi is similar to that of the trachea in that these airways are lined with a mucosal surface and supported by cartilagi-

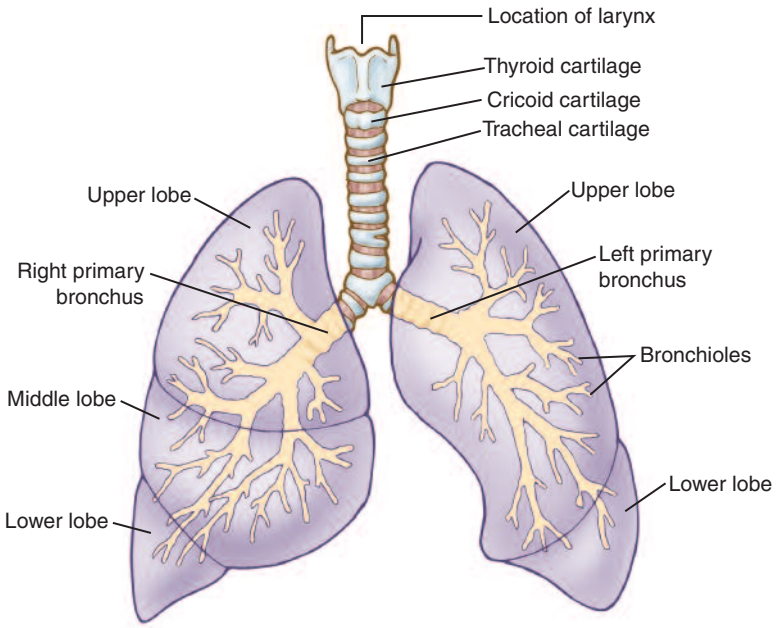


FIGURE 20-4 Larynx, trachea, and bronchial tree (anterior view).

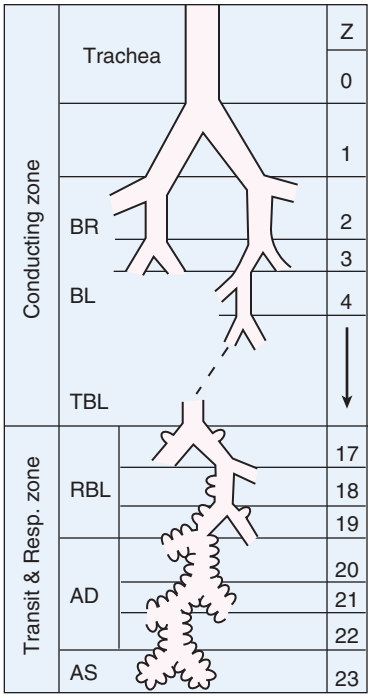


FIGURE 20-5 Idealization of the human airways. The first 16 generations of branching (Z) make up the conducting airways, and the last seven constitute the respiratory zone (or transitional and respiratory zone). BR, bronchus; BL, bronchiole; TBL, terminal bronchiole; RBL, respiratory bronchiole; AD, alveolar ducts; AS, alveolar sacs. (From Weibel E. R. [1962]. *Morphometry of the human lung* [p. 111]. Berlin: Springer-Verlag.)

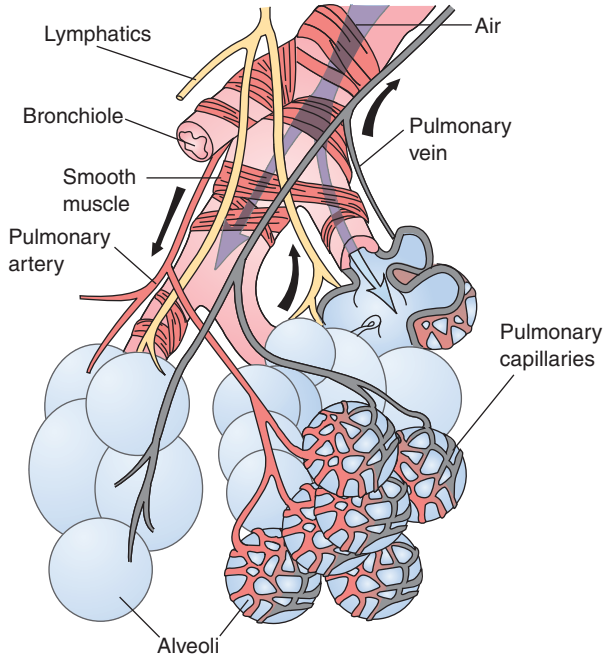


FIGURE 20-6 Lobule of the lung, showing the bronchial smooth muscle fibers, pulmonary blood vessels, and lymphatics.

nous rings. Each primary bronchus, accompanied by the pulmonary arteries, veins, and lymph vessels, enters the lung through a slit called the *hilus*.

Each primary bronchus divides into secondary or lobular bronchi that supply each of the lobes of the lung—three in the right lung and two in the left. The right middle lobe bronchus is of relatively small diameter and length and sometimes bends sharply near its bifurcation. It is surrounded by a collar of lymph nodes that drain the middle and the lower lobe and is particularly subject to obstruction. The secondary bronchi, in turn, divide to form the segmental bronchi, which supply the bronchopulmonary segments of the lung. These segments are identified according to their location in the lung (*e.g.*, the apical segment of the right upper lobe) and are the smallest named units in the lung. Lung lesions such as atelectasis and pneumonia often are localized to a particular bronchopulmonary segment. The structure of the secondary and segmental bronchi is similar to that of the primary bronchi, except the cartilage "C"-shaped rings are replaced by irregular plates of hyaline cartilage that completely surround the lumina of the bronchi and there are two layers of smooth muscle spiraling in opposite direction (Fig. 20-6).

The segmental bronchi continue to branch, forming smaller bronchi, until they become the terminal bronchioles, the smallest of the conducting airways. As these bronchi branch and become smaller, their wall structure changes. The cartilage gradually decreases and there is an increase in smooth muscle and elastic tissue (with respect to the thickness of the wall). By the time the bronchioles are reached, there is no cartilage present and their walls are composed mainly of smooth muscle and elastic fibers. Bronchospasm, or contraction of these muscles, causes narrowing of the bronchioles and impairs air flow. The elastic fibers, which radiate from the adventitia of the bronchial wall and connect with elastic fibers arising from other parts of the bronchial tree, exert tension on the bronchial walls; by pulling uniformly in all directions, they help maintain airway patency.

THE LUNGS AND RESPIRATORY AIRWAYS

The lungs are soft, spongy, cone-shaped organs located side by side in the chest cavity (see Fig. 20-1). They are separated from each other by the *mediastinum* (*i.e.*, the space between the lungs) and its contents—the heart, blood vessels, lymph nodes, nerve fibers, thymus gland, and esophagus. The upper part of the lung, which lies against the top of the thoracic cavity, is called the *apex*, and the lower part, which lies against the diaphragm, is called the *base*. The lungs are divided into lobes: three in the right lung and two in the left (see Fig. 20-4).

The lungs are the functional structures of the respiratory system. In addition to their gas exchange function, they inactivate vasoactive substances such as bradykinin; they convert angiotensin I to angiotensin II; and they serve as a reservoir for blood storage. Heparin-producing cells are particularly abundant in the capillaries of the lung, where small clots may be trapped.

Respiratory Lobules

The gas exchange function of the lung takes place in the lobules of the lungs. Each lobule, which is the smallest functional unit of the lung, is supplied by a terminal bronchiole, an arteriole, pulmonary capillaries, and a venule (see Fig. 20-6). Gas exchange takes place in the terminal respiratory bronchioles and the alveolar ducts and sacs. Blood enters the lobules through a pulmonary artery and exits through a pulmonary vein. Lymphatic structures surround the lobule and aid in the removal of plasma proteins and other particles from the interstitial spaces.

Unlike larger bronchi, the respiratory bronchioles are lined with simple epithelium, rather than ciliated pseudostratified epithelium. The alveolar sacs are cup-shaped, thin-walled structures that are separated from each other by thin alveolar septa. Most of the septa are occupied by a single network of capillaries so that blood is exposed to air on both sides. There are approximately 300 million alveoli in the adult lung, with a total surface area of approximately 50 to 100 m^2. In contrast to the bronchioles, which are tubes with their own separate walls, the alveoli are interconnecting spaces that have no separate walls (Fig. 20-7). As a result of this arrangement, there is a continual mixing of air in the alveolar structures.

The alveolar structures are composed of two types of cells: type I alveolar cells and type II alveolar cells (Fig. 20-8). The type I alveolar cells are flat squamous epithelial cells across which gas exchange takes place. The type II alveolar cells produce surfactant, a lipoprotein substance that decreases the surface tension in the alveoli. The alveoli also contain alveolar macrophages, which are responsible for the removal of offending substances from the alveolar epithelium.

Lung Circulation

The lungs are provided with a dual blood supply: the pulmonary and bronchial circulations. The pulmonary circulation arises from the pulmonary artery and provides for the gas exchange function of the lungs. Deoxygenated blood leaves the right heart through the pulmonary artery, which divides into a left pulmonary artery that enters the left lung and a right pulmonary artery that enters the right lung. Return of oxygenated blood to the heart occurs by way of the pulmonary veins, which empty into the left atrium. This is the only part of the circulation where arteries carry unoxygenated blood and veins carry oxygenated blood.

The bronchial circulation distributes blood to the conducting airways and supporting structures of the lung. The bronchial circulation has a secondary function of warming and humidifying incoming air as it moves through the conducting airways. The bronchial arteries arise from the thoracic aorta and enter the lungs with the major bronchi, dividing and subdividing along with the bronchi as they move out into the lung, supplying them and other lung structures with oxygen. The blood from the capillaries in the bronchial circulation drains into the

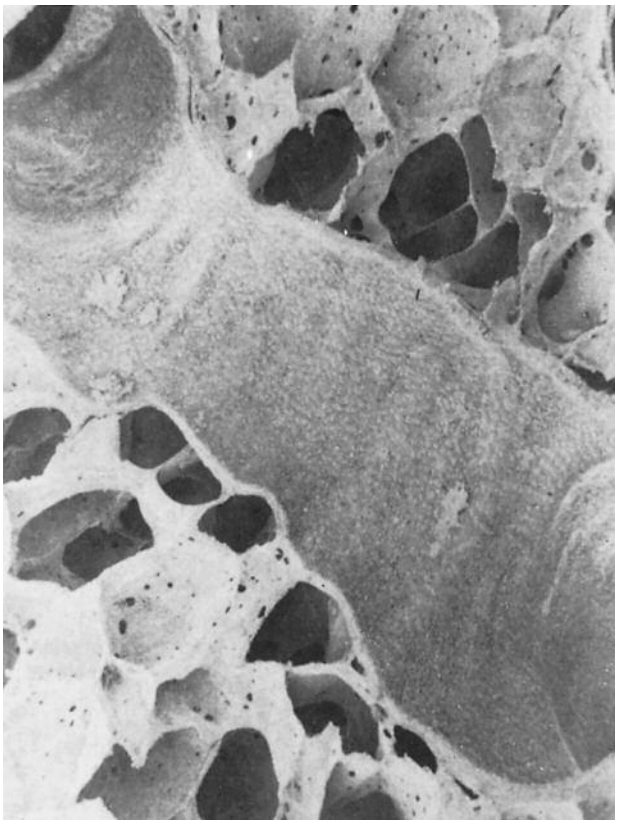


FIGURE 20-7 Close-up of a cross section of a small bronchus and surrounding alveoli. (Courtesy of Janice A. Nowell, University of California, Santa Cruz.)

