مقرر

GENERAL PHYSIOLOGY

3rd year of Zoology

Prepared By
Dr. Rana Abd-Elstar Ali
Assistant professor of animal physiology
Zoology department
Faculty of science
2022-2023

بيـــانـــات أساسية

الكلية: العلوم

الفرقة: الثالثة

التخصص: علم الحيوان

كود المقرر: ٣٠٤ح

القسم التابع له المقرر : قسم علم الحيوان كلية العلوم

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INTRODUCTION

Physiology tells us how the bodies of living organism's work. Physiology is based on the gross and microstructure. Both structure and function must be studied at all levels from the cellular to the molecular to the intact organism.

All aspects of human physiology evolved in the thousands of inherited units of DNA called genes. This genetic imprint is passed from parents to children. We all inherit a mixture of genes present in parents. There is immense genetic diversity, as a result of small spontaneous change in individual genes, called mutation, occurring from time to time. The natural selection concept of Charles Darwin emphasizes the predominance of the genes in the population that favors survival of the fittest and reproduction in a particular environment.

Early with life on earth cells developed the ability to react with oxygen and carbon compounds and use the energy released by these chemical reactions. With complexity of development cells evolved structure called mitochondria for efficient energy production. The efficiency of oxidative phosphorylation was maximized in natural selection of the best. The mitochondria of cells in mammals are same in appearance and function. Some aspects of human physiology may be rapidly changing on the evolutionary scale of time. Homosapiens have walked on the earth for perhaps 1.5 million years, but human brain has reached its present size only about 35,000 years back. The brain capabilities are probably still rapidly evolving as new pressures are faced. For pain with injury, a warning signal results in sudden

withdrawal of the injured part, protecting it from further injury. But step-by-step sequence of events starts with the injury and eventually ends with the contraction of group of muscles that flex the injured limb - stimulus, receptor, electric signals, spinal cord, flexor muscles. There are links between the nerve and the spinal cord, and the muscle. The circuit that creates this response is genetically determined and is formed during early development of the nervous system.

Life processes: The following are the important life processes of humans: **Metabolism:** includes catabolism and anabolism that provides energy and body's structural and functional components
Excitability: Ability to sense changes in and around us.
Conductivity: ability to carry the effects of stimulus from part of a cell to another.
Contractility: ability to contract in response to stimulus
Growth Differentiation Reproduction

COMPOSITION OF THE BODY

At an average, 60% of the body weight of young adult male is water. The remaining is composed of minerals, fat and proteins. The human body contains organic compounds such as lipids, proteins, carbohydrates and nucleic acids. The lipids are important forms of storage fuel in addition to providing insulation of the body as a whole or essential component in the structure of plasma membranes, myelin and other membranes. Carbohydrates serve as a lesser form of fuel storage (400-500 gms). Proteins serve as the structural basis for all enzymes, contractile muscle proteins, connective tissue, such as collagen and elastin and in addition as a fuel (about 15%), or precursor for carbohydrate in the process of gluconeogenesis. Ingested glucose is converted to glycogen and stored in the liver, muscle and adipose tissue.

Table 2. Components of Body System

System	**Components**
Circulation	Heart, blood vessels, blood

Digestive system	Mouth, pharynx, esophagus, stomach, small & large intestine, salivary glands, pancreas liver, and gallbladder
Respiratory system	Nose, pharynx, larynx, trachea, bronchi, lungs
Urinary system	Kidneys, ureters, urinary bladder, urethra
Skeletal system	Bones, cartilage, joints
Muscle system	Skeletal muscle
Integumentary system	Skin, hair, nails
Immune system	Leukocytes, thymus, bone marrow, tonsils, adenoids, lymph nodes, spleen, appendix, gut-associated lymphoid tissue, skin-associated lymphoid tissue muscosa associated lymphoid tissue
Nervous system	Brain, spinal cord, peripheral nervous system. Special sense organs
Endocrine system	All hormone-secreting tissues including hypothalamus, pituitary, thyroid, parathyroids, adrenals, endocrine pancreas, kidney, intestine, heart, thymus, pineal
Reproductive system	Male: testis, prostate, seminal vesicles, bulbourethral glands, associated ducts
	Female: ovary, oviduct, uterus, vagina, breast.

HOMEOSTASIS

Homeostasis is a delicately balanced state. Large part of physiology is concerned with regulation mechanisms that act to maintain the constancy of the internal environment. Many of these regulatory mechanisms operate on the negative feedback. Homeostasis is the

dynamic steady state of the internal environment. Departures from the steady state are opposed by negative feedback regulation. The structure and chemical reactions of living organisms are sensitive to the chemical and physical conditions within and around cells. Cells must be wet and surrounding fluid must be fresh or salty seawater. For multicellular organisms, the surrounding fluid is the interstitial fluid: a component of the extracellular fluid.

