Chapter Overview

The homeostatic role of the respiratory system overlaps that of the circulatory system: supplying oxygen to the cells of the body and removing carbon dioxide, a byproduct of cellular metabolism. While these are not the only functions of the respiratory system they are surely the most important. The entire ventilation-transport process, from air outside the body to the gaseous exchange at the systemic cellular level, involves diffusion down gradients. For the most part, they are pressure gradients.

The mechanics of ventilation rely heavily upon the physical properties of the alveolar wall and surface tension. Ventilation is controlled by the nervous system at both conscious and subconscious levels.

The bonding of oxygen and carbon dioxide to hemoglobin is important for transport by the blood. Oxygen bonds to the heme portion and carbon dioxide attaches to the globin fraction of the hemoglobin molecule. This is, however, only one step in the process of respiration.

From alveolar air to the mitochondria of the various cells involves many barriers through which oxygen and carbon dioxide must traverse. Crossing the numerous barriers oxygen and carbon dioxide diffuse down pressure gradients involving differences in their respective partial pressures. Using quite sophisticated control mechanisms, the respiratory system plays major role in maintaining homeostasis.

Chapter Outline

INTRODUCTION

The respiratory system does not participate in all steps of respiration.
- Internal or cellular respiration refers to the intracellular metabolic processes carried out within the mitochondria, which use oxygen and produce carbon dioxide during the derivation of energy from nutrient molecules.
- External respiration refers to the entire sequence or events in the exchange of oxygen and carbon dioxide between the external environment and the cells of the body.
- External respiration, the topic of this chapter, encompasses four steps: (1) Air is alternately moved in and out of the lungs so that exchange of air can occur between the atmosphere and the alveoli of the lungs; (2) Oxygen and carbon dioxide are exchanged between air in the alveoli, and blood within the pulmonary capillaries by the process of diffusion; (3) Oxygen and carbon dioxide are transported by the blood between the lungs and the tissues; and (4) The exchange of oxygen and carbon dioxide takes place between the tissues and the blood by the process of diffusion across the systemic capillaries.
- The respiratory system additionally performs the following nonrespiratory functions: (1) It provides a route for water loss and heat elimination; (2) It enhances venous return; (3) It enables speech, singing, and other vocalization; (4) It defends against inhaled foreign matter; (5) It removes, modifies, activates, or inactivates various materials passing through the pulmonary circulation; (6) The nose serves as the organ of smell;
and (7) It contributes to the maintenance of normal acid-base balance.

**The respiratory airways conduct air between the atmosphere and alveoli.**

- The respiratory system includes the respiratory airways leading into the lungs, the lungs themselves, and the structures of the thorax involved in producing movement of air through the airways into and out of the lungs.
- The airways include: (1) nasal passages, (2) pharynx, (3) larynx, (4) trachea, (5) bronchi, and (6) bronchioles.
- The term vocal chords has been replaced by the more descriptive term vocal folds.

**The gas-exchanging alveoli are small, thin-walled, inflatable air sacs encircled by a jacket of pulmonary capillaries.**

- The alveoli are clusters of thin walled, inflatable, grape like sacs at the terminal branches of the conducting airways.
- The alveolar walls consist of a single layer of flattened Type I alveolar cells.
- The interstitial space between an alveolus and the surrounding capillary network forms an extremely thin barrier.
- In addition to the Type I cells, the alveolar epithelium also contains Type II alveolar cells which secrete pulmonary surfactant.
- The minute pores of Kohn in the alveolar walls permit airflow between adjacent alveoli, a process known as collateral ventilation.

**The lungs occupy much of the thoracic cavity.**

- There is no muscle within the alveolar walls to cause them to innate or deflate during the breathing process.
- The lungs, heart and associated vessels, esophagus, thymus, and some nerves occupy the thoracic cavity.
- The outer chest wall is formed by twelve pairs of curved ribs, which join the sternum anteriorly and the thoracic vertebrae posteriorly.
- The diaphragm forms the floor of the thoracic cavity.

**A plural sac separates each lung from the thoracic wall.**

- Separating each lung from the thoracic wall and other surrounding structures is a doubled-walled, closed sac called the pleural sac.
- The surfaces of the pleura secrete a thin intrapleural fluid, which lubricates the pleural surfaces.

**Respiratory Mechanics**

**Interrelationships among atmospheric, intra-alveolar, and intrapleural pressures are important in respiratory mechanics.**

- Air tends to move from a region of higher pressure to a region of lower pressure down a pressure gradient.
- Three different pressure considerations are important in ventilation: (1) atmospheric pressure, (2) intra-alveolar pressure, and (3) intrapleural pressure.

**The intrapleural fluid's cohesiveness and the transmural pressure gradient hold the lungs and thoracic wall in tight apposition, even though the lungs are smaller than the thorax.**

- The polar water molecules in the intrapleural fluid resist being pulled apart because of their attraction to each other.
- The resultant cohesiveness of the intrapleural fluid tends to hold pleural surfaces together.
- An even more important reason that the lungs follow the movements of the chest wall is the transmural pressure gradient that exists across the lung wall.
- The intra-alveolar pressure is greater than the intrapleural pressure, so a greater pressure is pushing outward than is pushing inward across the lung wall.
- A similar transmural pressure gradient exists across the thoracic wall.
- The atmosphere pressure pushing inward on the thoracic wall is greater than the intrapleural pressure pushing outward on the same wall.
- The stretched lungs have a tendency to pull inward away from the thoracic wall, whereas the compressed thoracic wall tends to move away from the lungs.
- If the intrapleural pressure were ever to equilibrate with the atmospheric pressure, the
lungs and thorax would separate and assume their own inherent dimensions.