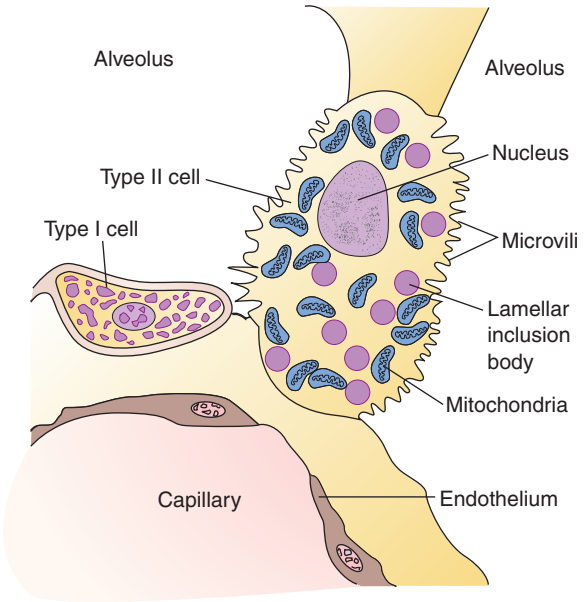


FIGURE 20-8 Schematic drawing of the two types of alveolar cells and their relation to alveoli and capillaries. Alveoli type I cells comprise most of the alveolar surface. Alveolar type II cells are located in the corner between two adjacent alveoli. Also shown are endothelial cells that line the pulmonary capillaries. (From Rhoades R.A., Tanner G.A. [2003]. *Medical physiology* [2nd ed., p. 329]. Philadelphia: Lippincott Williams & Wilkins.)

bronchial veins, with blood from the larger bronchial veins emptying into the vena cava. The blood from the smaller bronchial veins empties into the pulmonary veins. Because the bronchial circulation does not participate in gas exchange, this blood is unoxygenated. As a result, it dilutes the oxygenated blood returning to the left side of the heart by way of the pulmonary veins.

The bronchial blood vessels are the only ones that undergo angiogenesis (formation of new vessels) and develop collateral circulation when vessels in the pulmonary circulation are obstructed, as in pulmonary embolism. The development of new blood vessels helps to keep lung tissue alive until the pulmonary circulation can be restored.

PLEURA

A thin, transparent, double-layered serous membrane, called the *pleura,* lines the thoracic cavity and encases the lungs. The outer parietal layer lies adjacent to the chest wall, and the inner visceral layer adheres to the outer surface of the lung (see Fig. 20-1). The parietal pleura lines the pulmonary cavities and adheres to the thoracic wall, the mediastinum, and the diaphragm. The visceral pleura closely covers the lung and is adherent to all its surfaces. It is continuous with the parietal pleura at the hilum of the lung, where the major bronchus and pulmonary vessels enter and leave the lung. A thin film of serous fluid separates the two pleural layers, allowing the two layers to glide over each other and yet hold together, so there is no separation between the lungs and the chest wall. The pleural cavity is a potential space in which serous fluid or inflammatory exudate can accumulate. The term *pleural effusion* is used to describe an abnormal collection of fluid or exudate in the pleural cavity.

In summary, the respiratory system consists of the air passages and the lungs, where gas exchange takes place. Functionally and structurally, the air passages of the respiratory system can be divided into two parts: the conducting airways, through which air moves as it passes into and out of the lungs, and the respiratory tissues, where gas exchange actually takes place. The conducting airways include the nasal passages, mouth and nasopharynx, larynx, and tracheobronchial tree. Air is warmed, filtered, and humidified as it passes through these structures.

The lungs are the functional structures of the respiratory system. In addition to their gas exchange function, they inactivate vasoactive substances such as bradykinin; they convert angiotensin I to angiotensin II; and they serve as a reservoir for blood. The lobules, which are the functional units of the lung, consist of the respiratory bronchioles, alveoli, and pulmonary capillaries. It is here that gas exchange takes place. Oxygen from the alveoli diffuses across the alveolar-capillary membrane into the blood, and carbon dioxide from the blood diffuses into the alveoli.

The lungs are provided with a dual blood supply: the pulmonary circulation provides for the gas exchange function of the lungs, and the bronchial circulation distributes blood to the conducting airways and supporting structures of the lung. The lungs are encased in a thin, transparent, double-layered serous membrane called the *pleura.*

Exchange of Gases Between the Atmosphere and the Lungs

BASIC PROPERTIES OF GASES

The air we breathe is made up of a mixture of gases, mainly nitrogen and oxygen. These gases exert a combined pressure called the *atmospheric pressure*. The pressure at sea level is defined as 1 atmosphere, which is equal to 760 millimeters of mercury (mm Hg) or 14.7 pounds per square inch (PSI). When measuring respiratory pressures, atmospheric pressure is assigned a value of 0. This means that a respiratory pressure of +15 mm Hg is 15 mm Hg above atmospheric pressure, and a respiratory pressure of –15 mm Hg is 15 mm Hg less than atmospheric pressure. Respiratory pressures often are expressed in centimeters of water (cm H_2O) because of the small pressures involved (1 mm Hg = 1.35 cm H_2O pressure).

The pressure exerted by a single gas in a mixture is called the *partial pressure*. The capital letter "P" followed by the chemical symbol of the gas (*e.g.*, PO_2) is used to denote its partial pressure. The law of partial pressures states that the total pressure of a mixture of gases, as in the atmosphere, is equal to the sum of the partial pressures of the different gases in the mixture. If the concentration of oxygen at 760 mm Hg (1 atmosphere) is 20%, its partial pressure is 152 mm Hg (760×0.20).

Water vapor is different from other types of gases; its partial pressure is affected by temperature but not atmospheric pressure. The relative humidity refers to the percentage of moisture in the air compared with the amount that the air can hold without causing condensation (100% saturation). Warm air holds more moisture than cold air. This is the reason that precipitation in the form of rain or snow commonly occurs when the relative humidity is high and there is a sudden drop in atmospheric temperature. The air in the alveoli, which is 100% saturated at normal body temperature, has a water vapor pressure of 47 mm Hg. The water vapor pressure must be included in the sum of the total pressure of the gases in the alveoli (*i.e.*, the total pressure of the other gases in the alveoli is 760 – 47 = 713 mm Hg).

Air moves between the atmosphere and the lungs because of a pressure difference. According to the laws of physics, the pressure of a gas varies inversely with the volume of its container, provided the temperature remains constant. If equal amounts of a gas are placed in two

different-size containers, the pressure of the gas in the smaller container will be greater than the pressure in the larger container. The movement of gases is always from the container with the greater pressure to the one with the lesser pressure. The chest cavity can be viewed as a volume container. During inspiration, the size of the chest cavity increases and air moves into the lungs; during expiration, air moves out as the size of the chest cavity decreases.

VENTILATION AND THE MECHANICS OF BREATHING

Ventilation is concerned with the movement of gases into and out of the lungs. It relies on a system of open airways and the respiratory pressures created as the movements of the respiratory muscles change the size of the chest cage. The degree to which the lungs inflate and deflate depends on the respiratory pressures inflating the lung, compliance of the lungs, and airway resistance.

Respiratory Pressures

The pressure inside the airways and alveoli of the lungs is called the *intrapulmonary pressure* or *alveolar pressure*. The gases in this area of the lungs are in communication with atmospheric pressure (Fig. 20-9). When the glottis is open and air is not moving into or out of the lungs, as occurs just before inspiration or expiration, the intrapulmonary pressure is zero or equal to atmospheric pressure.

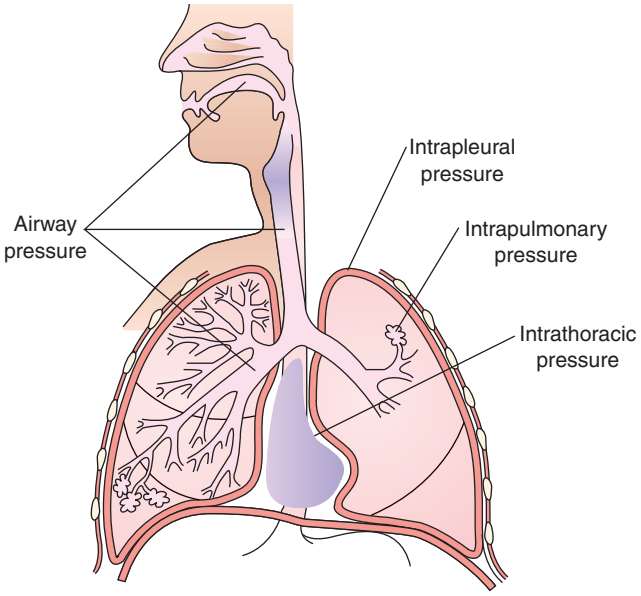


FIGURE 20-9 Partitioning of respiratory pressures.

The pressure in the pleural cavity is called the *intrapleural pressure*. The intrapleural pressure is always negative in relation to alveolar pressure in the normally inflated lung, approximately –4 mm Hg between breaths when the glottis is open and the alveolar spaces are open to the atmosphere. The lungs and the chest wall have elastic properties, each pulling in the opposite direction. If removed from the chest, the lungs would contract to a smaller size, and the chest wall, if freed from the lungs, would expand. The opposing forces of the chest wall and lungs create a pull against the visceral and parietal layers of the pleura, causing the pressure in the pleural cavity to become negative. During inspiration, the elastic recoil of the lungs increases, causing intrapleural pressure to become more negative than during expiration. Without the negative intrapleural pressure holding the lungs against the chest wall, their elastic recoil properties would cause them to collapse. Although the intrapleural pressure of the inflated lung is always negative in relation to alveolar pressure, it may become positive in relation to atmospheric pressure (*e.g.*, during forced expiration and coughing).

The *intrathoracic pressure* is the pressure in the thoracic cavity. It is essentially equal to intrapleural pressure and is the pressure to which the lungs, heart, and great vessels are exposed. Forced expiration against a closed glottis (Valsalva maneuver) compresses the air in the thoracic cavity and produces marked increases in intrathoracic and intrapleural pressures.

The Chest Cage and Respiratory Muscles

The lungs and major airways share the chest cavity with the heart, great vessels, and esophagus. The chest cavity is a closed compartment bounded on the top by the neck muscles and at the bottom by the diaphragm. The outer

KEY CONCEPTS

Ventilation and Gas Exchange

- Ventilation refers to the movement of gases into and out of the lungs through a system of open airways and along a pressure gradient resulting from a change in chest volume.
- During inspiration, air is drawn into the lungs as the respiratory muscles expand the chest cavity; during expiration, air moves out of the lungs as the chest muscles recoil and the chest cavity becomes smaller.
- The ease with which air is moved into and out of the lung depends on the resistance of the airways, which is inversely related to the fourth power of the airway radius, and lung compliance, or the ease with which the lungs can be inflated.
- The minute volume, which is determined by the metabolic needs of the body, is the amount of air that is exchanged each minute. It is the product of the tidal volume or amount of air that is exchanged with each breath multiplied by the respiratory rate.

walls of the chest cavity are formed by 12 pairs of ribs, the sternum, the thoracic vertebrae, and the intercostal muscles that lie between the ribs. Mechanically, ventilation or the act of breathing depends on the fact that the chest cavity is a closed compartment whose only opening to the exterior is the trachea.

Ventilation consists of inspiration and expiration. During *inspiration,* the size of the chest cavity increases, the intrathoracic pressure becomes more negative, and air is drawn into the lungs. *Expiration* occurs as the elastic components of the chest wall and lung structures that were stretched during inspiration recoil, causing the size of the chest cavity to decrease and the pressure in the chest cavity to increase (Fig. 20-10).

The diaphragm is the principal muscle of inspiration. When the diaphragm contracts, the abdominal contents are forced downward and the chest expands from top to bottom (see Fig. 20-10). During normal levels of inspiration, the diaphragm moves approximately 1 cm, but this can be increased to 10 cm on forced inspiration. The diaphragm is innervated by the phrenic nerve roots, which arise from the cervical level of the spinal cord, mainly from C4 but also from C3 and C5. Paralysis of one side of the diaphragm causes the chest to move up on that side rather than down during inspiration because of the negative pressure in the chest. This is called *paradoxical movement.*

The external intercostal muscles, which also aid in inspiration, connect to the adjacent ribs and slope downward and forward (Fig. 20-11). When they contract, they raise the ribs and rotate them slightly so that the sternum is pushed forward; this enlarges the chest from side to side and from front to back. The intercostal muscles receive their innervation from nerves that exit the central nervous system at the thoracic level of the spinal cord. Paralysis of these muscles usually does not have a serious effect on respiration because of the effectiveness of the diaphragm.

