CHAPTER 9: RESPIRATORY SYSTEM

At the end of this chapter, student will be able to:

a) State the general function of the respiratory system.
b) Describe the structure and functions of the nasal cavities and pharynx.
c) Describe the structure of the larynx and explain the speaking mechanism.
d) Describe the structure and functions of the trachea and bronchial tree.
e) State the locations of the pleural membranes, and explain the functions of serous fluid.
f) Describe the structure of the alveoli and pulmonary capillaries, and explain the importance of surfactant.
g) Name and describe the important air pressures involved in breathing.
h) Describe normal inhalation and exhalation and forced exhalation.
i) Name the pulmonary volumes and define each.
j) Explain the diffusion of gases in external respiration and internal respiration.
k) Describe how oxygen and carbon dioxide are transported in the blood.
l) Explain the nervous and chemical mechanisms that regulate respiration.
m) Explain how respiration affects the pH of body fluids.

9.1 INTRODUCTION TO THE RESPIRATORY SYSTEM

When the respiratory system is mentioned, people generally think of breathing, but breathing is only one of the activities of the respiratory system. The body cells need a continuous supply of oxygen for the metabolic processes that are necessary to maintain life. The respiratory system works with the circulatory system to provide this oxygen and to remove the waste products of metabolism. It also helps to regulate pH of the blood.

Respiration is the sequence of events that results in the exchange of oxygen and carbon dioxide between the atmosphere and the body cells. Every 3 to 5 seconds, nerve impulses stimulate the breathing process, or ventilation, which moves air through a series of passages into and out of the lungs. After this, there is an exchange of gases between the lungs and the blood. This is called external respiration. The blood transports the gases to and from the tissue cells. The exchange of gases between the blood and tissue cells is internal respiration. Finally, the cells utilize the oxygen for their specific activities. This is cellular metabolism, or cellular respiration. Together these activities constitute respiration.
9.2 FUNCTIONS

In brief, the respiratory system has the following functions:

1. Provides for gas exchange intake of O2 for delivery to body cells and elimination of CO2 produced by body cells.
2. Helps regulate blood pH.
3. Contains receptors for the sense of smell, filters inspired air, produces vocal sounds (phonation, olfaction), and excretes small amounts of water and heat.
4. Protection against some microorganisms.

Focus on Homeostasis
9.3 DIVISIONS OF THE RESPIRATORY SYSTEM

The respiratory system consists of the nose, pharynx (throat), larynx (voice box), trachea (windpipe), bronchi, and lungs. Also parts of the respiratory system are the pleural membranes and the respiratory muscles that form the chest cavity: the diaphragm and intercostal muscles.

Its parts can be classified according to either structure or function.

Structurally, the respiratory system consists of two parts:

1. The upper respiratory system consists of the parts outside the chest cavity: the air passages of the nose, nasal cavities, pharynx, larynx, and upper trachea.
2. The lower respiratory system includes the lower trachea and the lungs themselves, which include the bronchial tubes and alveoli.

Functionally, the respiratory system also consists of two parts:

1. The conducting zone consists of a series of interconnecting cavities and tubes both outside and within the lungs. These include the nose, pharynx, larynx, trachea, bronchi, bronchioles, and terminal bronchioles; their function is to filter, warm, and moisten air and conduct it into the lungs.
2. The respiratory zone consists of tissues within the lungs where gas exchange occurs. These include the respiratory bronchioles, alveolar ducts, alveolar sacs, and alveoli; they are the main sites of gas exchange between air and blood.
Figure: Midsagittal section of the head and neck showing the structures of the upper respiratory tract.
Nose and Nasal Cavities

The nose can be divided into external and internal portions:

- The external nose is the portion of the nose visible on the face and consists of a supporting framework of bone and hyaline cartilage covered with muscle and skin and lined by a mucous membrane.

  The bony framework of the external nose is formed by frontal bone, nasal bones, and maxillae.

  The cartilaginous framework of the external nose consists of the septal nasal cartilage, which forms the anterior portion of the nasal septum; the lateral nasal cartilages inferior to the nasal bones; and the alar cartilages, which form a portion of the walls of the nostrils.

  On the undersurface of the external nose are two openings called the external nares or nostrils.

  The interior structures of the external nose have three functions:

  1. warming, moistening, and filtering incoming air;
  2. detecting olfactory stimuli; and
  3. modifying speech vibrations as they pass through the large, hollow resonating chambers. Resonance refers to prolonging, amplifying, or modifying a sound by vibration.

- The internal nose is a large cavity beyond the nasal vestibule in the anterior aspect of the skull that lies inferior to the nasal bone and superior to the mouth; it is lined with muscle and mucous membrane.

  Anteriorly, the internal nose merges with the external nose, and posteriorly it communicates with the pharynx through two openings called the internal nares or choanae.

  Ducts from the paranasal sinuses (which drain mucus) and the nasolacrimal ducts (which drain tears) also open into the internal nose. Paranasal sinuses are air-filled cavities in the frontal, maxillae, ethmoid, and sphenoid bones. These sinuses, which have the same names as the bones in which they are located, surround the nasal cavity and open into it. Their function is to reduce the weight of the skull, to produce mucus, and to influence voice quality by acting as resonating chambers.
The lateral walls of the internal nose are formed by the ethmoid, maxillae, lacrimal, palatine, and inferior nasal conchae bones; the ethmoid bone also forms the roof. The palatine bones and palatine processes of the maxillae, which together constitute the hard palate, form the floor of the internal nose.

The space within the internal nose is called the nasal cavity.

The anterior portion of the nasal cavity just inside the nostrils, called the nasal vestibule, is surrounded by cartilage; the superior part of the nasal cavity is surrounded by bone.

A vertical partition, the nasal septum, divides the nasal cavity into right and left sides. The anterior portion of the nasal septum consists primarily of hyaline cartilage; the remainder is formed by the vomer, perpendicular plate of the ethmoid, maxillae, and palatine bones.

When air enters the nostrils, it passes first through the vestibule, which is lined by skin containing coarse hairs that filter out large dust particles. Drainage from the nasolacrimal ducts also helps moisten the air, and is sometimes assisted by secretions from the paranasal sinuses. The cilia move the mucus and trapped dust particles toward the pharynx, at which point they can be swallowed or spit out, thus removing the particles from the respiratory tract.

**Pharynx**

The pharynx, or throat, is a funnel-shaped tube about 13 cm (5 in.) long that starts at the internal nares and extends to the level of the cricoid cartilage, the most inferior cartilage of the larynx (voice box). The pharynx lies just posterior to the nasal and oral cavities, superior to the larynx, and just anterior to the cervical vertebrae.