The intracellular fluid has a high concentration of potassium and low concentration of Na^+ Cl^-, Mg^{++}, and Ca^+. In addition, cells need a ready supply of nutrients, that serve as structural building molecules, and source of energy as ATP (chemical energy). Body temperature is very crucial for intracellular physiological processes; enzymatic events need a very narrow range of temperature, within the physiological range of temperature compatible with life, cooler temperature favors preservations of cellular structure but slows the rate of chemical reactions carried out by cells. The higher temperature enhances chemical reactions, but may also disrupt the structure of the proteins and other macromolecules within cells. The production of energy for cellular activities requires oxygen and nutrients reaching the cell interior and carbon dioxide and other chemical wastes products be transferred to the environment. Extensive exchange between cells and immediate surroundings, interstitial fluid, occurs by diffusion based on a concentration gradient. Diffusion causes adequate movement of dissolved nutrients, gases and metabolic end products to meet the active needs of the cell, if the distance is short. If the distance increases, the time for diffusion increases too. For the efficiency of diffusion, the diameter of individual cells is usually not more than a few tenths of a millimeter. With the evolution of multicellular organisms, body plans include an internal fluid environment for the cells, called extracellular fluid (ECF). The ECF includes both the interstitial fluid and the plasma. In the circulatory system, blood rapidly moves between the respiratory system, where gases are exchanged; the kidney where wastes and excess of fluid and solutes are excreted; and the digestive system where nutrients are absorbed. These substances are rapidly transported by blood flow overcoming the diffusion limit on large body size. By maintaining a relatively constant internal environment, multicellular organisms are able to live freely in

changing external environment. Cannon called it ‘homeostasis’ (Greek, homeo = same; stasis = staying).

Homeostasis of the internal environment involves control of the chemical composition and volume of ECF; blood pressure and body temperature, etc. Most control systems use negative feedback (NFB). In NFB the control system compares a controlled variable with a set point value. Responses tend to oppose the change and restore the variable to its set point value. All organ systems have regulatory processes for maintaining a delicate balance in a dynamic steady state. If external environment stresses are very severe beyond the homeostatic processes, the balance can be overwhelmed. Prolonged exposure to cold may lead to an intolerable reduction in the body temperature. Exercise in very hot environment, may result in fluid depletion and an increase in the core temperature, resulting in heat stroke the cells are much adapted to a regulated core temperature that even a few degrees of temperature variations may have fatal consequences. Without clothes and proper protection humans can tolerate only a narrow difference between body temperature and environmental temperature.

Many diseases impair homeostasis. Factors homeostatically maintained include:

- Concentration of nutrient molecules
- Concentration of oxygen and carbondioxide
- Concentration of waste products
- pH
- Temperature
- Concentration of water, salt, and other electrolytes
- Volume (fluids), osmolality, and pressure

Homeostasis is essential for survival of cells in that:

- Cells need homeostasis for their own survival and for performing specialized function essential to survival of the whole body.
- Cells need a constant supply of nutrient and oxygen and going elimination of acid-forming carbon dioxide, to generate energy needed to power life sustaining cellular activities as follows:

Food + Oxygen = Carbondioxide + water + Energy

ROLE OF BODY SYSTEM IN MAINTAINING HOMEOSTASIS

Body systems are made up of cells organized according to specialization to maintain homeostasis.

Nervous System:

Information from the external environment relayed through the nervous system. Nervous system acts through electrical signals to control rapid responses for higher functions e.g., concentration, memory, and creativity

Endocrine System:

Acts by means of hormones secreted into the blood to control processes that require duration rather than speed, e.g., metabolic activity and water and electrolytes balances

Circulatory system:

Transports nutrients, oxygen, carbon dioxide, wastes, electrolytes, and hormones throughout the body

Respiratory system:

Obtains oxygen from and eliminates carbon dioxide to the external environment; helps regulate pH by adjusting the rate of removal of acid-forming carbon dioxide

Urinary system:

Important in regulating the volume, electrolyte composition, and pH of the internal environment; removes waste and excess water, salt, acid, and other electrolytes from the plasma and eliminates them into the urine.