The accessory muscles of inspiration include the scalene muscles and the sternocleidomastoid muscles. The scalene muscles elevate the first two ribs, and the sternocleidomastoid muscles raise the sternum to increase the size of the chest cavity. These muscles contribute little to quiet breathing but contract vigorously during exercise. For the accessory muscles to assist in ventilation, they must be stabilized in some way. For example, persons with bronchial asthma often brace their arms against a firm object during an attack as a means of stabilizing their shoulders so that the attached accessory muscles can exert their full effect on ventilation. The head commonly is bent backward so that the scalene and sternocleidomastoid muscles can elevate the ribs more effectively. Other muscles that play a minor role in inspiration are the alae nasi, which produce flaring of the nostrils during obstructed breathing.

Expiration is largely passive. It occurs as the elastic components of the chest wall and lung structures that were stretched during inspiration recoil, causing air to leave the lungs as the intrathoracic pressure increases. When needed, the abdominal and the internal intercostal muscles can be used to increase expiratory effort (see Fig. 20-11). The increase in intra-abdominal pressure that accompanies the forceful contraction of the abdominal muscles pushes the diaphragm upward and results in an increase in intrathoracic pressure. The internal intercostal muscles move inward, which pulls the chest downward, increasing expiratory effort.

Lung Compliance

Lung compliance refers to the ease with which the lungs can be inflated. Compliance can be appreciated by comparing the ease of blowing up a new balloon that is stiff and noncompliant with one that has been previously blown up and stretched. Specifically, lung compliance is a measure of the change in lung volume that occurs with a change in intrapulmonary pressure. The normal compliance of both lungs in the average adult is approximately 200 mL/cm H_2O. This means that every time the intrapulmonary pressure increases by 1 cm/H_2O, the lung volume expands by 200 mL. It would take more pressure to move the same amount of air into a noncompliant lung.

Lung compliance is determined by the elastin and collagen fibers of the lung, its water content, and surface

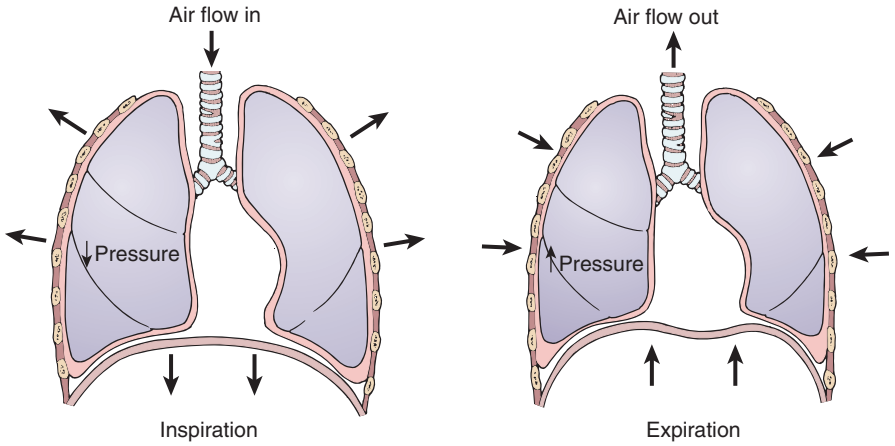


FIGURE 20-10 Movement of the diaphragm and changes in chest volume and pressure during inspiration and expiration. During inspiration, contraction of the diaphragm and expansion of the chest cavity produce a decrease in intrathoracic pressure, causing air to move into the lungs. During expiration, relaxation of the diaphragm and chest cavity produces an increase in intrathoracic pressure, causing air to move out of the lungs.

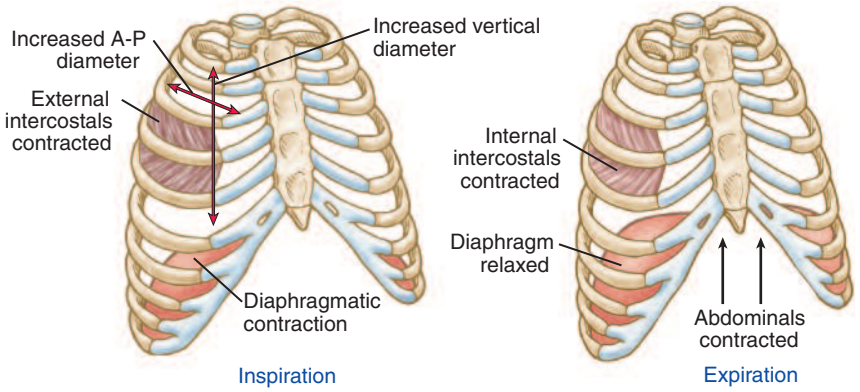


FIGURE 20-11 Expansion and contraction of the chest cage during expiration and inspiration, demonstrating especially diaphragmatic contraction, elevation of the rib cage, and function of the external and internal intercostals.

tension. It also depends on the compliance of the thoracic cage. It is diminished by conditions that reduce the natural elasticity of the lung; block the bronchi or smaller airways; increase the surface tension of the fluid film in the alveoli, or impair the flexibility of the thoracic cage.

Changes in Elastin/Collagen Composition of Lung Tissue. Lung tissue is made up of elastin and collagen fibers. The elastin fibers are easily stretched and increase the ease of lung inflation, whereas the collagen fibers resist stretching and make lung inflation more difficult. In lung diseases such as interstitial lung disease and pulmonary fibrosis, the lungs become stiff and noncompliant as the elastin fibers are replaced with scar tissue. Pulmonary congestion and edema produce a reversible decrease in pulmonary compliance.

Elastic recoil describes the ability of the elastic components of the lung to recoil to their original position after having been stretched. Overstretching of the elastic components, as occurs with emphysema, causes the elastic components of the lung to lose their recoil, making the lung easier to inflate but more difficult to deflate because of its inability to recoil.

Surface Tension. An important factor in lung compliance is the *surface tension* in the alveoli. The alveoli are lined with a thin film of liquid, and it is at the interface between this liquid film and the alveolar air that surface tension develops. This is because the forces that hold the liquid film molecules together are stronger than those that hold the air molecules together. In the alveoli, excess surface tension causes the liquid film to contract, making lung inflation more difficult.

The pressure in the alveoli (which are modeled as spheres with open airways projecting from them) can be predicted using Laplace law (pressure = 2 × surface tension/radius). If the surface tension were equal throughout the lungs, the alveoli with the smallest radii would have the greatest pressure, and this would cause them to empty into the larger alveoli (Fig. 20-12). This does not occur because special surface tension–lowering molecules, called *surfactant*, line the inner surface of the alveoli.

Surfactant is a complex mixture of lipoproteins (largely phospholipids) and small amounts of carbohydrates that is synthesized in type II alveolar cells. The surfactant molecule has two ends: a hydrophobic (water-insoluble) tail and a hydrophilic (water-soluble) head (Fig. 20-13). The hydrophilic head of the surfactant molecule attaches to the liquid molecules and the hydrophobic tail to the gas molecules, interrupting the intermolecular forces that are responsible for creating the surface tension.

Surfactant exerts four important effects on lung inflation: (1) it lowers the surface tension; (2) it increases lung compliance and ease of inflation; (3) it provides for stability and more even inflation of the alveoli; and (4) it assists in preventing pulmonary edema by keeping the alveoli dry. Without surfactant, lung inflation would be extremely difficult, requiring an intrapleural pressure of –20 to –30 mm Hg, compared with the –3 to –5 mm Hg pressure that normally is needed. The surfactant molecules are more densely packed in the small alveoli than in larger alveoli, where the density of the molecules is less. Therefore, surfactant reduces the surface tension more effectively in the small alveoli, which have the greatest tendency to collapse, providing for stability and more even distribution of ventilation. Surfactant also helps to keep the alveoli dry and prevent pulmonary edema. This is because water is pulled out of the pulmonary capillaries

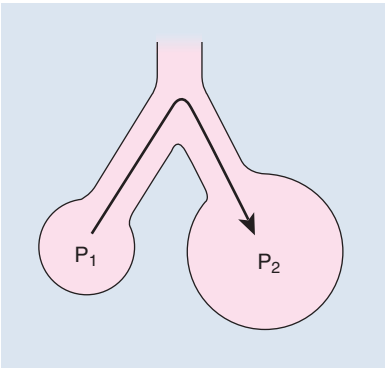


FIGURE 20-12 Law of Laplace (P = 2T/r; P = pressure, T = tension, r = radius). The effect of the radius on the pressure and movement of gases in the alveolar structures is depicted. Air moves from P_1 with a small radius and higher pressure to P_2 with its larger radius and lower pressure.

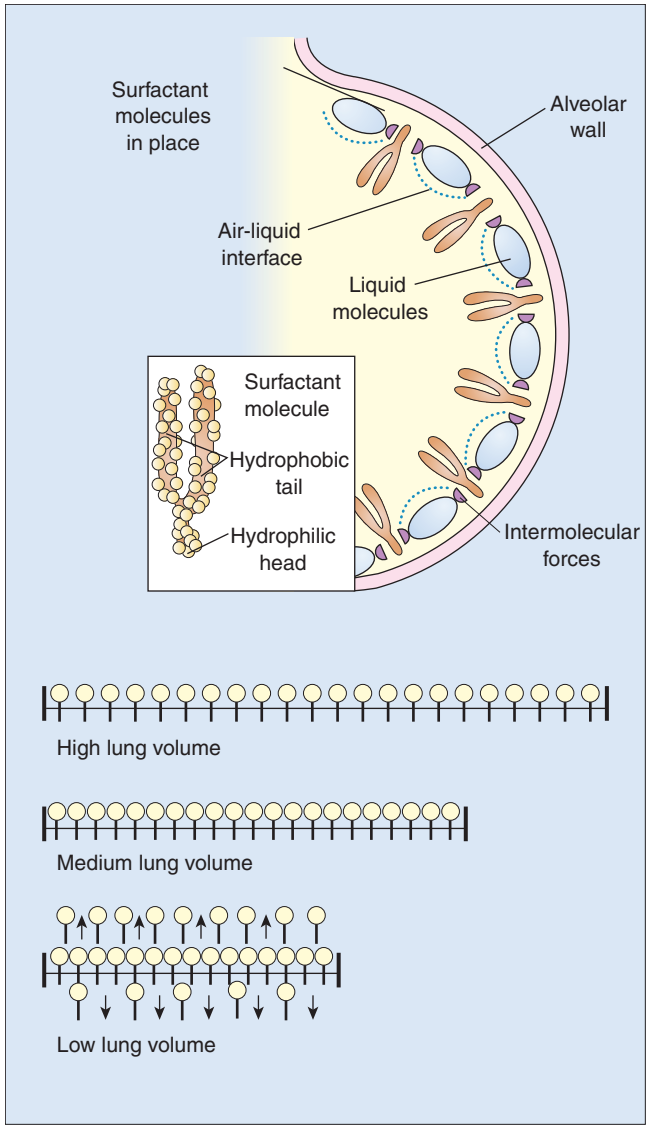


FIGURE 20-13 (**Top**) Alveolar wall depicting surface tension resulting from the intramolecular forces in the air–liquid film interface; the surfactant molecule with its hydrophobic tail and hydrophilic head; and its function in reducing surface tension by disrupting the intermolecular forces. (**Bottom**) The concentration of surfactant molecules at high, medium, and low lung volumes.

into the alveoli when increased surface tension causes the alveoli to contract.

The type II alveolar cells that produce surfactant do not begin to mature until the 26th to 28th week of gestation; consequently, many premature infants have difficulty producing sufficient amounts of surfactant. This can lead to alveolar collapse and severe respiratory distress. This condition, called *infant respiratory distress syndrome,* is the single most common cause of respiratory disease in premature infants. Surfactant dysfunction also is possible in the adult. This usually occurs as the result of severe injury or infection and can contribute to the development of a condition called *acute respiratory distress syndrome* (see Chapter 22).

Airway Resistance

The volume of air that moves into and out of the air exchange portion of the lungs is directly related to the pressure difference between the lungs and the atmosphere and inversely related to the resistance that the air encounters as it moves through the airways. The effects of airway resistance on airflow can be illustrated using *Poiseuille law*. According to Poiseuille law, the resistance to flow is inversely related to the fourth power of the radius ($R = 1/r^4$). If the radius is reduced by one half, the resistance increases 16-fold ($2 \times 2 \times 2 \times 2 = 16$). Because the resistance of the airways is inversely proportional to the fourth power of the radius, small changes in airway caliber, such as those caused by pulmonary secretions or bronchospasm, can produce a marked increase in airway resistance.