Its wall is composed of skeletal muscles and is lined with a mucous membrane. Contraction of the skeletal muscles assists in deglutition (swallowing).
The pharynx functions as a passageway for air and food, provides a resonating chamber for speech sounds, and houses the tonsils, which participate in immunological reactions against foreign invaders.

The pharynx can be divided into three anatomical regions:

(1) nasopharynx,
(2) oropharynx, and
(3) laryngopharynx.

The superior portion of the pharynx, called the nasopharynx, lies posterior to the nasal cavity and extends to the soft palate.

The soft palate, which forms the posterior portion of the roof of the mouth, is an arch-shaped muscular partition between the nasopharynx and oropharynx that is lined by mucous membrane, it is elevated during swallowing to block the nasopharynx and prevent food or saliva from going up rather than down.

There are five openings in its wall: two internal nares, two openings that lead into the auditory (pharyngotympanic) tubes (commonly known as the eustachian tubes), and the opening into the oropharynx.

The posterior wall also contains the pharyngeal tonsil (adenoid).

Through the internal nares, the nasopharynx receives air from the nasal cavity.

The nasopharynx is lined with pseudostratified ciliated columnar epithelium, and the cilia move the mucus down toward the most inferior part of the pharynx.

The nasopharynx also exchanges small amounts of air with the auditory tubes to equalize air pressure between the pharynx and the middle ear.

The intermediate portion of the pharynx, the oropharynx, lies posterior to the oral cavity and extends from the soft palate inferiorly to the level of the hyoid bone.

It has only one opening into it, the fauces (throat), the opening from the mouth.

This portion of the pharynx has both respiratory and digestive functions, serving as a common passageway for air, food, and drink.

Two pairs of tonsils, the palatine and lingual tonsils, are found in the oropharynx. a lymph nodule that contains macrophages.

The inferior portion of the pharynx, the laryngopharynx or hypopharynx, begins at the level of the hyoid bone.

At its inferior end it opens into the esophagus (food tube) posteriorly and the larynx (voice box) anteriorly.
Like the oropharynx, the laryngopharynx is both a respiratory and a digestive.

**Larynx**

The **larynx** or voice box, is a short passageway that connects the laryngopharynx with the trachea.
It lies in the midline of the neck anterior to the esophagus and the fourth through sixth cervical vertebrae (C4–C6).

As its name indicates one of its functions, which is speaking. The other function of the larynx is to be an air passageway between the pharynx and the trachea. The wall of the larynx is composed of **nine pieces of cartilage**. **Three** occur *singly* (thyroid cartilage, epiglottis, and cricoid cartilage), and **three** occur in *pairs* (arytenoid, cuneiform, and corniculate cartilages).

Of the paired cartilages, the **arytenoids** cartilages are the most important because they influence changes in position and tension of the vocal folds (true vocal cords for speech). The **extrinsic muscles** of the larynx connect the cartilages to other structures in the throat; the **intrinsic muscles** connect the cartilages to one another.

The **thyroid cartilage** (Adam’s apple) consists of two fused plates of hyaline cartilage that form the anterior wall of the larynx and give it a triangular shape. It is present in both males and females but is usually larger in males due to the influence of male sex hormones on its growth during puberty. The ligament that connects the thyroid cartilage to the hyoid bone is called the **thyrohyoid membrane**.

The **epiglottis** (epi-: over; glottis: tongue) is a large, leaf shaped piece of elastic cartilage that is covered with epithelium. The “stem: branch” of the epiglottis is the tapered inferior portion that is attached to the anterior border of the thyroid cartilage and hyoid bone. The broad superior “leaf” portion of the epiglottis is unattached and is free to move up and down like a trap door. During swallowing, the pharynx and larynx rise. Elevation of the pharynx widens it to receive food or drink; elevation of the larynx causes the epiglottis to move down and form a lid over the glottis, closing it off.

The **glottis** consists of a pair of folds of mucous membrane, the vocal folds (true vocal cords) in the larynx. The closing of the larynx in this way during swallowing routes liquids and foods into the esophagus and keeps them out of the larynx and airways. When small particles of dust, smoke, food, or liquids pass into the larynx, a cough reflex occurs, usually expelling the material.

During breathing, the vocal cords are held at the sides of the glottis, so that air passes freely into and out of the trachea. During speaking, the intrinsic muscles of the larynx pull the vocal cords across the glottis, and exhaled air vibrates the vocal cords to produce sounds that can be
turned into speech. It is also physically possible to speak while inhaling, but this is not what we are used to. The cranial nerves that are motor nerves to the larynx for speaking are the vagus and accessory nerves.

The **cricoid cartilage** (ringlike) is a ring of hyaline cartilage that forms the inferior wall of the larynx. It is attached to the first ring of cartilage of the trachea by the **cricotracheal ligament**. The thyroid cartilage is connected to the cricoid cartilage by the **cricothyroid ligament**. The cricoid cartilage is the landmark for making an emergency airway called a tracheotomy.

The paired **arytenoid cartilages** (ladlelike) are triangular pieces of mostly hyaline cartilage located at the posterior, superior border of the cricoid cartilage. They form synovial joints with the cricoid cartilage and have a wide range of mobility.

The paired **corniculate cartilages** (shaped like a small horn), horn-shaped pieces of elastic cartilage, are located at the apex of each arytenoid cartilage.

The paired **cuneiform cartilages** (wedge-shaped), clubshaped elastic cartilages anterior to the corniculate cartilages, support the vocal folds and lateral aspects of the epiglottis.

**Trachea**

The **trachea** or windpipe, is a tubular passageway for air that is about 12 cm (5 in.) long and 2.5 cm (1 in.) in diameter.

It is located anterior to the esophagus and extends from the larynx to the superior border of the fifth thoracic vertebra (T5), where it divides into right and left primary bronchi.

The **layers** of the tracheal wall, from **deep to superficial**, are the (1) **mucosa**, (2) **submucosa**, (3) **hyaline cartilage**, and (4) **adventitia**. The hyaline cartilage in the tracheal wall provides support and keeps the trachea from collapsing. The posterior soft tissue allows for expansion of the esophagus, which is immediately posterior to the trachea.

Goblet cells of the trachea produce mucus that traps airborne particles and microorganisms, and the cilia propel the mucus upward, where it is either swallowed or expelled.
Bronchi and Bronchial Tree

At the superior border of the fifth thoracic vertebra, the trachea divides into a right primary bronchus (windpipe), which goes into the right lung, and a left primary bronchus, which goes into the left lung.