**Bulk flow of air into and out of the lungs occurs because of cyclical intra-alveolar pressure changes brought about indirectly by respiratory muscle activity.**

- Because air flows down a pressure gradient, the intra-alveolar pressure must be less than atmospheric pressure for air to flow into the lungs during inspiration.
- At the onset of inspiration, the inspiratory muscles—the diaphragm and external intercostal muscles—are stimulated to contract, resulting in enlargement of the thoracic cavity.
- The intra-alveolar pressure is now less than atmospheric pressure, air flows into the lungs down the pressure gradient from higher to lower pressure.
- During inspiration, the intrapleural pressure falls.
- The resultant increase in the transmural pressure gradient during inspiration ensures that the lungs are stretched to fill the expanded thoracic cavity.
- At the end of inspiration, the inspiratory muscles relax.
- The chest wall and the stretched lungs recoil to their preinspiratory size because of their elastic properties.
- In a resting expiration, the intra-alveolar pressure increases.
- Air now leaves the lungs down a pressure gradient from high intra-alveolar pressure to lower atmospheric pressure.
-Expiration is normally a passive process.
- Inspiration is always an active process.
- To produce active expiration, the expiratory muscles must contract to further reduce the volume of the thoracic cavity and lungs.

**Airway resistance becomes an especially important determinant of airflow rates when the airways are narrowed by disease processes.**

- The primary determinant to resistance to airflow is the radius of the conducting airway.
- Normally, modest adjustments in airway size can be accomplished by autonomic nervous system regulation to suit the body's needs.
- Parasympathetic stimulation promotes bronchiolar smooth muscle contraction, which increases airway resistance by producing bronchoconstriction.
- Sympathetic stimulation and its associated hormone, epinephrine, bring about bronchodilation and decreased airway resistance by promoting bronchiolar smooth muscle relaxation.
- Resistance becomes an extremely important impediment to airflow when airway lumens become narrowed as a result of disease.
- Chronic obstructive pulmonary disease is a group of lung diseases characterized by increased airway resistance resulting from the narrowing of the lumen of the lower airways.
- Chronic obstructive pulmonary disease encompasses three chronic diseases: asthma, chronic bronchitis, and emphysema.
- In asthma, airway obstruction is due to (1) profound constriction of the smaller airways caused by allergy-induced spasm of the smooth muscle in the walls of these airways; (2) plugging of airways by excess secretion of very thick mucus; and (3) thickening of the walls of the airways due to inflammation and histamine-induced edema.
- Chronic bronchitis is a long-term inflammatory of the lower respiratory airways, generally triggered by irritating cigarette smoke, polluted air, or allergens.
- Emphysema is characterized by collapse of the smaller airways and a breakdown of alveolar walls.
- When airway resistance is increased as a result of chronic obstructive lung disease of any type, expiration is more difficult to accomplish than inspiration.

**Local controls act on smooth muscle of the airways and arterioles to maximally match blood flow to airflow.**

- If an alveolus is receiving too little airflow in comparison to its blood flow, carbon dioxide levels will increase in the alveolus.
- This local increase in carbon dioxide acts directly on the bronchiolar smooth muscle involved to induce the airway supplying the underaerated alveolus to relax.
• The result is an increased airflow to the involved alveolus, so its airflow now matches its blood supply.
• A localized decrease in carbon dioxide associated with an alveolus that is receiving too much air for its blood supply directly increases contractile activities.
• The result is a reduction in airflow to the overaerated alveolus.
• If the blood flow is greater than the airflow in a given alveolus, the oxygen level in the alveolus and surrounding tissue will fall below normal.
• The local decrease in oxygen concentration causes vasoconstriction of the pulmonary arteriole.
• The result is a reduction in blood flow to match the smaller airflow.
• An increase in alveolar oxygen concentration caused by a mismatched large airflow and small blood flow brings about pulmonary vasodilation, which increases blood flow to match the larger airflow.

Elastic behavior of the lungs is due to elastic connective tissue fibers and alveolar surface tension.
• Two interrelated concepts are involved in pulmonary elasticity: elastic recoil and compliance.
• Elastic recoil refers to how readily the lungs rebound after having been stretched.
• Compliance refers to how much effort is required to stretch or distort the lungs.
• A highly compliant lung stretches further for a given increase in the pressure difference than does a less compliant lung.
• Pulmonary elastic behavior depends mainly on two factors: highly elastic connective tissue in the lungs and alveolar surface tension.
• Pulmonary connective tissue contains large quantities of elastin fibers arranged into a meshwork that amplifies their elastic behavior.
• Surface tension is responsible for a twofold effect.
• First, the liquid layer resists any force that increases its surface area.
• Second, the liquid surface area tends to become as small as possible because the surface water molecules try to get as close together as possible.

Pulmonary surfactant decreases surface tension and contributes to lung stability.
• The tremendous surface tension of pure water is normally counteracted by secretion of pulmonary surfactant by the Type II alveolar cells.
• By lowering the alveolar surface tension, pulmonary surfactant provides two important benefits: (1) it increases pulmonary compliance, thus reducing the work of inflating the lungs; and (2) it reduces the lungs’ tendency to recoil, so that they do not collapse readily.
• Pulmonary surfactant’s role in reducing the alveoli’s tendency to recoil is important in helping maintain lung stability.
• A second factor that contributes to alveolar stability is the interdependence of neighboring alveoli.
• If an alveoli starts to collapse, the surrounding alveoli are stretched.
• By recoiling in resistance to being stretched, these neighboring alveoli exert expanding forces on the collapsing alveolus and thereby help keep it open.
• This phenomenon is termed interdependence.

A deficiency of pulmonary surfactant is responsible for newborn respiratory distress syndrome.
• In an infant born prematurely, pulmonary surfactant may be insufficient to reduce the alveolar surface tension to manageable levels.
• The resultant collection of symptoms that develop are referred to as newborn respiratory distress syndrome.
• It is more difficult to expand a collapsed alveolus by a given volume than to increase an already partially expanded alveolus by the same volume.
• With newborn respiratory distress syndrome, lung expansion may require considerably larger transmural pressure gradients.
• The problem is compounded by the fact that the newborn's muscles are still weak.
The work of breathing normally requires only about three percent of total energy expenditure.

- Normally, the lungs are highly compliant and the airway resistance is low, so only about three percent of the total energy expended by the body is used to accomplish quiet breathing.
- The work of breathing may be increased in four different situations: (1) when pulmonary compliance is decreased; (2) when airway resistance is increased; (3) when elastic recoil is decreased; and (4) when there is a need for increased ventilation.
- Because total energy expenditure by the body is increased up to fifteen- to twenty-fold during heavy exercise, the energy used to accomplish the increased ventilation still represents only about five percent of total energy expended.