Airway resistance is also affected by lung volumes, being less during inspiration than during expiration. This is because elastic-type fibers connect the outside of the airways to the surrounding lung tissues. As a result, these airways are pulled open as the lungs expand during inspiration, and they become narrower as the lungs deflate during expiration (Fig. 20-14). This is one of the reasons that persons with conditions that increase airway resistance, such as bronchial asthma, usually have less difficulty during inspiration than during expiration.

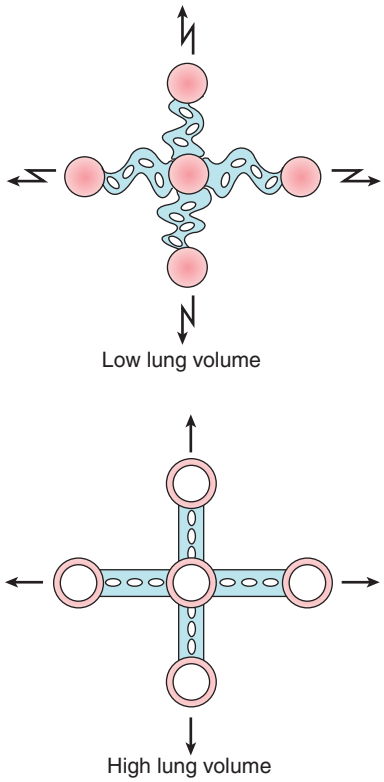


FIGURE 20-14 Interaction of tissue forces on airways during low and high lung volumes. At low lung volumes, the tissue forces promote folding or collapsing and place less tension on the airways, which become smaller; during high lung volumes, the tissue forces stretch and pull the airways open.

Airway Compression. Airflow through the collapsible airways in the lungs depends on the distending airway (intrapulmonary) pressures that hold the airways open and the external (intrapleural or intrathoracic) pressures that surround and compress the airways. The difference between these two pressures (airway pressure minus intrathoracic pressure) is called the *transpulmonary pressure*. For airflow to occur, the distending pressure inside the airways must be greater than the compressing pressure outside the airways (Fig. 20-15).

During forced expiration, the transpulmonary pressure is decreased because of a disproportionate increase in the intrathoracic pressure compared with airway pressure. The resistance that air encounters as it moves out of the lungs causes a further drop in airway pressure. If this drop in airway pressure is sufficiently great, the surrounding intrathoracic pressure will compress the collapsible airways (*i.e.*, those that lack cartilaginous support), causing airflow to be interrupted and air to be trapped in the alveoli (see Fig. 20-15). Although this type of airway compression usually is seen only during forced expiration in persons with normal respiratory function, it may occur during normal breathing in persons with lung disease. For example, in conditions that increase airway resistance, such as chronic obstructive pulmonary disease (COPD), the pressure drop along the smaller airways is magnified, and an increase in intra-airway pressure is needed to maintain airway patency (see Chapter 22). Measures such as pursed-lip breathing increase airway pressure and improve expiratory flow rates in persons with COPD.

LUNG VOLUMES

Lung volumes, or the amount of air exchanged during ventilation, can be subdivided into three components: (1) the tidal volume (TV), (2) the inspiratory reserve volume (IRV), and (3) the expiratory reserve volume (ERV). The TV, usually about 500 mL, is the amount of air that moves into and out of the lungs during a normal breath (Fig. 20-16). The IRV is the maximum amount of air that can be inspired in excess of the normal TV, and the ERV is the maximum amount that can be exhaled in excess of the normal TV. Approximately 1200 mL of air always remains in the lungs after forced expiration; this air is the *residual volume* (RV). The RV increases with age because there is more trapping of air in the lungs at the end of expiration. The lung volumes can be measured using an instrument called a *spirometer*.

Lung capacities include two or more lung volumes. The *vital capacity* (VC) equals the IRV plus the TV plus the ERV and is the amount of air that can be exhaled from the point of maximal inspiration. The *inspiratory capacity* (IC) equals the TV plus the IRV. It is the amount of air a person can breathe in beginning at the normal expiratory level and distending the lungs to the maximal amount. The *functional residual capacity* (FRC) is the sum of the RV and ERV; it is the volume of air that remains in the lungs at the end of normal expiration. The *total lung capacity* (TLC) is the sum of all the volumes in the lungs. The RV cannot be measured with the spirometer because this air cannot be expressed from the lungs. It is measured by indirect methods, such as the helium dilution methods, the nitrogen washout methods, or body plethysmography. Lung volumes and capacities are summarized in Table 20-1.

Pulmonary Function Studies

The previously described lung volumes and capacities are anatomic or static measures, determined by lung volumes and measured without relation to time. The

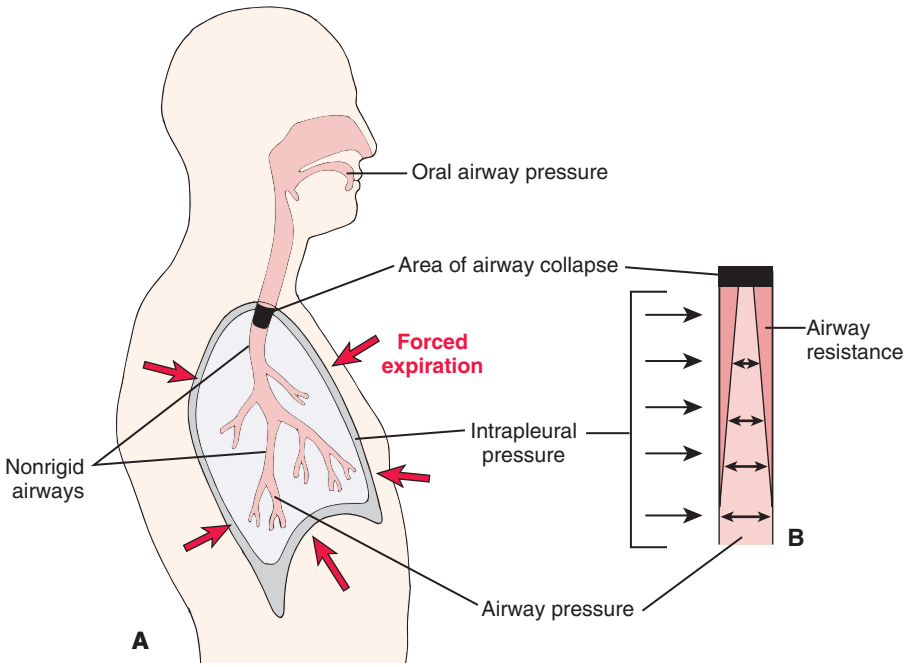


FIGURE 20-15 Mechanism that limits maximal expiratory flow rate. (**A**) Airway patency and airflow in the nonrigid airways of the lungs rely on a transpulmonary pressure gradient in which airway pressure is greater than intrapleural pressure. (**B**) Airway resistance normally produces a drop in airway pressure as air moves out of the lungs. The increased intrapleural pressure that occurs with forced expiration produces airway collapse in the nonrigid airways at the point where intrapleural pressure exceeds airway pressure.

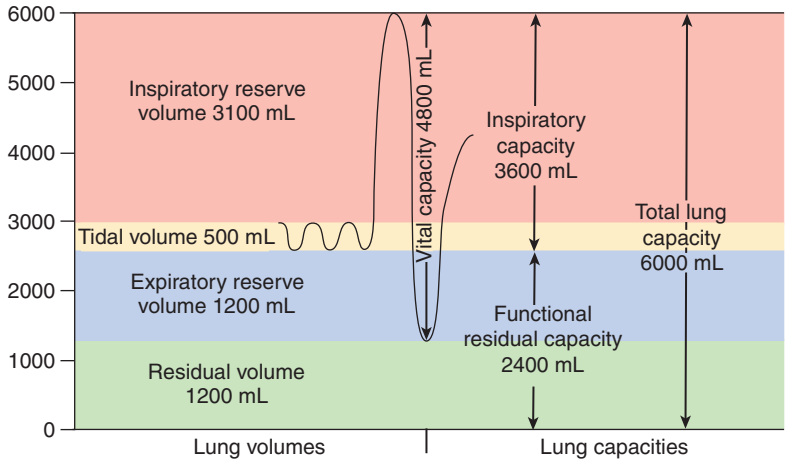


FIGURE 20-16 Tracings of respiratory volumes (**left**) and lung capacities (**right**) as they would appear if made using a spirometer. The tidal volume (*yellow*) represents the amount inhaled and exhaled during normal breathing; the inspiratory reserve volume (*pink*), the maximal amount of air in excess of the tidal volume that can be forcefully inhaled; the maximal expiratory reserve (*blue*), the maximal amount of air that can be exhaled in excess of the tidal volume; and the residual volume (*green*), the air that continues to remain in the lung after maximal expiratory effort. The inspiratory capacity represents the sum of the inspiratory reserve volume and the tidal volume; the functional residual capacity, the sum of the maximal expiratory reserve and residual volumes; and the total lung capacity, the sum of all the volumes.

spirometer also is used to measure dynamic lung function (*i.e.*, ventilation with respect to time); these tests often are used in assessing pulmonary function (Table 20-2). The *maximum voluntary ventilation* measures the volume of air that a person can move into and out of the lungs during maximum effort lasting for a specific period of time. This measurement usually is converted to liters per minute. Two other useful tests are the *forced vital capacity* (FVC) and the *forced expiratory volume* (FEV). The FVC involves full inspiration to total lung capacity followed by forceful maximal expiration. Obstruction of airways produces an FVC that is lower than that observed with more slowly performed vital capacity measurements. The FEV is the expiratory volume achieved in a given time period. The $FEV_{1.0}$ is the forced expiratory volume that can be exhaled in 1 second. The $FEV_{1.0}$ frequently is expressed as a percentage of the FVC. The $FEV_{1.0}$ and FVC are used in the diagnosis of obstructive lung disorders.

EFFICIENCY AND THE WORK OF BREATHING

The *minute volume*, or total ventilation, is the amount of air that is exchanged in 1 minute. It is determined by the metabolic needs of the body. The minute volume is equal to the TV multiplied by the respiratory rate. During normal activity it is about 6000 mL (500 mL TV × respiratory rate of 12 breaths per minute). The efficiency of breathing is determined by matching the TV and respiratory rate in a manner that provides an optimal minute volume while minimizing the work of breathing.

The work of breathing is determined by the amount of effort required to move air through the conducting airways and by the ease of lung expansion or compliance. Expansion of the lungs is difficult for persons with stiff and noncompliant lungs; they usually find it easier to breathe if they keep their TV low and breathe at a more rapid rate (*e.g.*, 300 × 20 = 6000 mL) to achieve their minute volume and meet their oxygen needs. In contrast,

TABLE 20-1 Lung Volumes and Capacities

Volume	Symbol	Measurement
Tidal volume (about 500 mL at rest)	TV	Amount of air that moves into and out of the lungs with each breath
Inspiratory reserve volume (about 3000 mL)	IRV	Maximum amount of air that can be inhaled from the point of maximal expiration
Expiratory reserve volume (about 1200 mL)	ERV	Maximum volume of air that can be exhaled from the resting end-expiratory level
Residual volume (about 1200 mL)	RV	Volume of air remaining in the lungs after maximal expiration. This volume cannot be measured with the spirometer; it is measured indirectly using methods such as the helium dilution method, the nitrogen washout technique, or body plethysmography.
Functional residual capacity (about 2400 mL)	FRC	Volume of air remaining in the lungs at end-expiration (sum of RV and ERV)
Inspiratory capacity (about 3600 mL)	IC	Sum of IRV and TV
Vital capacity (about 4800 mL)	VC	Maximal amount of air that can be exhaled from the point of maximal inspiration
Total lung capacity (about 6000 mL)	TLC	Total amount of air that the lungs can hold; it is the sum of all the volume components after maximal inspiration. This value is about 20% to 25% less in females than in males.