The right primary bronchus is more vertical, shorter, and wider than the left. As a result, an aspirated object is more likely to enter and lodge in the right primary bronchus than the left.

At the point where the trachea divides into right and left primary bronchi an internal ridge called the carina is formed by a posterior and somewhat inferior projection of the last tracheal cartilage.

The mucous membrane of the carina is one of the most sensitive areas of the entire larynx and trachea for triggering a cough reflex. Widening and distortion of the carina is a serious sign because it usually indicates a carcinoma of the lymph nodes around the region where the trachea divides.

On entering the lungs, the primary bronchi divide to form smaller bronchi: the secondary (lobar) bronchi, one for each lobe of the lung. (The right lung has three lobes; the left lung has two.) The secondary bronchi continue to branch, forming still smaller
bronchi, called tertiary (segmental) bronchi, that divide into bronchioles. Bronchioles in turn branch repeatedly, and the smallest ones branch into even smaller tubes called terminal bronchioles. This extensive branching from the trachea resembles an inverted tree and is commonly referred to as the bronchial tree.

The cartilage and mucous membrane of the primary bronchi are similar to that in the trachea. As the branching continues through the bronchial tree, the amount of hyaline cartilage in the walls decreases until it is absent in the smallest bronchioles. As the cartilage decreases, the amount of smooth muscle increases. The alveolar ducts and alveoli consist primarily of simple squamous epithelium, which permits rapid diffusion of oxygen and carbon dioxide. Exchange of gases between the air in the lungs and the blood in the capillaries occurs across the walls of the alveolar ducts and alveoli.

**Lungs and pleural membranes.**

The lungs are paired cone-shaped organs in the thoracic cavity. They are separated from each other by the heart and other structures in the mediastinum, which divides the thoracic cavity into two anatomically distinct chambers. Each lung is enclosed and protected by a double-layered serous membrane called the pleural membrane. The superficial layer, called the parietal pleura, lines the wall of the thoracic cavity; the deep layer, the visceral pleura, covers the lungs themselves. Between the visceral and parietal pleurae is a small space, the pleural cavity, which contains a small amount of lubricating fluid secreted by the membranes. This pleural fluid reduces friction between the membranes, allowing them to slide easily over one another during breathing. Pleural fluid also causes the two membranes to adhere to one another. Separate pleural cavities surround the left and right lungs.

The lungs extend from the diaphragm to just slightly superior to the clavicles and lie against the ribs anteriorly and posteriorly. The broad inferior portion of the lung, the base, is concave and fits over the convex area of the diaphragm. The narrow superior portion of the lung is the apex. The surface of the lung lying against the ribs, the costal surface, matches the rounded curvature of the ribs.
The mediastinal (medial) surface of each lung contains a region, the hilum, through which bronchi, pulmonary blood vessels, lymphatic vessels, and nerves enter and exit. These structures are held together by the pleura and connective tissue and constitute the root of the lung. Medially, the left lung also contains a concavity, the cardiac notch, in which the heart lies. Due to the space occupied by the heart, the left lung is about 10% smaller than the right lung.

Although the right lung is thicker and broader, it is also somewhat shorter than the left lung because the diaphragm is higher on the right side, accommodating the liver that lies inferior to it.

The lungs almost fill the thorax. The apex of the lungs lies superior to the medial third of the clavicles and is the only area that can be palpated. The anterior, lateral, and posterior surfaces of the lungs lie against the ribs. The base of the lungs extends from the sixth costal cartilage.
anteriorly to the spinous process of the tenth thoracic vertebra posteriorly. The pleura extends about 5 cm (2 in.) below the base from the sixth costal cartilage anteriorly to the twelfth rib posteriorly.

**Lobes, Fissures, and Lobules**

One or two fissures divide each lung into lobes. Both lungs have an oblique fissure, which extends inferiortly and anteriorly; the right lung also has a horizontal fissure. The oblique fissure in the left lung separates the superior lobe from the inferior lobe. In the right lung, the superior part of the oblique fissure separates the superior lobe from the inferior lobe; the inferior part of the oblique fissure separates the inferior lobe from the middle lobe, which is bordered superiorly by the horizontal fissure.

Each lobe receives its own secondary (lobar) bronchus. Thus, the right primary bronchus gives rise to three secondary (lobar) bronchi called the superior, middle, and inferior secondary (lobar) bronchi, and the left primary bronchus gives rise to superior and inferior secondary (lobar) bronchi. Within the lung, the secondary bronchi give rise to the tertiary (segmental) bronchi, which are constant in both origin and distribution, there are 10 tertiary bronchi in each lung.

The segment of lung tissue that each tertiary bronchus supplies is called a bronchopulmonary segment. Each bronchopulmonary segment of the lungs has many small compartments called lobules; each lobule is wrapped in elastic connective tissue and contains a lymphatic vessel, an arteriole, a venule, and a branch from a terminal bronchiole. Terminal bronchioles subdivide into microscopic branches called respiratory bronchioles. Respiratory bronchioles in turn subdivide into several (2–11) alveolar ducts. The respiratory passages from the trachea to the alveolar ducts contain about 25 orders of branching: branching from the trachea into primary bronchi is called first-order branching, from primary bronchi into secondary bronchi is called second-order branching, and so on down to the alveolar ducts.
Alveoli

The functional units of the lungs are the air sacs called **alveoli**. Around the circumference of the alveolar ducts are numerous **alveoli and alveolar sacs**. An **alveolus** is a cup-shaped outpouching lined by simple squamous epithelium and supported by a thin elastic basement membrane; an **alveolar sac** consists of two or more alveoli that share a common opening. The walls of alveoli consist of two types of alveolar epithelial cells. The more numerous **type I alveolar cells** are simple squamous epithelial cells that form a nearly continuous lining of the alveolar wall. **Type II alveolar cells**, also called **septal cells**, are fewer in number and are found between type I alveolar cells. The thin type I alveolar cells are the main sites of **gas exchange**. Type II alveolar cells, rounded or cuboidal epithelial cells with free surfaces containing microvilli, secrete **alveolar fluid**, which keeps the surface between the cells and the air moist. Included in the alveolar fluid is **surfactant**, a complex mixture of phospholipids and lipoproteins. Surfactant lowers the surface tension of alveolar fluid, which reduces the tendency of alveoli to collapse.
Associated with the alveolar wall are alveolar macrophages (dust cells), phagocytes that remove fine dust particles and other debris from the alveolar spaces.