Normally, the lungs contain about 2 to 2.5 liters of air during the respiratory cycle but can be filled to over 5.5 liters or emptied to about 1 liter.

- On average, the maximum amount of air that the lungs can hold is about 5.7 liters in males and 4.2 liters in females.
- Anatomical build, age, the distensibility of the lungs, and the presence or absence of respiratory disease affect this total lung capacity.
- At the end of a normal quiet expiration, the lungs still contain about 2,200 ml of air.
- About 500 ml of air are inspired and the same quantity expired during quiet breathing.
- Using a spirometer, the following lung volumes and lung capacities can be determined: (1) tidal volume, (2) inspiratory reserve volume, (3) inspiratory capacity, (4) expiratory reserve volume, (5) residual volume, (6) functional residual capacity, (7) vital capacity, (8) total lung capacity, and (9) forced expiratory volume in one second.
- Two general categories of respiratory dysfunction yield abnormal results during spirometry: obstructive and restrictive lung disease.
- To determine what abnormalities are present, the diagnostican relies on a variety or respiratory function tests in addition to spirometry, including X-ray examination, blood gas determinations, and tests to measure the diffusion capacity of the alveolar capillary membrane.

Alveolar ventilation is less than pulmonary ventilation because of the presence of dead space.

- Not all of the inspired air gets down to the site of gas exchange in the alveoli.
- Part of the air remains in the conducting airways, where it is not available for gas exchange.
- This volume is considered to be anatomic dead space.
- Alveolar ventilation—the volume of air exchanged between the atmosphere and the alveoli per minute—is more important than pulmonary ventilation.

GAS EXCHANGE
Gases move down partial pressure gradients.

- The ultimate purpose or breathing is to provide a continual supply of fresh oxygen for pickup by the blood and to constantly remove carbon dioxide unloaded from the blood.
- Gas exchange at both the pulmonary-capillary and tissue-capillary level involves simple passive diffusion of oxygen and carbon dioxide down partial pressure gradients.
- If, as in the case with oxygen, the alveolar partial pressure of a gas is higher than the partial pressure of that gas in the blood entering the pulmonary capillaries, the higher alveolar partial pressure drives more oxygen into the blood.
- Conversely, if the alveolar partial pressure of a gas is lower than its partial pressure in the entering blood—the situation that exists for carbon dioxide—the lower alveolar partial pressure permits some of the carbon dioxide to escape from solution in the blood.
- A gas always diffuses down its partial pressure gradient from the area of higher partial pressure to the area of lower partial pressure.
Oxygen enters and carbon dioxide leaves the blood in the lungs passively down partial pressure gradients.

- The alveolar partial pressure of oxygen remains relatively constant throughout the respiratory cycle.
- The partial pressure of oxygen in the blood likewise remains fairly constant at the same value.
- A similar situation in reverse exists for carbon dioxide.
- The appropriate partial pressure gradients between the alveoli and blood are maintained to ensure that oxygen enters the blood and carbon dioxide leaves the blood.
- The amount of oxygen picked up in the lungs matches the amount extracted and used by the tissues.
- The amount of carbon dioxide given up to the alveoli from the blood matches the amount of carbon dioxide picked up at the tissues.

Factors other than the partial pressure gradient influence the rate of gas transfer.

- According to Fick's law of diffusion, the rate of diffusion of a gas depends on the surface area and thickness of the membrane and on the diffusion coefficient of the gas.
- During exercise, the surface area available for exchange can be physiologically increased to enhance the rate of gas transfer.
- Many of the previously closed pulmonary capillaries are forced open.
- The alveolar membranes are stretched further than normal during exercise because of deeper breathing.
- Such stretching increases the alveolar surface area and decreases the thickness of the alveolar membrane.
- Collectively, these changes expedite gas exchange during exercise.
- Surface area is reduced in emphysema.
- Inadequate gas exchange can also occur when the thickness of the barrier separating the air and blood is pathologically increased.
- The thickness increases in (1) pulmonary edema, (2) pulmonary fibrosis, and (3) pneumonia.
- The rate of gas transfer is directly proportional to the diffusion coefficient.

- The diffusion coefficient for carbon dioxide is twenty times that of oxygen because carbon dioxide is much more soluble in body tissues than oxygen is.
- In a diseased lung in which diffusion is impeded because the surface area is decreased or the blood-air barrier is thickened, oxygen transfer is usually more impaired than carbon dioxide because of the larger carbon dioxide diffusion coefficient.

Gas exchange across the systemic capillaries also occurs down partial pressure gradient.

- Just as they do at the pulmonary capillaries, oxygen and carbon dioxide move between the systemic capillary blood and the tissue cells by simple passive diffusion down partial pressure gradients.
- The amount of oxygen transferred to the cells and the amount of carbon dioxide carried away from the cells depend on the rate of cellular metabolism.

GAS TRANSPORT

Most oxygen in the blood is transported bound to hemoglobin.

- Oxygen is present in the blood in two forms: physically dissolved and chemically bound to hemoglobin.
- Very little oxygen is physically dissolved in the plasma water because oxygen is poorly soluble in body fluids.
- Of the oxygen transported by the blood, 98.5 percent is transported in combination with hemoglobin.
- Hemoglobin, an iron-bearing protein molecule contained within the red blood cells, has the ability to form a loose easily reversible combination with oxygen.

The partial pressure of oxygen is the primary factor determining the percent hemoglobin saturation.

- Each hemoglobin molecule can carry up to four molecules of oxygen.
- The most important factor determining the percent of hemoglobin saturation is the partial pressure of oxygen of the blood, which in turn, is related to the concentration of oxygen physically dissolved in the blood.
• When the partial pressure or oxygen in the blood is increased, as it is in the pulmonary capillaries, the reaction is driven toward an increase in the formation of oxyhemoglobin.
• When the partial pressure of oxygen is decreased, as it is in the systemic capillaries, the reaction is driven toward an increase in the formation of reduced hemoglobin.