TABLE 20-2 Pulmonary Function Tests

Test	Symbol	Measurement*
Maximal voluntary ventilation	MVV	Maximum amount of air that can be breathed in a given time
Forced vital capacity	FVC	Maximum amount of air that can be rapidly and forcefully exhaled from the lungs after full inspiration. The expired volume is plotted against time.
Forced expiratory volume achieved in 1 second	$FEV_{1.0}$	Volume of air expired in the first second of FVC
Percentage of forced vital capacity	$FEV_{1.0}$/FVC%	Volume of air expired in the first second, expressed as a percentage of FVC

*By convention, all the lung volumes and rates of flow are expressed in terms of body temperature and pressure and saturated with water vapor (BTPS), which allows for a comparison of the pulmonary function data from laboratories with different ambient temperatures and altitudes.

persons with obstructive airway disease usually find it less difficult to inflate their lungs but expend more energy in moving air through the airways. As a result, these persons tend to take deeper breaths and breathe at a slower rate (*e.g.*, $600 \times 10 = 6000$ mL) to achieve their oxygen needs.

In summary, the movement of air between the atmosphere and the lungs follows the laws of physics as they relate to gases. The air in the alveoli contains a mixture of gases, including nitrogen, oxygen, carbon dioxide, and water vapor. With the exception of water vapor, each gas exerts a pressure that is determined by the atmospheric pressure and the concentration of the gas in the mixture. Water vapor pressure is affected by temperature but not atmospheric pressure. Air moves into the lungs along a pressure gradient. The pressure inside the airways and alveoli of the lungs is called *intrapulmonary* (or *alveolar*) *pressure;* the pressure in the pleural cavity is called *intrapleural pressure;* and the pressure in the thoracic cavity is called *intrathoracic pressure.*

Breathing is the movement of gases between the atmosphere and the lungs. It requires a system of open airways and pressure changes resulting from the action of the respiratory muscles in changing the volume of the chest cage. The diaphragm is the principal muscle of inspiration, assisted by the external intercostal muscles. The scalene and sternocleidomastoid muscles elevate the ribs and act as accessory muscles for inspiration. Expiration is largely passive, aided by the elastic recoil of the respiratory muscles that were stretched during inspiration. When needed, the abdominal and internal intercostal muscles can be used to increase expiratory effort.

Lung compliance describes the ease with which the lungs can be inflated. It reflects the elasticity of the lung tissue and the surface tension in the alveoli. Surfactant molecules, produced by type II alveolar cells, reduce the surface tension in the lungs, thereby increasing lung compliance. Airway resistance refers to the impediment to flow that the air encounters as it moves through the airways. The minute volume, which is determined by the metabolic needs of the body, is the amount of air that is exchanged in 1 minute (*i.e.,* respiratory rate × TV). The efficiency and work of breathing are determined by factors such as impaired lung compliance and airway diseases that increase the work involved in maintaining the minute volume. Lung volumes and lung capacities can be measured using a spirometer. Pulmonary function studies are used to assess ventilation with respect to time.

Exchange and Transport of Gases

The primary functions of the lungs are oxygenation of the blood and removal of carbon dioxide. Pulmonary gas exchange is conventionally divided into three processes: (1) ventilation or the flow of gases into and out of the alveoli of the lungs, (2) perfusion or flow of blood in the adjacent pulmonary capillaries, and (3) diffusion or transfer of gases between the alveoli and the pulmonary capillaries. The efficiency of gas exchange requires that alveolar ventilation occur adjacent to perfused pulmonary capillaries.

VENTILATION

Ventilation refers to the exchange of gases in the respiratory system. There are two types of ventilation: pulmonary and alveolar. *Pulmonary ventilation* refers to the total exchange of gases between the atmosphere and the lungs. *Alveolar ventilation* is the exchange of gases within the gas exchange portion of the lungs. Ventilation requires a system of open airways and a pressure difference that moves air into and out of the lungs. It is affected by body position and lung volume as well as by disease conditions that affect the heart and respiratory system.

Distribution of Ventilation

The distribution of ventilation between the base (bottom) and apex (top) of the lung varies with body position and reflects the effects of gravity on intrapleural pressure and

lung compliance. Compliance reflects the change in volume that occurs with a change in intrapleural pressure. It is less in fully expanded alveoli, which have difficulty accommodating more air, and greater in alveoli that are less inflated and can more easily expand to accommodate more air. In the seated or standing position, gravity exerts a downward pull on the lung, causing intrapleural pressure at the apex of the lung to become more negative. As a result, the alveoli at the apex of the lung are more fully expanded and less compliant than those at the base of the lung. The same holds true for lung expansion in the dependent portions of the lung in the supine or lateral position. In the supine position, ventilation in the lowermost (posterior) parts of the lung exceeds that in the uppermost (anterior) parts. In the lateral position (*i.e.,* lying on the side), the dependent lung is better ventilated.

The distribution of ventilation also is affected by lung volumes. During full inspiration (high lung volumes) in the seated or standing position, the airways are pulled open and air moves into the more compliant portions of the lower lung. At low lung volumes, the opposite occurs. At functional residual capacity, the intrapleural pressure at the base of the lung exceeds airway pressure, compressing the airways so that ventilation is greatly reduced. In contrast, the airways in the apex of the lung remain open, and this area of the lung is well ventilated.

PERFUSION

The term *perfusion* is used to describe the flow of blood through the pulmonary capillary bed. The primary functions of the pulmonary circulation are to perfuse or provide blood flow to the gas exchange portion of the lung and to facilitate gas exchange. The pulmonary circulation serves several important functions in addition to gas exchange. It filters all the blood that moves from the right to the left side of the circulation; it removes most of the thromboemboli that might form; and it serves as a reservoir of blood for the left side of the heart.

The gas exchange function of the lungs requires a continuous flow of blood through the respiratory portion of the lungs. Deoxygenated blood enters the lung through the pulmonary artery, which has its origin in the right side of the heart and enters the lung at the hilus, along with the primary bronchus. The pulmonary arteries branch in a manner similar to that of the airways. The small pulmonary arteries accompany the bronchi as they move down the lobules and branch to supply the capillary network that surrounds the alveoli (see Fig. 20-6). The oxygenated capillary blood is collected in the small pulmonary veins of the lobules, and then it moves to the larger veins to be collected in the four large pulmonary veins that empty into the left atrium.

Distribution of Blood Flow

As with ventilation, the distribution of pulmonary blood flow is affected by body position and gravity. In the upright position, the distance of the upper apices of the lung above the level of the heart may exceed the perfusion capabilities of the mean pulmonary arterial pressure (approximately 12 mm Hg); therefore, blood flow in the upper part of the lungs is less than that in the base or bottom part of the lungs. In the supine position, the lungs and the heart are at the same level, and blood flow to the apices and base of the lungs becomes more uniform. In this position, blood flow to the posterior or dependent portions (*e.g.,* bottom of the lung when lying on the side) exceeds flow in the anterior or nondependent portions of the lungs. In persons with left-sided heart failure, congestion develops in the dependent portions of the lungs exposed to increased blood flow.

Effects of Hypoxia

The blood vessels in the pulmonary circulation undergo marked vasoconstriction when they are exposed to hypoxia. When alveolar oxygen levels drop below 60 mm Hg, marked vasoconstriction may occur, and at very low oxygen levels, the local flow may be almost abolished. In regional hypoxia, as occurs with a localized airway obstruction (*e.g.,* atelectasis), vasoconstriction is localized to a specific region of the lung. In this situation, vasoconstriction has the effect of directing blood flow away from the hypoxic regions of the lungs.

Generalized hypoxia causes vasoconstriction throughout all of the vessels of the lung. Generalized vasoconstriction occurs when the partial pressure of oxygen is decreased at high altitudes, or it can occur in persons with chronic hypoxia caused by lung disease. Prolonged hypoxia can lead to pulmonary hypertension and increased workload on the right heart. A low blood pH also produces vasoconstriction, especially when alveolar hypoxia is present (*e.g.,* during circulatory shock).

DIFFUSION

Diffusion refers to the movement of gases in the alveoli and across the alveolar-capillary membrane. Diffusion of gases in the lung is affected by: (1) the difference in the pressure of gas across the membrane, (2) the surface area that is available for diffusion, (3) the thickness of the alveolar-capillary membrane through which the gas must pass, and (4) the characteristics of the gas. Administration of high concentrations of oxygen increases the pressure difference between the two sides of the membrane and increases the diffusion of the gas. Diseases that destroy lung tissue and the surface area for diffusion and those that increase the thickness of the alveolar-capillary membrane adversely influence the diffusing capacity of the lungs. For example, the removal of one lung reduces the diffusing capacity by one half. The thickness of the alveolar-capillary membrane and the distance for diffusion are increased in persons with pulmonary edema or pneumonia. The characteristics of the gas and its molecular weight and solubility constitute the diffusion coefficient and determine how rapidly the gas diffuses through the respiratory membranes. For example, carbon dioxide diffuses 20 times more rapidly than oxygen because of its greater solubility in the respiratory membranes.

MATCHING OF VENTILATION AND PERFUSION

The gas exchange properties of the lung depend on the matching of ventilation and perfusion, ensuring that equal amounts of air and blood are entering the respiratory portion of the lungs (Fig. 20-17). There are two factors that may interfere with the matching of ventilation and perfusion: (1) dead air space, and (2) shunt.

Dead Air Space

Dead space refers to the air that must be moved with each breath but does not participate in gas exchange. The movement of air through dead space contributes to the work of breathing but not to gas exchange. There are two types of dead space: that contained in the conducting airways, called the *anatomic dead space,* and that contained in the respiratory portion of the lung, called the *alveolar dead space*. The volume of anatomic airway dead space is fixed at approximately 150 to 200 mL, depending on body size. It constitutes air contained in the nose, pharynx, trachea, and bronchi. The creation of an opening in the trachea to facilitate ventilation (tracheostomy) decreases anatomic dead space ventilation because air does not have to move through the nasal and oral airways. Alveolar dead space, normally about 5 to 10 mL, constitutes alveolar air that does not participate in gas exchange. When alveoli are ventilated but deprived of blood flow, they do not contribute to gas exchange and thereby constitute alveolar dead space.

The *physiologic dead space* includes the anatomic dead space plus alveolar dead space. In persons with normal respiratory function, physiologic dead space is about the same as anatomic dead space. Only in lung disease does physiologic dead space increase.

Shunt

Shunt refers to blood that moves from the right to the left side of the circulation without being oxygenated. There are two types of shunts: physiologic and anatomic. In a *physiologic shunt,* there is mismatching of ventilation and perfusion, resulting in insufficient ventilation to provide the oxygen needed to oxygenate the blood flowing through the alveolar capillaries. Physiologic shunting of blood usually results from destructive lung disease that impairs ventilation or from heart failure that interferes with movement of blood through sections of the lungs. In an *anatomic shunt,* blood moves from the venous to the arterial side of the circulation without moving through the lungs. Anatomic intracardiac shunting of blood caused by congenital heart defects is discussed in Chapter 18.

Mismatching of Ventilation and Perfusion

Mismatching of ventilation and perfusion occurs when there is perfusion without ventilation or ventilation without perfusion (see Fig. 20-17). Perfusion without ventilation (shunt) results in a low ventilation–perfusion ratio. This is the type of situation that occurs when there is incomplete expansion of the lung, such as in atelectasis (see Chapter 22). Ventilation without perfusion (dead air space) results in a high ventilation–perfusion ratio. An example of this type of situation is pulmonary embolism, when a blood clot obstructs flow (see Chapter 22). The PO_2 in the arterial blood leaving the pulmonary circula-

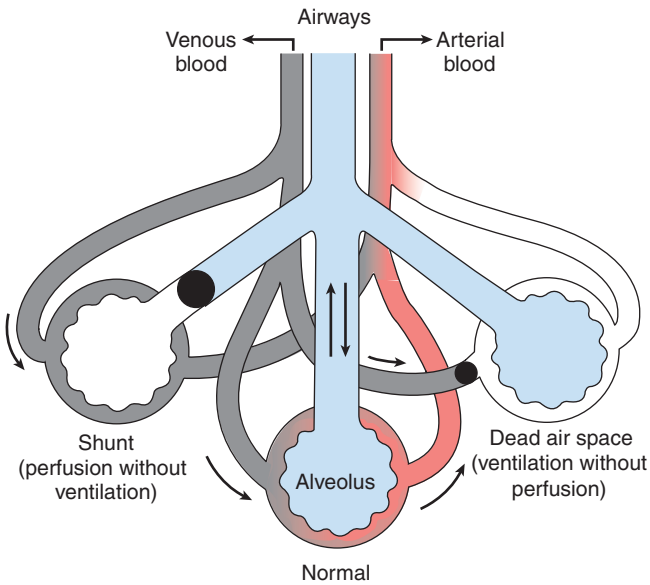


FIGURE 20-17 Matching of ventilation and perfusion. (**Center**) Normal matching of ventilation and perfusion; (**left**) perfusion without ventilation (*i.e.,* shunt); (**right**) ventilation without perfusion (*i.e.,* dead air space).