On the outer surface of the alveoli, the lobule’s arteriole and venule disperse into a network of blood capillaries that consist of a single layer of endothelial cells and basement membrane.

The exchange of O2 and CO2 between the air spaces in the lungs and the blood takes place by diffusion across the alveolar and capillary walls, which together form the respiratory membrane.

Blood Supply to the Lungs

The lungs receive blood via two sets of arteries: pulmonary arteries and bronchial arteries. Deoxygenated blood passes through the pulmonary trunk, which divides into a left pulmonary artery that enters the left lung and a right pulmonary artery that enters the right lung. (The pulmonary arteries are the only arteries in the body that carry deoxygenated blood.)

Return of the oxygenated blood to the heart occurs by way of the four pulmonary veins, which drain into the left atrium. A unique feature of pulmonary blood vessels is their constriction in response to localized hypoxia (low O2 level). In all other body tissues, hypoxia causes dilatation of blood vessels to increase blood flow. In the lungs, however, vasoconstriction in response to hypoxia diverts pulmonary blood from poorly ventilated areas of the lungs to well ventilated regions. This phenomenon is known as ventilation–perfusion coupling because the perfusion (blood flow) to each area of the lungs matches the extent of ventilation (airflow) to alveoli in that area.

Bronchial arteries, which branch from the aorta, deliver oxygenated blood to the lungs. This blood mainly perfuses the muscular walls of the bronchi and bronchioles. Connections exist between branches of the bronchial arteries and branches of the pulmonary arteries, however; most blood returns to the heart via pulmonary veins. Some blood, however, drains into bronchial veins, branches of the azygos system, and returns to the heart via the superior vena cava.
**9.4 MECHANISM OF BREATHING**

**Ventilation** is the term for the movement of air to and from the alveoli. The two aspects of ventilation are **inhalation and exhalation**, which are brought about by the nervous system and the respiratory muscles. The respiratory centers are located in the medulla and pons. It is the medulla that generates impulses to the respiratory muscles. These muscles are the diaphragm and the external and internal intercostal muscles. The **diaphragm** is a dome-shaped muscle below the lungs; when it contracts, the diaphragm flattens and moves downward. The intercostal muscles are found between the ribs. The **external intercostal**...
muscles pull the ribs upward and outward, and the internal intercostals muscles pull the ribs downward and inward.

Ventilation is the result of the respiratory muscles producing changes in the pressure within the alveoli and bronchial tree.

With respect to breathing, three types of pressure are important:

1. **Atmospheric pressure**: the pressure of the air around us. At sea level, atmospheric pressure is 760 mmHg. At higher altitudes, of course, atmospheric pressure is lower.

2. **Intrapleural pressure**: the pressure within the potential pleural space between the parietal pleura and visceral pleura. This is a potential rather than a real space. A thin layer of serous fluid causes the two pleural membranes to adhere to one another. Intrapleural pressure is always slightly below atmospheric pressure (about 756 mmHg), and is called a *negative* pressure. The elastic lungs are always tending to collapse and pull the visceral pleura away from the parietal pleura. The serous fluid, however, prevents actual separation of the pleural membranes.

3. **Intrapulmonic pressure**: the pressure within the bronchial tree and alveoli. This pressure fluctuates below and above atmospheric pressure during each cycle of breathing.

**INHALATION**

Inhalation, also called *inspiration*, is a precise sequence of events that may be described as follows: Motor impulses from the medulla travel along the phrenic nerves to the diaphragm and along the intercostals nerves to the external intercostal muscles. The diaphragm contracts, moves downward, and expands the chest cavity from top to bottom. The external intercostal muscles pull the ribs up and out, which expands the chest cavity from side to side and front to back. As the chest cavity is expanded, the parietal pleura expands with it. Intrapleural pressure becomes even more negative as a sort of suction is created between the pleural membranes. The adhesion created by the serous fluid, however, permits the visceral pleura to be expanded too, and this expands the lungs as well. As the lungs expand, intrapulmonic pressure falls below atmospheric pressure, and air enters the nose and travels through the respiratory passages to the alveoli. Entry of air continues until intrapulmonic pressure is equal to atmospheric pressure; this is a normal inhalation. Of course, inhalation can be continued beyond normal, that is, a deep breath. This requires a more forceful
contraction of the respiratory muscles to further expand the lungs, permitting the entry of more air.

EXHALATION

Exhalation may also be called expiration and begins when motor impulses from the medulla decrease and the diaphragm and external intercostal muscles relax. As the chest cavity becomes smaller, the lungs are compressed, and their elastic connective tissue, which was stretched during inhalation, recoils and also compresses the alveoli. As intrapulmonic pressure rises above atmospheric pressure, air is forced out of the lungs until the two pressures are again equal.

Notice that inhalation is an active process that requires muscle contraction, but normal exhalation is a passive process, depending to a great extent on the normal elasticity of healthy lungs. In other words, under normal circumstances we must expend energy to inhale but not to exhale. We can, however, go beyond a normal exhalation and expel more air, such as when talking, singing, or blowing up a balloon. Such a forced exhalation is an active process that requires contraction of other muscles. Contraction of the internal intercostal muscles pulls the ribs down and in and squeezes even more air out of the lungs. Contraction of abdominal muscles, such as the rectus abdominis, compresses the abdominal organs and pushes the diaphragm upward, which also forces more air out of the lungs.
9.5 PULMONARY VOLUMES

The capacity of the lungs varies with the size and age of the person. Taller people have larger lungs than do shorter people. Also, as we get older our lung capacity diminishes as lungs lose their elasticity and the respiratory muscles become less efficient. For the following pulmonary volumes, the values given are those for healthy young adults.

1. **Tidal volume**: the amount of air involved in one normal inhalation or exhalation. The average tidal volume is 500 mL, but many people often have lower tidal volumes because of superficial breathing.

2. **Minute respiratory volume** (MRV): the amount of air inhaled and exhaled in 1 minute. MRV is calculated by multiplying tidal volume by the number of respirations per minute (average range: 12 to 20 per minute). If tidal volume is 500 mL and the respiratory rate is 12 breaths per minute, the MRV is 6000 mL, or 6 liters of air per minute, which is average.
Superficial breathing usually indicates a smaller than average tidal volume, and would thus require more respirations per minute to obtain the necessary MRV.

3. **Inspiratory reserve**: the amount of air, beyond tidal volume, that can be taken in with the deepest possible inhalation. Normal inspiratory reserve ranges from 2000 to 3000 mL.