By acting as a storage depot, hemoglobin promotes the net transfer of oxygen from the alveoli to the blood.
• Net diffusion of oxygen from alveoli to blood occurs continuously until the hemoglobin becomes saturated with oxygen as completely as it can be at that particular partial pressure.
• At a normal partial pressure for oxygen, hemoglobin is 97.5 percent saturated.
• Not until hemoglobin can store no more oxygen does all of the oxygen transferred into the blood remain dissolved and directly contribute to the partial pressure.
• Once the partial pressure of oxygen in the blood equilibrates with the alveolar partial pressure, no further oxygen transfer can take place.
• The reverse situation occurs at the tissue level.
• When the partial pressure of oxygen in the blood falls, hemoglobin is forced to unload some of its stored oxygen because the percent of hemoglobin saturation is reduced.
• Only when hemoglobin is no longer able to release any more oxygen into solution can the partial pressure of oxygen in the blood become as low as in the surrounding tissue.
• At this time, further transfer of oxygen ceases.
• Hemoglobin plays an important role in the total quantity of oxygen that the blood can pick up in the lungs and drop off in the tissues.

Increased carbon dioxide, acidity, temperature, and 2,3-bisphosphoglycerate shift the oxygen-hemoglobin dissociation curve to the right.
• An increase in the partial pressure of carbon dioxide reduces the amount of oxygen and hemoglobin that can be combined.
• An increase in acidity also reduces the amount of oxygen and hemoglobin that can be combined.
• The influence of carbon dioxide and acid on the release of oxygen is known as the Bohr effect.
• Local elevation in temperature enhances oxygen release from hemoglobin for use by the more active tissues.
• Thus, increases in carbon dioxide, acidity, and temperature at the tissue level enhances the effect of a drop in the partial pressure of oxygen in facilitating the release of oxygen and hemoglobin.
• These effects are largely reversed at the pulmonary level, where the extra acid-forming carbon dioxide is blown off and the local environment is cooler.
• Inside the red blood cell, 2,3-diphosphoglycerate is produced during cellular metabolism.
• This erythrocyte constituent can bind reversibly with hemoglobin and reduce its affinity for oxygen.

Oxygen-binding sites on hemoglobin have a much higher affinity for carbon monoxide than for oxygen.
• Carbon monoxide and oxygen compete for the same binding sites on hemoglobin, but the affinity of hemoglobin for carbon monoxide is two hundred forty times that of the bond strength between hemoglobin and oxygen.
• Fortunately, carbon monoxide is not a normal constituent of inspired air.
• If carbon monoxide is being produced in a closed environment, it can reach lethal levels without the victim ever being aware of the danger.

The majority of carbon dioxide is transported in the blood as bicarbonate.
• Carbon dioxide is transported in the blood in three ways: (1) physically dissolved, (2) bound to hemoglobin, and (3) as bicarbonate.
• The amount of carbon dioxide physically dissolved in the blood is only ten percent of the blood's total carbon dioxide content at normal systemic venous partial pressure levels.
Another thirty percent of the carbon dioxide combines with hemoglobin to form carbamino hemoglobin.

Carbon dioxide binds with the globin portion of hemoglobin.

By far the most important means of carbon dioxide transport is as bicarbonate.

Carbon dioxide combines with water to form carbonic acid.

This reaction proceeds swiftly within red blood cells because of the presence of the erythrocyte enzyme carbonic anhydrase which catalyzes the reaction.

The one carbon and two oxygen atoms of the original carbon dioxide molecule are thus present in the blood as an integral part of the bicarbonate ion.

Bicarbonate and hydrogen start to accumulate within the red blood cells in the systemic capillaries.

Bicarbonate diffuses down its concentration gradient out of erythrocytes into the plasma.

Chloride ions the dominant plasma anions, diffuse into the red blood cells down the electrical gradient to restore neutrality.

This inward shift of chloride ions in exchange for the outflux of carbon dioxide-generated bicarbonate ions is known as the chloride shift.

Reduced hemoglobin has a greater affinity for hydrogen ions than does oxyhemoglobin.

The fact that removal of oxygen from hemoglobin increases the ability of hemoglobin to pick up carbon dioxide and carbon dioxide-generated hydrogen is known as the Haldane effect.

The Haldane effect and Bohr effect work in synchrony to facilitate oxygen liberation and the uptake of carbon dioxide and carbon dioxide-generated hydrogen ions.

**Various respiratory states are characterized by abnormal blood gas levels.**

- Hypoxia refers to insufficient oxygen at the cellular level.
- There are four general categories of hypoxia: (1) hypoxic hypoxia, (2) anemic hypoxia, (3) circulatory hypoxia, and (4) histotoxic hypoxia.
- Hypercapnia refers to excess carbon dioxide in the arterial blood.

- Hypercapnia is caused by hypoventilation.

**CONTROL OF RESPIRATION**

*Respiratory centers in the brain stem establish a rhythmic breathing cycle.*

- Respiratory control centers housed in the brain stem are responsible for generating the rhythmic pattern of breathing.
- The primary respiratory control center is the medullary respiratory center.
- There are two other respiratory centers higher in the brain stem in the pons—the apneustic center and the pneumotaxic center.
- The medullary respiratory center consists of two neuronal clusters known as the dorsal respiratory group and the ventral respiratory group.
- The dorsal respiratory group consists mostly of inspiratory neurons whose descending fibers terminate on the motor neurons that supply the inspiratory muscles.
- This ventral respiratory group is composed of inspiratory neurons and expiratory neurons.
- The ventral respiratory group is called into play by the dorsal respiratory group as an "overdrive" mechanism during periods when demands for ventilation are increased.
- The generation of respiratory rhythm is now widely believed to lie in the rostral ventromedial medulla, a region located near the upper end of the ventral respiratory group.
- The pontine centers exert "fine-tuning" influences over the medullary center to help produce normal, smooth inspirations and expirations.
- The pneumotaxic center sends impulses to the dorsal respiratory group that help "switch off" the inspiratory neurons, thereby limiting the duration of inspiration.
- The apneustic center prevents the inspiratory neurons from being switched off.
- The pneumotaxic center is dominant over the apneustic center.
- When the tidal volume is large, as during exercise, the Hering-Breuer reflex is triggered to prevent overinflation of the lungs.
- Action potentials from the pulmonary stretch receptors travel through afferent nerve fibers
to the medullary center and inhibit the inspiratory neurons.