KEY CONCEPTS

Matching of Ventilation and Perfusion

- Exchange of gases between the air in the alveoli and the blood in pulmonary capillaries requires a matching of ventilation and perfusion.
- Dead air space refers to air that is moved with each breath but is not ventilated. Anatomic dead space is that contained in the conducting airways that normally do not participate in gas exchange. Alveolar dead space results from alveoli that are ventilated but not perfused.
- Shunt refers to blood that moves from the right to the left side of the circulation without being oxygenated. With an anatomic shunt, blood moves from the venous to the arterial side of the circulation without going through the lungs. Physiologic shunting results from blood moving through unventilated parts of the lung.

tion reflects the mixing of blood from areas of shunt and dead air space.

OXYGEN AND CARBON DIOXIDE TRANSPORT

The lungs enable inhaled air to come in contact with blood flowing through the pulmonary capillaries so that exchange of gases between the external environment and the internal environment of the body can occur. The lungs restore the oxygen content of the arterial blood and remove carbon dioxide from the venous blood.

The blood carries oxygen and carbon dioxide as dissolved gases and in combination with hemoglobin. Carbon dioxide also is converted to bicarbonate and transported in that form (see Chapter 6). In the clinical setting, blood gas measurements are used to determine the partial pressure of the dissolved oxygen (PO_2) and carbon dioxide (PCO_2) in the blood. Arterial blood usually is used for measuring blood gases. Venous blood is not used because venous levels of oxygen and carbon dioxide reflect the metabolic demands of the tissues, rather than the gas exchange function of the lungs. The PO_2 of arterial blood normally is greater than 80 mm Hg, and the PCO_2 is in the range of 35 to 45 mm Hg. Normally, the arterial blood gases are the same or nearly the same as the partial pressure of the gases in the alveoli. The arterial PO_2 often is written PaO_2, and the alveolar PO_2 as PAO_2, with the same types of designations being used for PCO_2. This text uses PO_2 and PCO_2 to designate both arterial and alveolar levels of the gases.

The PO_2 and PCO_2 in the blood reflect the partial pressure of the gas in the alveoli, increasing as the alveolar pressure increases and decreasing as the pressure decreases. The effect of alveolar pressures on dissolved gases in the blood can be compared with the dissolved carbon dioxide in a capped bottle of a carbonated drink. In the case of the carbonated drink, carbon dioxide is added under increased pressure as a means of increasing the amount of carbon dioxide that can be dissolved. When the bottle cap is removed and the pressure reduced, tiny bubbles can be seen as the carbon dioxide moves from the dissolved to the gaseous state.

Oxygen Transport

Oxygen is transported in two forms: (1) in chemical combination with hemoglobin, and (2) in the dissolved state. Hemoglobin carries about 98% to 99% of oxygen in the blood and is the main transporter of oxygen. The remaining 1% to 2% of the oxygen is carried in the dissolved state. Only dissolved oxygen that is not bound to hemoglobin can pass through the capillary wall, diffuse through the cell membrane, and make itself available for use in cell metabolism. The oxygen content of the blood (measured in milliliters per 100 milliliters of blood) includes the oxygen carried by hemoglobin and the dissolved form of the gas.

Hemoglobin Transport. Hemoglobin is a highly efficient carrier of oxygen. Hemoglobin with bound oxygen is called *oxyhemoglobin,* and when oxygen is removed, it is called *deoxygenated* or *reduced hemoglobin.* Each gram of hemoglobin carries approximately 1.34 mL of oxygen when it is fully saturated. This means that a person with 14 g/100 mL hemoglobin carries 18.8 mL of oxygen per milliliter of blood when the hemoglobin is completely saturated (100 mL = 1 deciliter [dL]). In the lungs, oxygen moves across the alveolar-capillary membrane, through the plasma, and into the red blood cell, where it forms a loose and reversible bond with the hemoglobin molecule. In normal lungs, this process is rapid, so that even with a fast heart rate, the hemoglobin is almost completely saturated with oxygen during the short time it spends in the pulmonary capillaries.

The oxygenated hemoglobin is transported in the arterial blood to the peripheral capillaries, where the oxygen is released and made available to the tissues for use in cell metabolism. As the oxygen moves out of the capillaries in response to the needs of the tissues, the hemoglobin saturation, which usually is approximately 95% to 97% as the blood leaves the left side of the heart, drops to approximately 75% as the mixed venous blood returns to the right side of the heart.

Dissolved Oxygen. The PO_2 represents the level of dissolved oxygen in plasma. The amount of gas that can be dissolved in a liquid depends on the solubility of the gas and its partial pressure. The solubility of oxygen in plasma is fixed and very small. For every 1 mm Hg of PO_2 present in the alveoli, 0.003 mL of oxygen becomes dissolved in 100 mL of plasma. This means that at a normal alveolar PO_2 of 100 mm Hg, the blood carries only 0.3 mL of dissolved oxygen in each 100 mL of plasma. This amount is very small compared with the amount that can be carried in an equal amount of blood when oxygen is attached to hemoglobin. Although the amount of oxygen carried in plasma under normal conditions is small, it can become a lifesaving mode of transport in carbon monoxide poisoning, when most of the hemoglobin sites are occupied by carbon monoxide and are unavailable for transport of oxygen. The use of a hyperbaric chamber, in which 100% oxygen can be administered at high atmospheric pressures, increases the amount of oxygen that can be carried in the dissolved state.

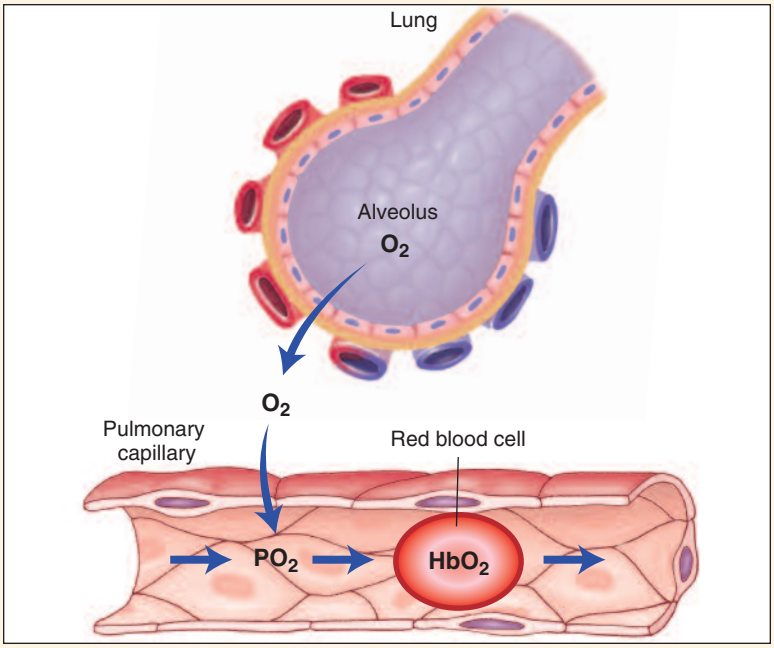
Oxygen-Hemoglobin Dissociation Curve. The relation between the oxygen carried in combination with hemoglobin and the PO_2 of the blood can be described using the *oxygen-hemoglobin dissociation curve,* which is shown in Figure 20-18. The *x* axis of the graph depicts the PO_2 of the dissolved oxygen; the left *y* axis, hemoglobin saturation; and the right *y* axis, the oxygen content. The PO_2 reflects the partial pressure of the gas in the lung and can vary from 60 mm Hg under hypoxic conditions to greater than 100 mm Hg in hyperoxic conditions such as breathing oxygen-enriched air. The hemoglobin saturation reflects the percentage of hemoglobin that is saturated with oxygen. The saturation of arterial blood is normally 97% to 98% rather than 100% because of

Understanding ➤ Oxygen Transport

All body tissues rely on oxygen (O_2) that is transported in the blood to meet their metabolic needs. Oxygen is carried in two forms: dissolved and bound to hemoglobin. About 98% of O_2 is carried by hemoglobin and the remaining 2% is carried in the dissolved state. Dissolved oxygen is the only form that diffuses across cell membranes and produces a partial pressure (PO_2), which, in turn, drives diffusion. The transport of O_2 involves (1) transfer from the alveoli to the pulmonary capillaries in the lung; (2) hemoglobin binding and transport; and (3) the dissociation from hemoglobin in the tissue capillaries.

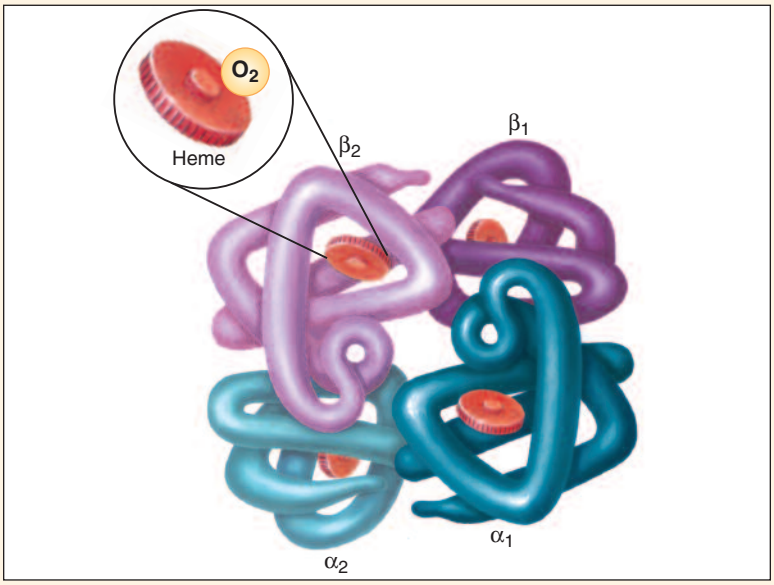
1

Alveoli-to-capillary transfer. In the lung, O_2 moves from the alveoli to the pulmonary capillaries as a dissolved gas. Its movement occurs along a concentration gradient, moving from the alveoli, where the partial pressure of PO_2 is about 100 mm Hg, to the venous end of the pulmonary capillaries with their lesser O_2 concentration and lower PO_2. The dissolved O_2 moves rapidly between the alveoli and the pulmonary capillaries, such that the PO_2 at the arterial end of the capillary is almost if not the same as that in the alveoli.



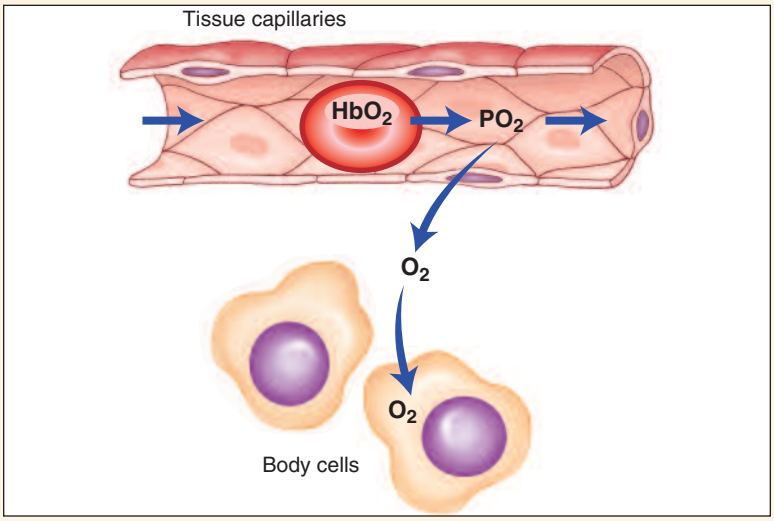
2

Hemoglobin binding and transport. Oxygen, which is relatively insoluble in plasma, relies on hemoglobin for transport in the blood. Once oxygen has diffused into the pulmonary capillary, it moves rapidly into the red blood cells and reversibly binds to hemoglobin to form HbO_2. The hemoglobin molecule contains four heme units, each capable of attaching an oxygen molecule. Hemoglobin is 100% saturated when all four units are occupied and is usually about 97% saturated in the systemic arterial blood. The capacity of the blood to carry O_2 is dependent both on hemoglobin levels and the ability of the lungs to oxygenate the hemoglobin.