4. **Expiratory reserve**: the amount of air, beyond tidal volume, that can be expelled with the most forceful exhalation. Normal expiratory reserve ranges from 1000 to 1500 mL.

5. **Vital capacity**: the sum of tidal volume, inspiratory reserve, and expiratory reserve. Stated another way, vital capacity is the amount of air involved in the deepest inhalation followed by the most forceful exhalation. Average range of vital capacity is 3500 to 5000 mL.

6. **Residual air**: the amount of air that remains in the lungs after the most forceful exhalation; the average range is 1000 to 1500 mL. Residual air is important to ensure that there is some air in the lungs at all times, so that exchange of gases is a continuous process, even between breaths.

Some of the volumes just described can be determined with instruments called spirometers, which measure movement of air. Trained singers and musicians who play wind instruments often have vital capacities much larger than would be expected for their height and age, because their respiratory muscles have become more efficient with “practice.” The same is true for athletes who exercise regularly. A person with emphysema, however, must “work” to exhale, and vital capacity and expiratory reserve volume are often much lower than average.

Another kind of pulmonary volume is **alveolar** reaches the alveoli and participates in gas exchange. An average tidal volume is 500 mL, of which 350 to 400 mL is in the alveoli at the end of an inhalation. The remaining 100 to 150 mL of air is **anatomic dead space**, the air still within the respiratory passages. Despite the rather grim name, anatomic dead space is normal; everyone has it. **Physiological dead space** is not normal, and is the volume of non-functioning alveoli that decrease gas exchange. Causes of increased physiological dead space include bronchitis, pneumonia, tuberculosis, emphysema, asthma, pulmonary edema, and a collapsed lung.

The **compliance** of the thoracic wall and the lungs, that is, their normal expansibility, is necessary for sufficient alveolar ventilation. Thoracic compliance may be decreased by fractured ribs, scoliosis, pleurisy, or ascites. Lung compliance will be decreased by any condition that increases physiologic dead space. Normal compliance thus promotes sufficient gas exchange in the alveoli.
9.6 EXCHANGE OF GASES

There are two sites of exchange of oxygen and carbon dioxide: the lungs and the tissues of the body. The exchange of gases between the air in the alveoli and the blood in the pulmonary capillaries is called external respiration. This term may be a bit confusing at first, because we often think of “external” as being outside the body. In this case, however, “external” means the exchange that involves air from the external environment, though the exchange takes place within the lungs. Internal respiration is the exchange of gases between the blood in the systemic capillaries and the tissue fluid (cells) of the body. The air we inhale (the earth’s atmosphere) is approximately 21% oxygen and 0.04% carbon dioxide. Although most (78%) of the atmosphere is nitrogen, this gas is not physiologically available to us, and we simply exhale it. This exhaled air also contains about 16% oxygen and 4.5% carbon dioxide, so it is apparent that some oxygen is retained within the body and the carbon dioxide produced by cells is exhaled.

9.7 DIFFUSION OF GASES - PARTIAL PRESSURES

Within the body, a gas will diffuse from an area of greater concentration to an area of lesser concentration. The concentration of each gas in a particular site (alveolar air, pulmonary blood, and so on) is expressed in a value called partial pressure. The partial pressure of a gas, measured in mmHg, is the pressure it exerts within a mixture of gases, whether the mixture is actually in a gaseous state or is in a liquid such as blood.

1. The abbreviation for partial pressure is “P,” which is used, for example, on hospital lab slips for blood gases and will be used here.

Because partial pressure reflects concentration, a gas will diffuse from an area of higher partial pressure to an area of lower partial pressure. The air in the alveoli has a high PO\textsubscript{2} and a low PCO\textsubscript{2}. The blood in the pulmonary capillaries, which has just come from the body, has a low PO\textsubscript{2} and a high PCO\textsubscript{2}. Therefore, in external respiration, oxygen diffuses from the air in the alveoli to the blood, and carbon dioxide diffuses from the blood to the air in the alveoli.
The blood that returns to the heart now has a high PO$_2$ and a low PCO$_2$ and is pumped by the left ventricle into systemic circulation. The arterial blood that reaches systemic capillaries has a high PO$_2$ and a low PCO$_2$. The body cells and tissue fluid have a low PO$_2$ and a high PCO$_2$ because cells continuously use oxygen in cell respiration (energy production) and produce carbon dioxide in this process. Therefore, in internal respiration, oxygen diffuses from the blood to tissue fluid (cells), and carbon dioxide diffuses from tissue fluid to the blood. The blood that enters systemic veins to return to the heart now has a low PO$_2$ and a high PCO$_2$ and is pumped by the right ventricle to the lungs to participate in external respiration.

**9.8 TRANSPORT OF GASES IN THE BLOOD**

Although some oxygen is dissolved in blood plasma and does create the PO$_2$ values, it is only about 1.5% of the total oxygen transported, not enough to sustain life. As you already know,
most oxygen is carried in the blood bonded to the hemoglobin in red blood cells (RBCs). The mineral iron is part of hemoglobin and gives this protein its oxygen-carrying ability.

The oxygen–hemoglobin bond is formed in the lungs where PO₂ is high. This bond, however, is relatively unstable, and when blood passes through tissues with a low PO₂, the bond
breaks, and oxygen is released to the tissues. The lower the oxygen concentration in a tissue, the more oxygen the hemoglobin will release. This ensures that active tissues, such as exercising muscles, receive as much oxygen as possible to continue cell respiration. Other factors that increase the release of oxygen from hemoglobin are a high PCO₂ (actually a lower pH) and a high temperature, both of which are also characteristic of active tissues. Another measure of blood oxygen is the percent of oxygen saturation of hemoglobin (SaO₂). The higher the PO₂, the higher the SaO₂, and as PO₂ decreases, so does SaO₂, though not as rapidly. A PO₂ of 100 is an SaO₂ of about 97%, as is found in systemic arteries. A PO₂ of 40, as is found in systemic veins, is an SaO₂ of about 75%. Some carbon dioxide is dissolved in the plasma, and some is carried by hemoglobin (carbaminohemoglobin), but these account for only about 20% of total CO₂ transport. Most carbon dioxide is carried in the plasma in the form of bicarbonate ions (HCO₃⁻). Let us look at the reactions that transform CO₂ into a bicarbonate ion. When carbon dioxide enters the blood, most diffuses into red blood cells, which contain the enzyme carbonic anhydrase. This enzyme (which contains zinc) catalyzes the reaction of carbon dioxide and water to form carbonic acid:

\[ \text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{CO}_3 \]

The carbonic acid then dissociates:

\[ \text{H}_2\text{CO}_3 \rightarrow \text{H}^+ + \text{HCO}_3^- \].