*Carbon dioxide-generated hydrogen-ion concentration in the brain extracellular fluid is normally the primary regulator of the magnitude of ventilation.*

- The medullary respiratory center receives inputs that provide information about the body's needs for gas exchange.
- The arterial partial pressure of oxygen is monitored by peripheral chemoreceptors known as the carotid bodies and aortic bodies, which are located at the bifurcation of the common carotid arteries and in the arch of the aorta, respectively.
- The peripheral chemoreceptors are not sensitive to modest reductions in the arterial partial pressure of oxygen.
- Reflex stimulation of respiration by the peripheral chemoreceptors serves as an important emergency mechanism in dangerously low arterial partial pressures of oxygen conditions.
- The arterial partial pressure of carbon dioxide is the most important input regulating the magnitude of ventilation under resting conditions.
- An increase in the arterial partial pressure of carbon dioxide reflexly stimulates the respiratory center, with the resultant increase in ventilation promoting elimination of excess carbon dioxide.
- Conversely, a fall in arterial partial pressure of carbon dioxide reflexly reduces respiratory drive.
- There are no important receptors that monitor the arterial partial pressure of carbon dioxide.
- Located in the medulla in the vicinity of the respiratory center, central chemoreceptors are sensitive to changes in carbon dioxide-induced hydrogen ion concentration in the brain extracellular fluid.
- Increased partial pressure of carbon dioxide within the brain extracellular fluid causes a corresponding increase in the concentration of hydrogen ions.
- An elevation in the hydrogen ion concentration in the brain extracellular fluid directly stimulates the central chemoreceptors, which in turn increase ventilation by stimulating the respiratory center.
- A decline in arterial partial pressure of carbon dioxide below normal is paralleled by a fall in partial pressure of carbon dioxide and hydrogen ions in the brain extracellular fluid, the result of which is a central chemoreceptor-mediated decrease in ventilation.
- The powerful influence of the central chemoreceptors on the respiratory center is responsible for your inability to deliberately hold your breath for more than about a minute.
- Carbon dioxide induced changes in the hydrogen ion concentration in the arterial blood are detected by the peripheral chemoreceptors.
- The result is reflex stimulation of ventilation in response to an increase in arterial hydrogen ions and depression of ventilation is association with a decrease in arterial hydrogen ion concentration.

*Exercise profoundly increases ventilation, but the mechanisms involved are unclear.*

- The cause of increased ventilation during exercise is still largely speculative.
- Researchers have suggested that a number of other factors, including the following, play a role in the ventilatory response to exercise: (1) reflexes originating from body movements, (2) increase in body temperature, (3) epinephrine release, and (4) impulses from the cerebral cortex.

*Ventilation can be influenced by factors unrelated to the need to supply oxygen or remove carbon dioxide.*

- Protective reflexes such as sneezing and coughing temporarily govern respiratory activity in an effort to expel irritant materials from the respiratory passages.
- Inhalation of particularly noxious agents frequently triggers immediate cessation of ventilation.
- Voluntary control of breathing is accomplished by the cerebral cortex, which does not act on the respiratory center in the brain stem but instead sends impulses
directly to the motor neurons in the spinal cord that supply the respiratory muscles.

*During apnea, a person subconsciously "forgets to breathe," whereas during dyspnea, a person consciously feels that ventilation is inadequate.*

- Apnea is the transient cessation of ventilation with the expectation that breathing will resume spontaneously.
- The condition is called respiratory arrest.
- In exaggerated cases of sleep apnea, the victim may be unable to recover from an apneic period, and death results.
- This is the case of sudden infant death syndrome.

*Most evidence suggests that the baby "forgets to breathe" as a result of the immaturity of the respiratory control mechanisms.*

- Certain risk factors make babies more vulnerable to sudden infant death syndrome (SIDS).
- Among them are sleeping position (a higher incidence of SIDS is associated with sleeping on the abdomen rather than on the back or side) and exposure to nicotine during fetal life or after birth.
- People who have dyspnea have the subjective sensation that they are not getting enough air.

**Key Terms**

- Alveolar surface tension
- Alveoli
- Alveolar ventilation
- Anatomical dead space
- Aortic bodies
- Apneusis
- Apneustic center
- Apnea
- Asthma
- Atelectasis
- 2,3-bisphosphoglycerate
- Bohr effect
- Boyle's law
- Breathing (ventilation)
- Bronchi
- Bronchioles
- Bronchoconstriction
- Bronchodilation
- Carbamino hemoglobin
- Carboxyhemoglobin (HbCO₂)
- Carotid bodies
- Central chemoreceptors
- Chloride (Cl⁻) shift
- Chronic bronchitis
- Chronic obstructive pulmonary disease
- Collateral ventilation
- Compliance
- Dorsal respiratory group
- Dyspnea
- Elastic recoil
- Emphysema
- Expiratory reserve volume

- External respiration
- Forced expiratory volume in one second (FEV₁)
- Functional residual capacity
- Haldane effect
- Hering-Breuer reflex
- Hypercapnia
- Hyperoxia
- Hyperpnea
- Hyperventilation
- Hypocapnia
- Hypoxia
- Intrapleural fluid
- Intrapleural pressure
- Intrapulmonary pressure (intra-alveolar pressure)
- Inspiration
- Inspiratory capacity
- Inspiratory reserve volume
- Internal (cellular) respiration
- LaPlace's law
- Larynx
- Newborn respiratory distress syndrome
- Oxygen-hemoglobin dissociation curve
- Oxyhemoglobin
- Partial pressure
- Partial pressure gradient
- Percent (%Hb) hemoglobin saturation
- Pleural sac
- Pleurisy
- Pneumotaxic center
- Pneumothorax
- Pressure gradient
The Respiratory System 221

Pores of Kohn
Pulmonary stretch receptors
Pulmonary surfactant
Pulmonary ventilation
Reduced hemoglobin
Residual volume
Respiratory airways
Respiratory quotient (R.Q.)
Spirometer

Sudden infant death syndrome (SIDS)
Total lung capacity
Tidal volume
Trachea (windpipe)
Transmural pressure gradient
Type I alveolar cells
Type II alveolar cells
Ventral respiratory group
Vital capacity

Review Exercises
Answers are in the appendix

True/False

____ 1. Pulmonary connective tissue contains large quantities of elastin fibers.

____ 2. The work of breathing may be increased when pulmonary compliance is increased.

____ 3. The energy used to accomplish the increased ventilation still represents only about three percent of total energy expended.