3

Oxygen dissociation in the tissues. The dissociation or release of O_2 from hemoglobin occurs in the tissue capillaries where the PO_2 is less than that of the arterial blood. As oxygen dissociates from hemoglobin, it dissolves in the plasma and then moves into the tissues where the PO_2 is less than that in the capillaries. The affinity of hemoglobin for O_2 is influenced by the carbon dioxide (PCO_2) content of the blood and its pH temperature, and 2,3-diphosphoglycerate (2,3-DPG), a byproduct of glycolysis in red blood cells. Under conditions of high metabolic demand, in which the PCO_2 is increased and the pH is decreased, the binding affinity of hemoglobin is decreased, and during decreased metabolic demand, when the PCO_2 is decreased and the pH is increased, the affinity is increased.



the dilution with unoxygenated blood that occurs in the left heart.

The S-shaped oxygen dissociation curve has a flat top portion representing binding of oxygen by the hemoglobin in the lungs and a steep portion representing its release into the tissue capillaries (see Fig. 20-18A). The "S" shape of the curve reflects the effect that oxygen saturation has on the conformation of the hemoglobin molecule and its affinity for oxygen. At approximately 100 mm Hg PO_2, a plateau occurs, at which point the hemoglobin is approximately 98% saturated. Increasing the alveolar PO_2 above this level does not increase the hemoglobin saturation. Even at high altitudes, when the partial pressure of oxygen is considerably decreased, the hemoglobin remains relatively well saturated. At 60 mm Hg PO_2, for example, the hemoglobin is still approximately 89% saturated.

The steep portion of the dissociation curve—between 60 and 40 mm Hg—represents the removal of oxygen from hemoglobin as it moves through the tissue capillaries. This portion of the curve reflects the fact that there is considerable transfer of oxygen from hemoglobin to the tissues with only a small drop in PO_2, thereby ensuring an adequate concentration gradient for movement of oxygen from the capillary to the tissues. The tissues normally remove approximately 5 mL of oxygen per 100 mL of blood, with the hemoglobin of mixed venous blood being approximately 75% saturated as it returns to the right side of the heart. At hemoglobin saturation levels below 75%, the rate at which oxygen is released from hemoglobin is determined largely by tissue uptake.

Hemoglobin can be regarded as a buffer system that regulates the delivery of oxygen to the tissues. To function as a buffer system, the affinity of hemoglobin for oxygen must change with the metabolic needs of the tissues. This change is represented by a shift to the right or left in the dissociation curve (see Fig. 20-18B). A shift to the right indicates that the tissue PO_2 is greater for any given level of hemoglobin saturation and represents reduced affinity of hemoglobin for oxygen. It usually is caused by conditions such as fever or acidosis or by an increase in PCO_2, which reflects increased tissue metabolism. High altitude and conditions such as pulmonary insufficiency, heart failure, and severe anemia also cause the oxygen dissociation curve to shift to the right. A shift to the left on the oxygen dissociation curve represents an increased affinity

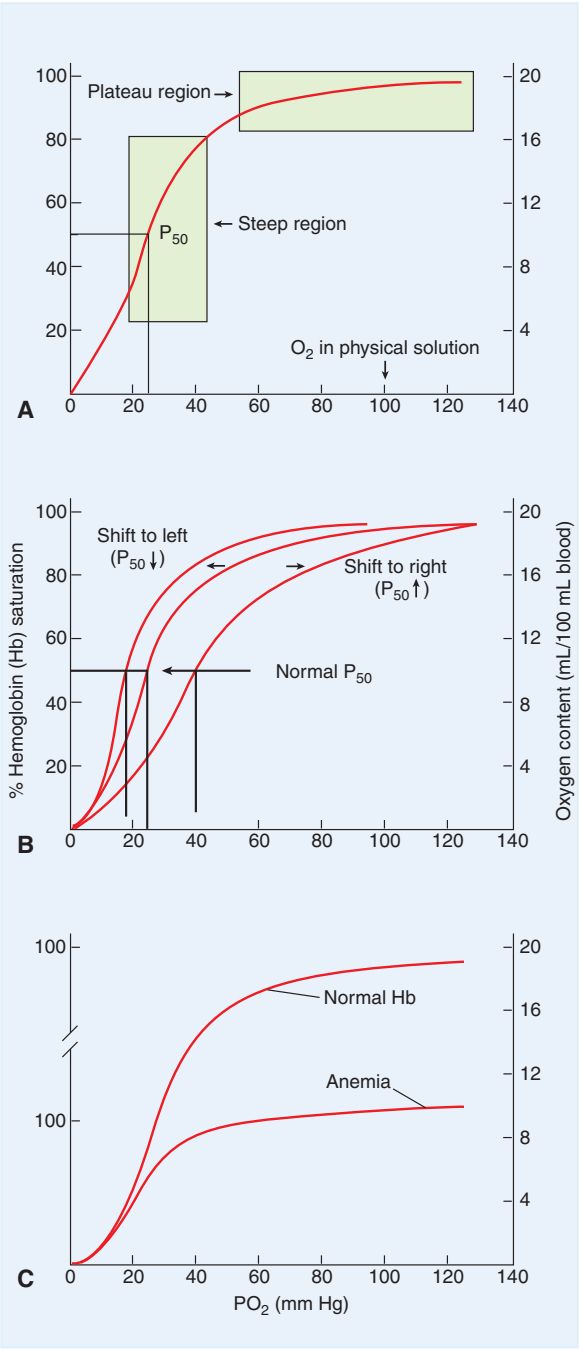


FIGURE 20-18 Oxygen-hemoglobin dissociation curve (**A**) Left boxed area represents the steep portion of the curve where oxygen is released from hemoglobin (Hb) to the tissues, and the top boxed area the plateau of the curve where oxygen is loaded onto hemoglobin in the lung. P_{50} is the partial pressure of oxygen required to saturate 50% of hemoglobin with oxygen. (**B**) The effect of body temperature, arterial PCO_2, and pH on hemoglobin affinity for oxygen as indicated by a shift in the curve and position of the P_{50}. A shift of the curve to the right due to an increase in temperature, PCO_2, or decreased pH favors release of oxygen to the tissues. A decrease in temperature, PCO_2, or increase in pH shifts the curve to the left. (**C**) Effect of anemia on the oxygen-carrying capacity of blood. The hemoglobin can be completely saturated, but the oxygen content of the blood is reduced. (Adapted from Rhoades R. A., Tanner G. A. [1996]. *Medical physiology.* Boston: Little, Brown.)

of hemoglobin for oxygen and occurs in situations associated with a decrease in tissue metabolism, such as alkalosis, decreased body temperature, and decreased PCO_2 levels. The degree of shift can be determined by the P_{50}, or the partial pressure of oxygen that is needed to achieve a 50% saturation of hemoglobin. Returning to Figure 20-18B, the dissociation curve on the left has a P_{50} of approximately 20 mm Hg; the normal curve, a P_{50} of 26; and the curve on the right, a P_{50} of 39 mm Hg.

The oxygen content of the blood (measured in milliliters per 100 milliliters of blood) represents the total amount of oxygen carried in the blood, including the dissolved oxygen and that carried by the hemoglobin (see Fig. 20-18C). It is the oxygen content of the blood rather than the PO_2 or hemoglobin saturation that determines the amount of oxygen that is carried in the blood and delivered to the tissues. An anemic person may have a normal PO_2 and hemoglobin saturation level but decreased oxygen content because of the lower amount of hemoglobin for binding oxygen.

Carbon Dioxide Transport

Carbon dioxide is transported in the blood in three forms: as dissolved carbon dioxide (10%), attached to hemoglobin (30%), and as bicarbonate (60%). Acid-base balance is influenced by the amount of dissolved carbon dioxide and the bicarbonate level in the blood (see Chapter 6).

As carbon dioxide is formed during the metabolic process, it diffuses out of cells into the tissue spaces and then into the capillaries. The amount of dissolved carbon dioxide that can be carried in plasma is determined by the partial pressure of the gas and its solubility coefficient (0.03 mL/100 mL/1 mm Hg PCO_2). Carbon dioxide is 20 times more soluble in plasma than oxygen. Thus, the dissolved state plays a greater role in transport of carbon dioxide compared with oxygen.

Most of the carbon dioxide diffuses into the red blood cells, where it forms carbonic acid or combines with hemoglobin. Carbonic acid (H_2CO_3) is formed when carbon dioxide combines with water ($CO_2 + H_2O = H^+ + HCO_3^-$). The process is catalyzed by an enzyme called *carbonic anhydrase*, which greatly increases the rate of the reaction. Carbonic acid readily ionizes to form a bicarbonate (HCO_3^-) and a hydrogen (H^+) ion. The hydrogen ion that is generated combines with the hemoglobin, which is a powerful acid-base buffer, and the bicarbonate ion diffuses into plasma in exchange for a chloride ion.

In addition to the carbonic anhydrase–mediated reaction with water, carbon dioxide reacts directly with hemoglobin to form *carbaminohemoglobin*. The combination of carbon dioxide with hemoglobin is a reversible reaction involving a loose bond that allows transport of carbon dioxide from tissues to the lungs, where it is released into the alveoli for exchange with the external environment. The release of oxygen from hemoglobin in the tissues enhances the binding of carbon dioxide to hemoglobin; in the lungs, the combining of oxygen with hemoglobin displaces carbon dioxide. The binding of carbon dioxide to hemoglobin is determined by the acidic nature of hemoglobin. Binding with carbon dioxide causes the hemoglobin to become a stronger acid. In the lungs, the highly

acidic hemoglobin has a lesser tendency to form carbaminohemoglobin, and carbon dioxide is released from hemoglobin into the alveoli. In the tissues, the release of oxygen from hemoglobin causes hemoglobin to become less acid, thereby increasing its ability to combine with carbon dioxide and form carbaminohemoglobin.

In summary, the primary functions of the lungs are oxygenation of the blood and removal of carbon dioxide. Pulmonary gas exchange is conventionally divided into three processes: ventilation, or the flow of gases into the alveoli of the lungs; perfusion, or movement of blood through the adjacent pulmonary capillaries; and diffusion, or transfer of gases between the alveoli and the pulmonary capillaries.

Ventilation is the movement of air between the atmosphere and the lungs. Pulmonary ventilation refers to the total exchange of gases between the atmosphere and the lungs, and alveolar ventilation refers to ventilation in the gas exchange portion of the lungs. The distribution of alveolar ventilation and pulmonary capillary blood flow varies with lung volume and body position. In the upright position and at high lung volumes, ventilation is greatest in the lower parts of the lungs. The upright position also produces a decrease in blood flow to the upper parts of the lung, resulting from the distance above the level of the heart and the low mean arterial pressure in the pulmonary circulation.

The diffusion of gases in the lungs is influenced by four factors: the surface area available for diffusion; the thickness of the alveolar-capillary membrane, through which the gases diffuse; the differences in the partial pressure of the gas on either side of the membrane; and the characteristics of the gas. The efficiency of gas exchange requires matching of ventilation and perfusion so that equal amounts of air and blood enter the respiratory portion of the lungs. Two factors—dead air space and shunt—interfere with matching of ventilation and perfusion and do not contribute to gas exchange. Dead air space occurs when areas of the lungs are ventilated but not perfused. Shunt is the condition under which areas of the lungs are perfused but not ventilated.

The blood transports oxygen to the cells and returns carbon dioxide to the lungs. Oxygen is transported in two forms: in chemical combination with hemoglobin and physically dissolved in plasma (PO_2). Hemoglobin is an efficient carrier of oxygen, and approximately 98% to 99% of oxygen is transported in this manner. Carbon dioxide is carried in three forms: carbaminohemoglobin (30%), dissolved carbon dioxide (10%), and bicarbonate (60%).