The bicarbonate ions diffuse out of the red blood cells into the plasma, leaving the hydrogen ions (H⁺) in the red blood cells. The many H⁺ ions would tend to make the red blood cells too acidic, but hemoglobin acts as a buffer to prevent acidosis. To maintain an ionic equilibrium, chloride ions (Cl⁻) from the plasma enter the red blood cells; this is called the chloride shift. Where is the CO₂? It is in the plasma as part of HCO₃⁻ ions. When the blood reaches the lungs, an area of lower PCO₂, these reactions are reversed, and CO₂ is re-formed and diffuses into the alveoli to be exhaled.

**9.9 REGULATION OF RESPIRATION**

Two types of mechanisms regulate breathing: nervous mechanisms and chemical mechanisms. Because any changes in the rate or depth of breathing are ultimately brought about by nerve impulses, we will consider nervous mechanisms first.
Nervous regulation

The respiratory centers are located in the medulla and pons, which are parts of the brain stem. Within the medulla are the inspiration center and expiration center. The inspiration center automatically generates impulses in rhythmic spurts. These impulses travel along nerves to the respiratory muscles to stimulate their contraction. The result is inhalation. As the lungs inflate, baroreceptors in lung tissue detect this stretching and generate sensory impulses to the medulla; these impulses begin to depress the inspiration center. This is called the Hering-Breuer inflation reflex, which also helps prevent overinflation of the lungs. As the inspiration center is depressed, the result is a decrease in impulses to the respiratory muscles, which relax to bring about exhalation. Then the inspiration center becomes active again to begin another cycle of breathing. When there is a need for more forceful exhalations, such as during exercise, the inspiration center activates the expiration center, which generates impulses to the internal intercostal and abdominal muscles. The two respiratory centers in the pons work with the inspiration center to produce a normal rhythm of breathing. The apneustic center prolongs inhalation, and is then interrupted by impulses from the pneumotaxic center, which contributes to exhalation. In normal breathing, inhalation lasts 1 to 2 seconds, followed by a slightly longer (2 to 3 seconds) exhalation, producing the normal respiratory rate range of 12 to 20 breaths per minute. What has just been described is normal breathing, but variations are possible and quite common. Emotions often affect respiration; a sudden fright may bring about a gasp or a scream, and anger usually increases the respiratory rate. In these situations, impulses from the hypothalamus modify the output from the medulla. The cerebral cortex enables us to voluntarily change our breathing rate or rhythm to talk, sing, breathe faster or slower, or even to stop breathing for 1 or 2 minutes. Such changes cannot be continued indefinitely, however, and the medulla will eventually resume control.

Coughing and sneezing are reflexes that remove irritants from the respiratory passages; the medulla contains the centers for both of these reflexes. Sneezing is stimulated by an irritation of the nasal mucosa, and coughing is stimulated by irritation of the mucosa of the pharynx, larynx, or trachea. The reflex action is essentially the same for both: An inhalation is followed by exhalation beginning with the glottis closed to build up pressure. Then the glottis opens suddenly, and the exhalation is explosive. A cough directs the exhalation out the mouth, while a sneeze directs the exhalation out the nose. Hiccups, also a reflex, are spasms of the diaphragm. The result is a quick inhalation that is stopped when the glottis snaps shut, causing the “hic” sound. The stimulus may be irritation...
of the phrenic nerves or nerves of the stomach. Excessive alcohol is an irritant that can cause hiccups. Some causes are simply unknown. Yet another respiratory reflex is yawning. Most of us yawn when we are tired, but the stimulus for and purpose of yawning are not known with certainty. There are several possibilities, such as lack of oxygen or accumulation of carbon dioxide, but we really do not know. Nor do we know why yawning is contagious, but seeing someone yawn is almost sure to elicit a yawn of one’s own. You may even have yawned while reading this paragraph about yawning.

Chemical regulation

Chemical regulation refers to the effect on breathing of blood pH and blood levels of oxygen and carbondioxide. Chemoreceptors that detect changes in blood gases and pH are located in the carotid and aortic bodies and in the medulla itself. A decrease in the blood level of oxygen (hypoxia) is detected by the chemoreceptors in the carotid and aortic bodies. The sensory impulses generated by these receptors travel along the glossopharyngeal and vagus nerves to the medulla, which responds by increasing respiratory rate or depth (or both). This response will bring more air into the lungs so that more oxygen can diffuse into the blood to correct the hypoxic state. Carbon dioxide becomes a problem when it is present in excess in the blood, because excess CO₂ (hypercapnia) lowers the pH when it reacts with water to form carbonic acid (a source of H+ ions). That is, excess CO₂ makes the blood or other body fluids less alkaline (or more acidic). The medulla contains chemoreceptors that are very sensitive to changes in pH, especially decreases. If accumulating CO₂ lowers blood pH, the medulla responds by increasing respiration. This is not for the purpose of inhaling, but rather to exhale more CO₂ to raise the pH back to normal. Of the two respiratory gases, which is the more important as a regulator of respiration? Our guess might be oxygen, because it is essential for energy production in cell respiration. However, the respiratory system can maintain a normal blood level of oxygen even if breathing decreases to half the normal rate or stops for a few moments. Recall that exhaled air is 16% oxygen. This oxygen did not enter the blood but was available to do so if needed. Also, the residual air in the lungs supplies oxygen to the blood even if breathing rate slows. Therefore, carbon dioxide must be the major regulator of respiration, and the reason is that carbon dioxide affects the pH of the blood. As was just mentioned, an excess of CO₂ causes the blood pH to decrease, a process that must not be allowed to continue. Therefore, any increase in the blood CO₂ level is quickly compensated for by increased breathing to exhale more CO₂. If, for example, you
hold your breath, what is it that makes you breathe again? Have you run out of oxygen? Probably not, for the reasons mentioned. What has happened is that accumulating CO₂ has lowered blood pH enough to stimulate the medulla to start the breathing cycle again. In some situations, oxygen does become the major regulator of respiration. People with severe, chronic pulmonary diseases such as emphysema have decreased exchange of both oxygen and carbon dioxide in the lungs. The decrease in pH caused by accumulating CO₂ is corrected by the kidneys, but the blood oxygen level keeps decreasing. Eventually, the oxygen level may fall so low that it does provide a very strong stimulus to increase the rate and depth of respiration.