____ 4. The maximum amount of air that the lungs can hold is about 4.2 liters in males.

____ 5. The lungs still contain about 2,200 ml of air, at the end of a normal quiet expiration.

____ 6. Alveolar ventilation is more important than pulmonary ventilation.

____ 7. A gas always diffuses down its partial pressure gradient from the area of higher to the area of lower partial pressure.

____ 8. The alveolar parial pressure of oxygen remains relatively constant at about 150 mm Hg throughout the respiratory cycle.

____ 9. Surface area is reduced in emphysema.

____ 10. The rate of gas transfer is directly proportional to the diffusion coefficient.

____ 11. The amount of oxygen transferred to the cells and the amount of carbon dioxide carried away from the cells depend on the rate of cellular metabolism.

____ 12. The net diffusion of oxygen occurs first between the blood and the tissues.

____ 13. Respiratory control centers housed in the brain stem are responsible for generating the rhythmic pattern of breathing.

____ 14. VRG is generally regarded as being responsible for the basic rhythm of ventilation.

____ 15. The pneumotaxic center is dominant over the apneustic center.
16. Arterial partial pressure of carbon dioxide is the most important input regulating the magnitude of ventilation under resting conditions.

17. A fall in arterial partial pressure of carbon dioxide reflexly reduces the respiratory drive.

18. A decrease in hydrogen ion concentrations in the brain ECF directly stimulates the central chemoreceptors.

19. The cause of increased ventilation during exercise is still largely speculative.

20. In sudden infant death syndrome (SIDS) babies two to five months are victims of poorly developed carotid bodies.

21. Only 2.5 percent of the carbon dioxide in the blood is dissolved.

22. Each hemoglobin molecule can carry up to four molecules of oxygen.

23. In the systemic capillaries the blood partial pressure of carbon dioxide is increased.

24. At a normal partial pressure of oxygen of 100 mm Hg, hemoglobin is 98.5 percent saturated.

25. Local elevation in temperature enhances oxygen release from hemoglobin for use by the more active tissues.

26. Carbon dioxide binds with the globin portion of hemoglobin.

27. Histotoxic hypoxia arises when too little oxygenated blood is delivered to the tissues.

28. There are no muscles within the alveolar walls.

29. Air tends to move from a region of lower pressure to a region of higher pressure.

30. The intrapleural pressure is greater than the intra-alveolar pressure.

31. The stretched lungs have a tendency to pull inward.

32. During inspiration, the intrapleural pressure increases.

33. At resting expiration, the intra-alveolar pressure decreases.

34. Expiration is normally a passive process.

35. If the blood flow is greater than the airflow to a given alveolus, the oxygen level in the alveolus and surrounding tissues will fall below normal.

Fill in the Blank

36. ________________ oxygen delivery to the tissues is normal, but the cells are unable to use the oxygen available to them.
37. __________ refers to excess carbon dioxide in the arterial blood that is caused by hypoventilation.

38. The relationship between partial pressure of oxygen and percent hemoglobin saturation is depicted by an S-shaped curve known as the ________________.

39. The influence of carbon dioxide and acid on the release of oxygen is known as the ________________.

40. The combination of carbon monoxide and hemoglobin is known as ________________.

41. The fact that removal of oxygen from hemoglobin increases the ability of hemoglobin to pick up CO2 and CO2-generated H+ is known as the ________________.

42. ________________ is characterized by a low arterial blood partial pressure of oxygen accompanied by inadequate hemoglobin saturation.

43. ________________ is characterized by inflammatory fluid accumulation within or around the alveoli.

44. The individual pressure exerted independently by a particular gas within a mixture of gases is known as its ________________.

45. A difference in partial pressure between pulmonary blood and alveolar air is known as ________________.

46. Across systemic capillaries: oxygen partial pressure gradient from blood to tissue cell is ____________ and carbon dioxide partial pressure gradient from tissue cell to blood is ____________.

47. ____________ is the volume of air in the lungs at the end of a normal passive expiration.

48. Two general categories of respiratory dysfunction yield abnormal results during spirometry; ________________ and ________________ lung disease.

49. Not all of the inspired air gets down to the site of gas exchange in the alveoli. Part of it remains in the conducting airways, where it is not available for gas exchange. The volume is considered to be ________________.
50. ___________ is the pressure exerted by the weight of the air in the atmosphere on objects on the earth's surface.

51. ___________ refers to decreased airway resistance by promoting bronchiolar smooth muscle relaxation.

52. ___________ is characterized by collapse of the smaller airways and a breakdown of alveolar walls.

53. ___________ refers to how much effort is required to stretch or distend the lungs.

54. A second factor that contributes to alveolar stability is the ___________ of neighboring alveoli.

55. ___________ refers to the magnitude of the inward-directed collapsing pressure directly proportional to the surface tension and inversely proportional to the radius of the bubble.

56. ___________ is the volume of air entering or leaving the lung during a single breath.

57. The primary respiratory control center is the ___________.

58. There are two other respiratory centers higher in the brain stem in the pons:

(1) ___________ and (2) ___________.

59. The ___________ consists mostly of inspiratory neurons.

60. ___________ is when the breathing pattern consists of prolonged inspiratory gasps abruptly interrupted by very brief expirations.

61. Arterial partial pressure of oxygen is monitored by peripheral chemoreceptors known as the ___________ and ___________.

62. ___________ is the transient cessation of ventilation with the expectation that breathing will resume spontaneously.

63. People who have ___________ have the subjective sensation that they are not getting enough air.

64. ___________ involves the sum of the processes that accomplish ongoing passive movement of oxygen from the atmosphere to the tissues to support cellular metabolism.
65. Two tubes lead from the pharynx: the ______________ through which air is conducted to the lungs, and the ______________, the tube through which food passes to the stomach.