Control of Breathing

Unlike the heart, which has inherent rhythmic properties and can beat independently of the nervous system, the muscles that control respiration require continuous input from the nervous system. Movement of the diaphragm, intercostal muscles, sternocleidomastoid, and other accessory muscles that control ventilation is integrated by neurons located in the pons and medulla. These neurons are collectively referred to as the *respiratory center* (Fig. 20-19).

RESPIRATORY CENTER

The respiratory center consists of two dense, bilateral aggregates of respiratory neurons involved in initiating inspiration and expiration and incorporating afferent impulses into motor responses of the respiratory muscles. The first, or dorsal, group of neurons in the respiratory center is concerned primarily with inspiration. These neurons control the activity of the phrenic nerves that innervate the diaphragm and drive the second, or ventral, group of respiratory neurons. They are thought to integrate sensory input from the lungs and airways into the ventilatory response. The second group of neurons, which contains inspiratory and expiratory neurons, controls the spinal motor neurons of the intercostal and abdominal muscles.

The pacemaker properties of the respiratory center result from the cycling of the two groups of respiratory neurons: the *pneumotaxic center* in the upper pons and the *apneustic center* in the lower pons. These two groups of neurons contribute to the function of the respiratory center in the medulla. The apneustic center has an excitatory effect on inspiration, tending to prolong inspiration. The pneumotaxic center switches inspiration off, assisting in the control of respiratory rate and inspiratory volume. Brain injury, which damages the connections between the pneumotaxic and apneustic centers, results in an irregular breathing pattern consisting of prolonged inspiratory gasps interrupted by expiratory efforts.

Axons from the neurons in the respiratory center cross in the midline and descend in the ventrolateral columns of the spinal cord. The tracts that control expiration and inspiration are spatially separated in the cord, as are the tracts that transmit specialized reflexes (*i.e.*, coughing and hiccuping) and voluntary control of ventilation. Only at the level of the spinal cord are the respiratory impulses integrated to produce a reflex response.

REGULATION OF BREATHING

The control of breathing has automatic and voluntary components. The automatic regulation of ventilation is controlled by input from two types of sensors or receptors: chemoreceptors and lung receptors. Chemoreceptors monitor blood levels of oxygen, carbon dioxide, and pH and adjust ventilation to meet the changing metabolic needs of the body. Lung receptors monitor breathing patterns and lung function.

Voluntary regulation of ventilation integrates breathing with voluntary acts such as speaking, blowing, and singing. These acts, which are initiated by the motor and premotor cortex, cause a temporary suspension of automatic breathing. The automatic and voluntary components of respiration are regulated by afferent impulses that are transmitted to the respiratory center from a number

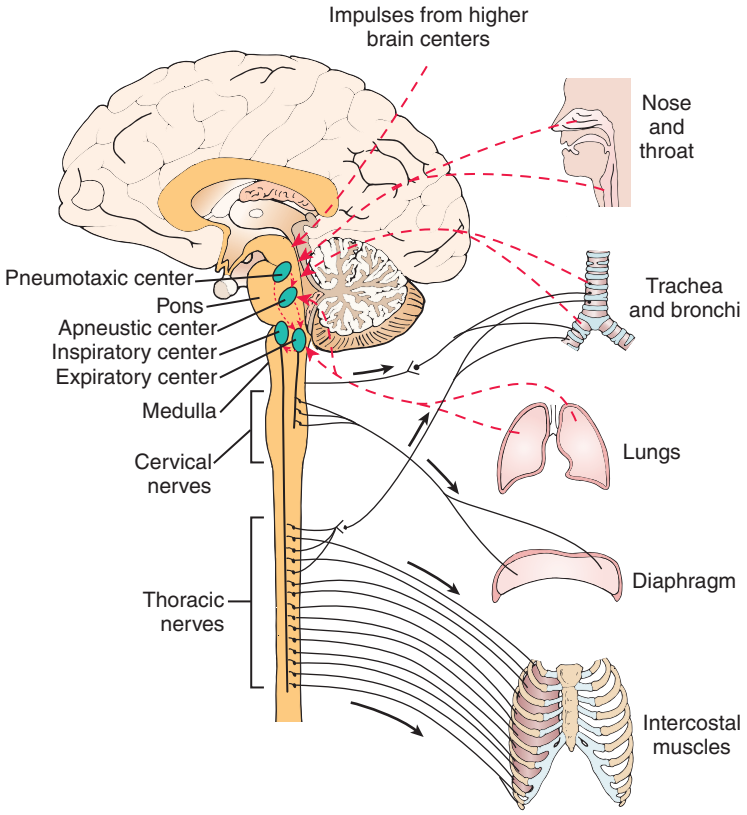


FIGURE 20-19 Schematic representation of activity in the respiratory center. Impulses traveling over afferent neurons (*dashed lines*) communicate with central neurons, which activate efferent neurons that supply the muscles of respiration. Respiratory movements can be altered by a variety of stimuli.

of sources. Afferent input from higher brain centers is evidenced by the fact that a person can consciously alter the depth and rate of respiration. Fever, pain, and emotion exert their influence through lower brain centers. Vagal afferents from sensory receptors in the lungs and airways are integrated in the dorsal area of the respiratory center.

Chemoreceptors

Tissue needs for oxygen and the removal of carbon dioxide are regulated by chemoreceptors that monitor blood levels of these gases. Input from these sensors is transmitted to the respiratory center, and ventilation is adjusted to maintain the arterial blood gases within a normal range.

There are two types of chemoreceptors: central and peripheral. The most important chemoreceptors for sensing changes in blood carbon dioxide content are the *central chemoreceptors*. These receptors are located in chemosensitive regions near the respiratory center in the medulla and are bathed in cerebrospinal fluid (CSF). Although the central chemoreceptors monitor carbon dioxide levels, the actual stimulus for these receptors is provided by hydrogen ions in the CSF. The CSF is separated from the blood by the blood-brain barrier, which permits free diffusion of carbon dioxide but not bicarbonate or hydrogen ions. The carbon dioxide combines rapidly with water to form carbonic acid, which dissociates into hydrogen and bicarbonate ions. The carbon dioxide content in the blood regulates ventilation through its effect on the pH of the extracellular fluid of the brain.

The central chemoreceptors are extremely sensitive to short-term changes in carbon dioxide. An increase in carbon dioxide levels produces an increase in ventilation that reaches its peak within a minute or so and then declines if the carbon dioxide level remains elevated. Thus, persons with chronically elevated levels of carbon dioxide no longer have a response to this stimulus for increased ventilation but rely on the stimulus provided by a decrease in blood oxygen levels.

The *peripheral chemoreceptors* are located in the carotid and aortic bodies, which are found at the bifurcation of the common carotid arteries and in the arch of the aorta, respectively. These chemoreceptors monitor arterial blood oxygen levels. Although the peripheral chemoreceptors also monitor carbon dioxide, they play a much more important role in monitoring oxygen levels. These receptors exert little control over ventilation until the PO_2 has dropped below 60 mm Hg. Thus, hypoxia is the main stimulus for ventilation in persons with chronically elevated levels of carbon dioxide. If these patients are given oxygen therapy at a level sufficient to increase the PO_2 above that needed to stimulate the peripheral chemoreceptors, their ventilation may be seriously depressed.

Lung Receptors

Lung and chest wall receptors monitor the status of breathing in terms of airway resistance and lung expansion. There are three types of lung receptors: stretch, irritant, and juxtacapillary receptors.

Stretch receptors are located in the smooth muscle layers of the conducting airways. They respond to changes in pressure in the walls of the airways. When the lungs are inflated, these receptors inhibit inspiration and promote expiration. They are important in establishing breathing patterns and minimizing the work of breathing by adjusting respiratory rate and TV to accommodate changes in lung compliance and airway resistance.

The *irritant receptors* are located between the airway epithelial cells. They are stimulated by noxious gases, cigarette smoke, inhaled dust, and cold air. Stimulation of the irritant receptors leads to airway constriction and a pattern of rapid, shallow breathing. This pattern of breathing probably protects respiratory tissues from the damaging effects of toxic inhalants. It also is thought that the mechanical stimulation of these receptors may ensure more uniform lung expansion by initiating periodic sighing and yawning. It is possible that these receptors are involved in the bronchoconstriction response that occurs in some persons with bronchial asthma.

The *juxtacapillary* or *J receptors* are located in the alveolar wall, close to the pulmonary capillaries. It is thought that these receptors sense lung congestion. These receptors may be responsible for the rapid, shallow breathing that occurs with pulmonary edema, pulmonary embolism, and pneumonia.

COUGH REFLEX

Coughing is a neurally mediated reflex that protects the lungs from the accumulation of secretions and from entry of irritating and destructive substances. It is one of the primary defense mechanisms of the respiratory tract. The cough reflex is initiated by receptors located in the tracheobronchial wall; these receptors are extremely sensitive to irritating substances and to the presence of excess secretions. Afferent impulses from these receptors are transmitted through the vagus to the medullary center, which integrates the cough response.

Coughing itself requires the rapid inspiration of a large volume of air (usually about 2.5 L), followed by rapid closure of the glottis and forceful contraction of the abdominal and expiratory muscles. As these muscles contract, intrathoracic pressures are elevated to levels of 100 mm Hg or more. The rapid opening of the glottis at this point leads to an explosive expulsion of air.

Many conditions can interfere with the cough reflex and its protective function. The reflex is impaired in persons whose abdominal or respiratory muscles are weak. This problem can be caused by disease conditions that lead to muscle weakness or paralysis, by prolonged inactivity, or as an outcome of surgery involving these muscles. Bed rest interferes with expansion of the chest and limits the amount of air that can be taken into the lungs in preparation for coughing, making the cough weak and ineffective. Disease conditions that prevent effective closure of the glottis and laryngeal muscles interfere with production of the marked increase in intrathoracic pressure that is needed for effective coughing. For example, the presence of a nasogastric tube may prevent closure of the upper airway structures and may fatigue the receptors for the cough reflex that are located in the area. The cough reflex also is impaired when there is depressed function of the medullary centers in the brain that integrate the cough reflex. Interruption of the central integration aspect of the cough reflex can arise as the result of disease of this part of the brain or the action of drugs that depress the cough center.

Although the cough reflex is a protective mechanism, frequent and prolonged coughing can be exhausting and painful and can have undesirable effects on the cardiovascular and respiratory systems and on the elastic tissues of the lungs. This is particularly true in young children and elderly persons.

In summary, the respiratory system requires continuous input from the nervous system. Movement of the diaphragm, intercostal muscles, and other respiratory muscles is controlled by neurons of the respiratory center located in the pons and medulla. The control of breathing has automatic and voluntary components. Voluntary respiratory control is needed for integrating breathing and actions such as speaking, blowing, and singing. These acts, which are initiated by the motor and premotor cortex, cause temporary suspension of automatic breathing.

The automatic regulation of ventilation is controlled by two types of receptors: lung receptors, which protect respiratory structures, and chemoreceptors, which monitor the gas exchange function of the lungs by sensing changes in blood levels of carbon dioxide, oxygen, and pH. There are three types of lung receptors: stretch receptors, which monitor lung inflation; irritant receptors, which protect against the damaging effects of toxic inhalants; and J receptors, which are thought to sense lung congestion. There are two groups of chemoreceptors: central and peripheral. The central chemoreceptors are the most important in sensing changes in carbon dioxide levels, and the peripheral chemoreceptors function in sensing arterial blood oxygen levels.

The cough reflex protects the lungs from the accumulation of secretions and from the entry of irritating and destructive substances; it is one of the primary defense mechanisms of the respiratory tract.

Review Exercises

Use the solubility coefficient for oxygen and the oxygen dissociation curve depicted in Figure 20-18 to answer the following questions:

A. What is the hemoglobin saturation at a high altitude in which the barometric pressure is 500 mm Hg (consider oxygen to represent 21% of the total gases)?

B. It is usually recommended that the hemoglobin saturation of persons with chronic lung disease

be maintained at about 89% when they are receiving supplemental low-flow oxygen. What would their PO_2 be at this level of hemoglobin saturation, and what is the rationale for keeping the PO_2 at this level?

C. What is the oxygen content of a person with a hemoglobin level of 6 g/dL who is breathing room air?

D. What is the oxygen content of a person with carbon monoxide poisoning who is receiving 100% oxygen at 3 atmospheres pressure in a hyperbaric chamber? Consider that most of the person's hemoglobin is saturated with carbon monoxide.

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