9.10 RESPIRATION AND ACID–BASE BALANCE

As you have just seen, respiration affects the pH of body fluids because it regulates the amount of carbon dioxide in these fluids. Remember that CO₂ reacts with water to form carbonic acid (H₂CO₃), which ionizes into H⁺ ions and HCO₃⁻ ions. The more hydrogen ions present in a body fluid, the lower the pH, and the fewer hydrogen ions present, the higher the pH. The respiratory system may be the cause of a pH imbalance, or it may help correct a pH imbalance created by some other cause.

Respiratory acidosis and alkalosis

Respiratory acidosis occurs when the rate or efficiency of respiration decreases, permitting carbon dioxide to accumulate in body fluids. The excess CO₂ results in the formation of more H⁺ ions, which decrease the pH. Holding one’s breath can bring about a mild respiratory acidosis, which will soon stimulate the medulla to initiate breathing again. More serious causes of respiratory acidosis are pulmonary diseases such as pneumonia and emphysema, or severe asthma. Each of these impairs gas exchange and allows excess CO₂ to remain in body fluids. Respiratory alkalosis occurs when the rate of respiration increases, and CO₂ is very
rapidly exhaled. Less CO₂ decreases H+ ion formation, which increases the pH. Breathing faster for a few minutes can bring about a mild state of respiratory alkalosis. Babies who cry for extended periods (crying is a noisy exhalation) put themselves in this condition. In general, however, respiratory alkalosis is not a common occurrence. Severe physical trauma and shock, or certain states of mental or emotional anxiety, may be accompanied by hyperventilation and also result in respiratory alkalosis. In addition, traveling to a higher altitude (less oxygen in the atmosphere) may cause a temporary increase in breathing rate before compensation occurs

**Respiratory compensation**

If a pH imbalance is caused by something other than a change in respiration, it is called metabolic acidosis or alkalosis. In either case, the change in pH stimulates a change in respiration that may help restore the pH of body fluids to normal. **Metabolic acidosis** may be caused by untreated diabetes mellitus (ketoacidosis), kidney disease, or severe diarrhea. In such situations, the H+ ion concentration of body fluids is increased. Respiratory compensation involves an increase in the rate and depth of respiration to exhale more CO₂ to decrease H+ ion formation, which will raise the pH toward the normal range. **Metabolic alkalosis** is not a common occurrence but may be caused by ingestion of excessive amounts of alkaline medications such as those used to relieve gastric disturbances. Another possible cause is vomiting of stomach contents only. In such situations, the H+ ion concentration of body fluids is decreased. Respiratory compensation involves a decrease in respiration to retain CO₂ in the body to increase H+ ion formation, which will lower the pH toward the normal range. Respiratory compensation for an ongoing metabolic pH imbalance cannot be complete, because there are limits to the amounts of CO₂ that may be exhaled or retained. At most, respiratory compensation is only about 75% effective.

**AGING AND THE RESPIRATORY SYSTEM**

Perhaps the most important way to help your respiratory system age gracefully is not to smoke. In the absence of chemical assault, respiratory function does diminish but usually remains adequate. The respiratory muscles, like all skeletal muscles, weaken with age. Lung tissue loses its elasticity and alveoli are lost as their walls deteriorate. All of this results in decreased ventilation and lung capacity, but the remaining capacity is usually sufficient for
ordinary activities. The cilia of the respiratory mucosa deteriorate with age, and the alveolar macrophages are not as efficient, which make elderly people more prone to pneumonia, a serious pulmonary infection. Chronic alveolar hypoxia from diseases such as emphysema or chronic bronchitis may lead to pulmonary hypertension, which in turn overworks the right ventricle of the heart. Systemic hypertension often weakens the left ventricle of the heart, leading to congestive heart failure and pulmonary edema, in which excess tissue fluid collects in the alveoli and decreases gas exchange. Though true at any age, the interdependence of the respiratory and circulatory systems is particularly apparent in elderly people.

- **Applications to the nursing care**

  1) **Asthma**

  Asthma is usually triggered by an infection or allergic reaction that affects the smooth muscle and glands of the bronchioles. Allergens include foods and inhaled substances such as dust and pollen. Wheezing and dyspnea (difficult breathing) characterize an asthma attack, which may range from mild to fatal. As part of the allergic response, the smooth muscle of the bronchioles constricts. Because there is no cartilage present in their walls, the bronchioles may close completely. The secretion of mucus increases, perhaps markedly, so the already constricted bronchioles may become clogged or completely obstructed with mucus. Chronic asthma is a predisposing factor for emphysema. When obstructed bronchioles prevent ventilation of alveoli, the walls of the alveoli begin to deteriorate and break down, leaving large cavities that do not provide much surface area for gas exchange. One possible way to prevent such serious lung damage is to prevent asthma attacks with a medication that blocks the release of IgE antibodies. An allergy is an immune overreaction, and blocking such a reaction would prevent the damaging effects of inflammation.

  2) **Hyaline membrane disease**

  Hyaline membrane disease is also called respiratory distress syndrome (RDS) of the newborn, and most often affects premature infants whose lungs have not yet produced sufficient quantities of pulmonary surfactant. The first few breaths of a newborn inflate most of the previously collapsed lungs, and the presence of surfactant permits the alveoli to remain
open. The following breaths become much easier, and normal breathing is established. Without surfactant, the surface tension of the tissue fluid lining the alveoli causes the air sacs to collapse after each breath rather than remain inflated. Each breath, therefore, is difficult, and the newborn must expend a great deal of energy just to breathe. Premature infants may require respiratory assistance until their lungs are mature enough to produce surfactant. Use of a synthetic surfactant has significantly helped some infants, and because they can breathe more normally, their dependence on respirators is minimized. Still undergoing evaluation are the effects of the long-term use of this surfactant in the most premature babies, who may require it for much longer periods of time.

3) **Pneumothorax**

**Pneumothorax** is the presence of air in the pleural space, which causes collapse of the lung on that side. Recall that the pleural space is only a potential space because the serous fluid keeps the pleural membranes adhering to one another, and the intrapleural pressure is always slightly below atmospheric pressure. Should air at atmospheric pressure enter the pleural cavity, the suddenly higher pressure outside the lung will contribute to its collapse (the other factor is the normal elasticity of the lungs). A spontaneous pneumothorax, without apparent trauma, may result from rupture of weakened alveoli on the lung surface. Pulmonary diseases such as emphysema may weaken alveoli. Puncture wounds of the chest wall also allow air into the pleural space, with resulting collapse of a lung. In severe cases, large amounts of air push the heart, great vessels, trachea, and esophagus toward the opposite side (mediastinal shift), putting pressure on the other lung and making breathing difficult. This is called tension pneumothorax, and requires rapid medical intervention to remove the trapped air.