66. ______________ are two bands of elastic tissue that lie across the opening of the larynx, which can be stretched and positioned in different shapes by laryngeal muscles.

67. The alveolar walls consist of a single layer of flattened ______________.

68. ______________ secrete pulmonary surfactant.

69. ______________ are present in the alveolar walls to permit airflow between adjacent alveoli.

**Matching**

*Match the description of the lung volume or lung capacity to the name of lung volume or capacity.*

a. total lung capacity  
b. tidal volume  
c. vital capacity  
d. functional residual capacity  
e. inspiratory reserve volume  
f. residual volume  
g. inspiratory capacity  
h. expiratory reserve volume

____ 70. The vital capacity plus the residual volume

____ 71. The minimum volume of air remaining in the lungs even after maximal expiration

____ 72. The extra volume of air that can be maximally inspired over and above the typically resting tidal volume

____ 73. The maximum volume of air that the lungs can hold

____ 74. The tidal volume plus the inspiratory reserve volume

____ 75. The volume of air in the lungs at the end of a normal passive expiration

____ 76. The volume of air entering or leaving the lungs during a single breath

____ 77. The extra volume of air that can be actively expired by maximal contraction of the expiratory muscles beyond that normally passively expired at the end of a typical resting tidal volume

____ 78. The tidal volume plus the inspiratory reserve volume plus the expiratory reserve volume

____ 79. The expiratory reserve volume plus the residual volume

____ 80. The maximum volume of air that can be inspired at the end of a normal quiet expiration
81. The maximum volume of air that can be moved out during a single breath following a maximal inspiration

**Multiple Choice**

82. Which condition is characterized by the person “forgetting to breathe?”
   a. newborn respiratory distress syndrome
   b. atelectasis
   c. sudden infant death syndrome
   d. dyspnea
   e. hypercapnia

83. Which of the following conditions is characterized by air entering the pleural cavity?
   a. apnea
   b. pleurisy
   c. dyspnea
   d. asthma
   e. pneumothorax

84. Which of the following conditions refers to insufficient oxygen at the cellular level?
   a. hypoxia
   b. hypercapnia
   c. hyperpnea
   d. emphysema
   e. atelectasis

85. Which of the following conditions indicates that the partial pressure of carbon dioxide is above normal in arterial blood?
   a. hyperoxia
   b. hypercapnia
   c. hyperpnea
   d. atelectasis
   e. hypercarbonium

86. Which of the following is classified as a chronic obstructive pulmonary disease?
   a. pneumothorax
   b. pleurisy
   c. atelectasis
   d. hypoxia
   e. asthma

87. Which of the following conditions is characterized by the lungs collapsing to its unstretched size?
   a. pleurisy
   b. atelectasis
   c. emphysema
   d. dyspnea
   e. pneumothorax
88. Which of the following refers to an inflammation of the pleural sac?
   a. pleuritis
   b. pneumothorax
   c. pleurisy
   d. emphysema
   e. hyperpnea

89. Which of the following is classified as a chronic obstructive pulmonary disease?
   a. pleuritis
   b. pleurisy c. sleep apnea
   d. pneumothorax
   e. emphysema

90. Which of the following conditions refers to a situation in alveolar surface tension due to insufficient pulmonary surfactant?
   a. sudden infant death syndrome
   b. newborn respiratory distress syndrome
   c. pleurisy
   d. pleuritis
   e. pulmonary insufficiency

91. Which of the following conditions is characterized by transient cessation of ventilation?
   a. apnea
   b. hypocapnia
   c. hyperoxia
   d. hyperdypnea
   e. atelectasis

92. Which of the following conditions refers to increased ventilation to meet increased oxygen needs?
   a. hypopnea
   b. apnea
   c. dyspnea
   d. hyperpnea
   e. hypoxia

93. Which of the following conditions is characterized by inflammation of the lower respiratory airways?
   a. dyspnea
   b. chronic bronchitis
   c. asthma
   d. pleuritis
   e. pleurisy

94. Which of the following conditions is a subjective sensation of not getting enough air?
   a. dyspnea
   b. emphysema
   c. apnea
   d. hyperpnea
   e. pleurisy
95. At high altitudes
   a. the alveolar \( \text{PO}_2 \) is higher than normal.
   b. the alveolar \( \text{PO}_2 \) is lower than normal.
   c. the alveolar \( \text{PCO}_2 \) is higher than normal.
   d. Both a and c above are correct.
   e. Both b and c above are correct.

96. The receptors that are stimulated by a large drop in the blood partial pressure of oxygen are located where?
   a. In the respiratory center of the brain.
   b. In the carotid and aortic bodies.
   c. In the tissue capillaries.
   d. Two of the above are correct.
   e. All of the above (a-c) are correct.

97. The apneustic center
   a. is located in the medulla.
   b. stimulates the inspiratory neurons.
   c. inhibits inspiratory activity.
   d. Both a and b above are correct.
   e. Both a and c above are correct.

98. Hypercapnia
   a. refers to excess carbon dioxide in the arterial blood.
   b. occurs when carbon dioxide is blown off to the atmosphere at a rate faster than it is being produced by the tissues.
   c. always accompanies hypoxia.
   d. Two of the above are correct.
   e. All of the above (a-c) are correct.

99. Which of the following conditions exists at high altitudes?
   a. Histotoxic hypoxia
   b. Hypoxic hypoxia
   c. Anemic hypoxia
   d. Hypocapnia
   e. None of the above are correct.