4) **Emphysema**

**Emphysema**, a form of chronic obstructive pulmonary disease (COPD), is a degenerative disease in which the alveoli lose their elasticity and cannot recoil. Perhaps the most common (and avoidable) cause is cigarette smoking; other causes are longterm exposure to severe air pollution or industrial dusts, or chronic asthma. Inhaled irritants damage the alveolar walls and cause deterioration of the elastic connective tissue surrounding the alveoli. Macrophages migrate to the damaged areas and seem to produce an enzyme that contributes to the destruction of the protein elastin. This is an instance of a useful body response (for cleaning
up damaged tissue) becoming damaging when it is excessive. As the alveoli break down, larger air cavities are created that are not efficient in gas exchange. In progressive emphysema, damaged lung tissue is replaced by fibrous connective tissue (scar tissue), which further limits the diffusion of gases. Blood oxygen level decreases, and blood carbon dioxide level increases. Accumulating carbon dioxide decreases the pH of body fluids; this is a respiratory acidosis. One of the most characteristic signs of emphysema is that the affected person must make an effort to exhale. The loss of lung elasticity makes normal exhalation an active process, rather than the passive process it usually is. The person must expend energy to exhale in order to make room in the lungs for inhaled air. This extra “work” required for exhalation may be exhausting for the person and contribute to the debilitating nature of emphysema.

5) **Heimlich maneuver**

The **Heimlich maneuver** has received much well deserved publicity, and indeed it is a life-saving technique. If a person is choking on a foreign object (such as food) lodged in the pharynx or larynx, the air in the lungs may be utilized to remove the object. The person performing the maneuver stands behind the choking victim and puts both arms around the victim’s waist. One hand forms a fist that is placed between the victim’s navel and rib cage (below the diaphragm), and the other hand covers the fist. It is important to place hands correctly, in order to avoid breaking the victim’s ribs. With both hands, a quick, forceful upward thrust is made and repeated if necessary. This forces the diaphragm upward to compress the lungs and force air out. The forcefully expelled air is often sufficient to dislodge the foreign object.

6) **Pulmonary edema**

**Pulmonary edema** is the accumulation of fluid in the alveoli. This is often a consequence of congestive heart failure in which the left side of the heart (or the entire heart) is not pumping efficiently. If the left ventricle does not pump strongly, the chamber does not empty as it should and cannot receive all the blood flowing in from the left atrium. Blood flow, therefore, is “congested,” and blood backs up in the pulmonary veins and then in the pulmonary capillaries. As blood pressure increases in the pulmonary capillaries, filtration creates tissue fluid that collects in the alveoli. Fluid-filled alveoli are no longer sites of efficient gas
exchange, and the resulting hypoxia leads to the symptoms of dyspnea and increased respiratory rate. The most effective treatment is that which restores the pumping ability of the heart to normal.

7) Pneumonia

Pneumonia is a bacterial infection of the lungs. Although many bacteria can cause pneumonia, the most common one is probably Streptococcus pneumoniae. This species is estimated to cause at least 500,000 cases of pneumonia every year in the United States, with 50,000 deaths. *S. pneumoniae* is a transient inhabitant of the upper respiratory tract, but in otherwise healthy people, the ciliated epithelium and the immune system prevent infection. Most cases of pneumonia occur in elderly people following a primary infection such as influenza. When the bacteria are able to establish themselves in the alveoli, the alveolar cells secrete fluid that accumulates in the air sacs. Many neutrophils migrate to the site of infection and attempt to phagocytize the bacteria. The alveoli become filled with fluid, bacteria, and neutrophils (this is called consolidation); this decreases the exchange of gases. Pneumovax is a vaccine for this type of pneumonia. It contains only the capsules of *S. pneumoniae* and cannot cause the disease. The vaccine is recommended for people over the age of 60 years, and for those with chronic pulmonary disorders or any debilitating disease. It has also been approved for administration to infants.

8) Carbon monoxide

Carbon monoxide (CO) is a colorless, odorless gas that is produced during the combustion of fuels such as gasoline, coal, oil, and wood. As you know, CO is a poison that may cause death if inhaled in more than very small quantities or for more than a short period of time. The reason CO is so toxic is that it forms a very strong and stable bond with the hemoglobin in RBCs (carboxyhemoglobin). Hemoglobin with CO bonded to it cannot bond to and transport oxygen. The effect of CO, therefore, is to drastically decrease the amount of oxygen carried in the blood. As little as 0.1% CO in inhaled air can saturate half the total hemoglobin with CO. Lack of oxygen is often apparent in people with light skin as cyanosis, a bluish cast to the skin, lips, and nail beds. This is because hemoglobin is dark red unless something (usually oxygen) is bonded to it. When hemoglobin bonds to CO, however, it becomes a bright, cherry red. This color may be seen in light skin and may be very misleading; the
person with CO poisoning is in a severely hypoxic state. Although CO is found in cigarette smoke, it is present in such minute quantities that it is not lethal. Heavy smokers, however, may be in a mild but chronic hypoxic state because much of their hemoglobin is firmly bonded to CO. As a compensation, RBC production may increase, and a heavy smoker may have a hematocrit over 50%.

9) **Cystic Fibrosis**

Cystic fibrosis (CF) is a genetic disorder (there are many forms) of certain exocrine glands including the salivary glands, the sweat glands, the pancreas, and the mucous glands of the respiratory tract.

In the pancreas, thick mucus clogs the ducts and prevents pancreatic enzymes from reaching the small intestine, thus impairing digestion, especially of fats. But the most serious effects of CF are in the lungs. The genetic mistake in CF often involves a gene called CFTR, which codes for chloride ion channels (proteins) in the membranes of epithelial cells. In the lungs, the defective channels are destroyed (by proteasomes), which causes a change in the composition of the tissue fluid around the cells.

This change inactivates defensin, a natural antibiotic produced by lung tissue. In the absence of defensin, a bacterium called *Pseudomonas aeruginosa* stimulates the lung cells to produce copious thick mucus, an ideal growth environment for bacteria. Defensive white blood cells cannot get through the thick mucus, and their activity mistakenly destroys lung tissue. A person with CF has thickened bronchial tubes, frequent episodes of pneumonia, and, ultimately, lungs that cannot carry out gas exchange. CF is a chronic, progressive disease that is eventually fatal unless a lung transplant is performed. CF is one of several disorders believed to be correctable by gene therapy, but because it involves human subjects, this kind of work proceeds very slowly.