100. The normal percent saturation of hemoglobin in venous blood is
   a. 97%.
   b. 75%.
   c. 50%.
   d. 40%.
   e. 10%.
Modified Multiple Choice

Indicate which lung volume or capacity is being described in the column by filling in the appropriate letter in the blank. There is only one correct answer for each question and each answer may be used more than once.

a. vital capacity  
b. respiratory rate  
c. FEV₁  
d. tidal volume  
e. residual volume  
f. total lung capacity  
g. functional residual capacity  
h. alveolar ventilation  
i. pulmonary ventilation  
j. inspiratory reserve volume  
k. expiratory reserve volume  
l. inspiratory capacity  
m. anatomic dead space volume

101. _____ respiratory rate \( X (\text{tidal volume} \ - \ \text{dead space volume}) \)
102. _____ maximum volume of air that the lungs can hold
103. _____ the volume of air entering or leaving the lungs in a single breath during quiet breathing
104. _____ the minimum volume of air remaining in the lungs after maximal expiration
105. _____ the extra volume of air that can be maximally inspired over and above the tidal volume
106. _____ amount of air breathed in and out in one minute
107. _____ maximum volume of air that can be moved in and out during a single breath
108. _____ volume of air that can be expired during the first second of expiration in a vital-capacity determination
109. _____ the maximum volume of air that can be inspired at the end of a normal expiration
110. _____ inspiratory reserve volume + tidal volume + expiratory reserve volume
111. _____ vital capacity + residual volume
112. _____ volume of air in the respiratory airways
113. _____ the extra volume of air that can be actively expired by contraction of the expiratory muscles
114. _____ respiratory rate \( X \) tidal volume
115. _____ volume of air in the lungs at the end of a normal passive expiration
116. _____ amount of air that is available for exchange of gases with the blood per minute
117. _____ breaths/minute

Indicate which type of hypoxia would be present in each of the circumstances listed below by writing the appropriate letter in the blank using the following answer code.

A = anemic hypoxia  
B = circulatory hypoxia  
C = histotoxic hypoxia  
D = hypoxic hypoxia

118. _____ cyanide poisoning  
119. _____ high altitude  
120. _____ carbon monoxide poisoning  
121. _____ emphysema  
122. _____ hemoglobin deficiency  
123. _____ congestive heart failure
Points to Ponder

1. The lung of a frog is quite different when compared to that of a human. The frog lung is a thin cylindrical tube much like a finger on a rubber glove. How does this very simple structure adequately serve the frog whereas humans require millions of alveoli to survive?

2. How would you explain the position of the trachea being ventral to the esophagus: the food must pass over the trachea to be swallowed?

3. What should you do when a small child declares that he will hold his breath until he dies if his demands are not met?

4. Why do some athletes breathe pure oxygen on the sidelines?

5. Why do we yawn?

6. Why is it important for the respiratory system to have a dual blood supply?

7. Why is it important that the capillaries surrounding the alveoli have a small diameter?

8. Under normal conditions, why is the first breath of life difficult?

9. After driving from sea level to a trail high in the Sierras, you get out of your SUV and feel dizzy. What do you suppose is causing your dizziness?

10. Nicototne from cigarette smoke causes the buildup of mucus and paralyzes the ciliated epithelial cells that line the bronchioles. How might these conditions affect pulmonary function tests?

Clinical Perspectives

1. How do you avoid carbon monoxide in a closed environment?

2. How would you relate drowning to this chapter?

3. How does taking a dive in a hyperbaric chamber enhance treatment against certain anaerobic bacteria?

4. You have just come upon an accident victim. After summoning help you see that the victim has a pneumothorax. How could you possibly help this person until medical help arrives?

5. Your college roommate has just returned from a football game and is very hoarse from all of the cheering he did. He knows you are taking a physiology course and wants to know why he is hoarse. How would you explain to him that yelling makes us hoarse?

6. Are common colds spread mostly through sneezes? Explain why or why not.

7. Why is the disease asthma often treated with glucocorticoid drugs?
8. When or under what conditions would the use of hyperbaric oxygen therapy be useful?

9. People who hyperventilate during psychological stress are sometimes told to breathe into a paper bag. What is the physiological basis for this act?

10. Your friend asks you to explain to her what “mountain sickness” is. How would you explain this to her?

**Experiments of the Day**

1. Exhale normally, then exhale a little more and a little more until you can no longer exhale. From which of the lung volumes or capacities are you exhaling? Repeat using inhalation until you can no longer inhale. Into which lung volumes or capacities are you inhaling?

2. Do some exercise until you are ventilating rapidly. Place a bag over your mouth and nose. What are the results and why?
Chapter 13: Respiratory System

True/False

1. True
2. False—When compliance is decreased.
3. False—Five percent.
4. False—5.7 liters.
5. True
6. True
7. True
8. False—100 mmHg.
9. True
10. True
11. True
12. False—Between the alveoli and the blood.
13. True
14. False—DRG.
15. True
16. True
17. True
18. False—Increase.
19. True
20. True
21. False—1.5 percent.
22. True
23. False—Decreased.
24. False—97.5 % saturated.
25. True
26. True
27. False—Circulatory hypoxia.
28. True
29. False—Higher pressure to lower pressure.
30. False—Lower.
31. True
32. False—Decreases.
33. False—Increases.
34. True
35. True

Multiple Choice

40. Carboxyhemoglobin
41. Haldane effect
42. Hypoxic hypoxia
43. Pneumonia
44. Partial pressure
45. Partial pressure gradient
46. 60 mm Hg, 6 mm Hg
47. Functional residual capacity
48. Obstructive, restrictive
49. Anatomic dead space
50. Atmospheric (barometric) pressure
51. Bronchodilation
52. Emphysema
53. Compliance
54. Interdependence
55. LaPlace’s law
56. Tidal volume
57. Medullary respiratory center
58. Apneustic center, pneumotaxic center
59. Dorsal respiratory group
60. Apneusis
61. Carotid bodies, aortic bodies
62. Apnea
63. Dyspnea
64. Respiration
65. Esophagus
66. Vocal folds
67. Type I alveolar cells
68. Type II alveolar cells
69. Pores of Kohn

Matching

70. a
71. f
72. e
73. a
74. g
75. d
76. b
77. h
78. c
79. d
80. g
81. c

Modified

101. h
102. f
103. d
104. e
105. j
106. I
107. A
108. C
109. L
110. A
111. F
112. m
113. k
114. I
115. G
116. H
117. B
118. C
119. D
120. A
121. D
122. A
123. b

Fill in the Blank

36. Histotoxic hypoxia
37. Hypercapnia
38. Oxygen-hemoglobin dissociation curve
39. Bohr effect