Digestive system:

Obtains nutrients, water and electrolytes from the external environment and transfers them into the plasma; eliminates undigested food residues to the external environment

Muscular and Skeletal system:

Supports and protects body parts and allows body movements; heat generated by muscular contraction are important in temperature regulation; calcium is stored in the bones Immune system:

Defense against foreign invaders and cancer cells; paves way for tissue repair

Integumentary system:

keeps internal fluids in and foreign materials out serves as a protective barrier between the external environment and the remainder of the body; the sweat glands and adjustment in blood flow are important in temperature regulation

The Digestive System

The digestive system includes the organs of the alimentary canal and accessory structures. The alimentary canal forms a continuous tube that is open to the outside environment at both ends. The organs of the alimentary canal are the mouth, pharynx, esophagus, stomach, small intestine, and large intestine. The accessory digestive structures include the teeth, tongue, salivary glands, liver, pancreas, and gallbladder. The wall of the alimentary canal is composed of four basic tissue layers: mucosa, submucosa, muscularis, and serosa. The enteric nervous system provides intrinsic innervation, and the autonomic nervous system provides extrinsic innervation.

Digestive System Processes and Regulation

The digestive system ingests and digests food, absorbs released nutrients, and excretes food components that are indigestible. The six activities involved in this process are ingestion, motility, mechanical digestion, chemical digestion, absorption, and defecation. These processes are regulated by neural and hormonal mechanisms.

The Mouth, Pharynx, and Esophagus

In the mouth, the tongue and the teeth begin mechanical digestion, and saliva begins chemical digestion. The pharynx, which plays roles in breathing and vocalization as well as digestion, runs from the nasal and oral cavities superiorly to the esophagus inferiorly (for digestion) and to the larynx anteriorly (for respiration). During deglutition (swallowing), the soft palate rises to close off the nasopharynx, the larynx elevates, and the epiglottis folds over the glottis. The esophagus includes an upper esophageal sphincter made of skeletal muscle, which regulates the movement of food from the pharynx to the esophagus. It also has a lower esophageal sphincter, made of smooth muscle, which controls the passage of food from the esophagus to the stomach. Cells in the esophageal wall secrete mucus that eases the passage of the food bolus.

The Stomach

The stomach participates in all digestive activities except ingestion and defecation. It vigorously churns food. It secretes gastric juices that break down food and absorbs certain drugs, including aspirin and some alcohol. The stomach begins the digestion of protein and continues the digestion of carbohydrates and fats. It stores food as an acidic liquid called chyme, and releases it gradually into the small intestine through the pyloric sphincter.

The Small and Large Intestines

The three main regions of the small intestine are the duodenum, the jejunum, and the ileum. The small intestine is where digestion is completed and virtually all absorption occurs. These two activities are facilitated by structural

adaptations that increase the mucosal surface area by 600-fold, including circular folds, villi, and microvilli. There are around 200 million microvilli per square millimeter of small intestine, which contain brush border enzymes that complete the digestion of carbohydrates and proteins. Combined with pancreatic juice, intestinal juice provides the liquid medium needed to further digest and absorb substances from chyme. The small intestine is also the site of unique mechanical digestive movements. Segmentation moves the chyme back and forth, increasing mixing and opportunities for absorption. Migrating motility complexes propel the residual chyme toward the large intestine. The main regions of the large intestine are the cecum, the colon, and the rectum. The large intestine absorbs water and forms feces, and is responsible for defecation. Bacterial flora break down additional carbohydrate residue, and synthesize certain vitamins. The mucosa of the large intestinal wall is generously endowed with goblet cells, which secrete mucus that eases the passage of feces. The entry of feces into the rectum activates the defecation reflex.

Accessory Organs in Digestion: The Liver, Pancreas, and Gallbladder

Chemical digestion in the small intestine cannot occur without the help of the liver and pancreas. The liver produces bile and delivers it to the common hepatic duct. Bile contains bile salts and phospholipids, which emulsify large lipid globules into tiny lipid droplets, a necessary step in lipid digestion and absorption. The gallbladder stores and concentrates bile, releasing it when it is needed by the small intestine. The pancreas produces the enzyme- and bicarbonate-rich pancreatic juice and delivers it to the small intestine through ducts. Pancreatic juice buffers the acidic gastric juice in chyme, inactivates pepsin from the stomach, and enables the optimal functioning of digestive enzymes in the small intestine.

Chemical Digestion and Absorption

- Identify the locations and primary secretions involved in the chemical digestion of carbohydrates, proteins, lipids, and nucleic acids.

- Compare and contrast absorption of the hydrophilic and hydrophobic nutrients

As you have learned, the process of mechanical digestion is relatively simple. It involves the physical breakdown of food but does not alter its chemical makeup. Chemical digestion, on the other hand, is a complex process that reduces food into its chemical building blocks, which are then absorbed to nourish the cells of the body (**Figure 1**). In this section, you will look more closely at the processes of chemical digestion and absorption.

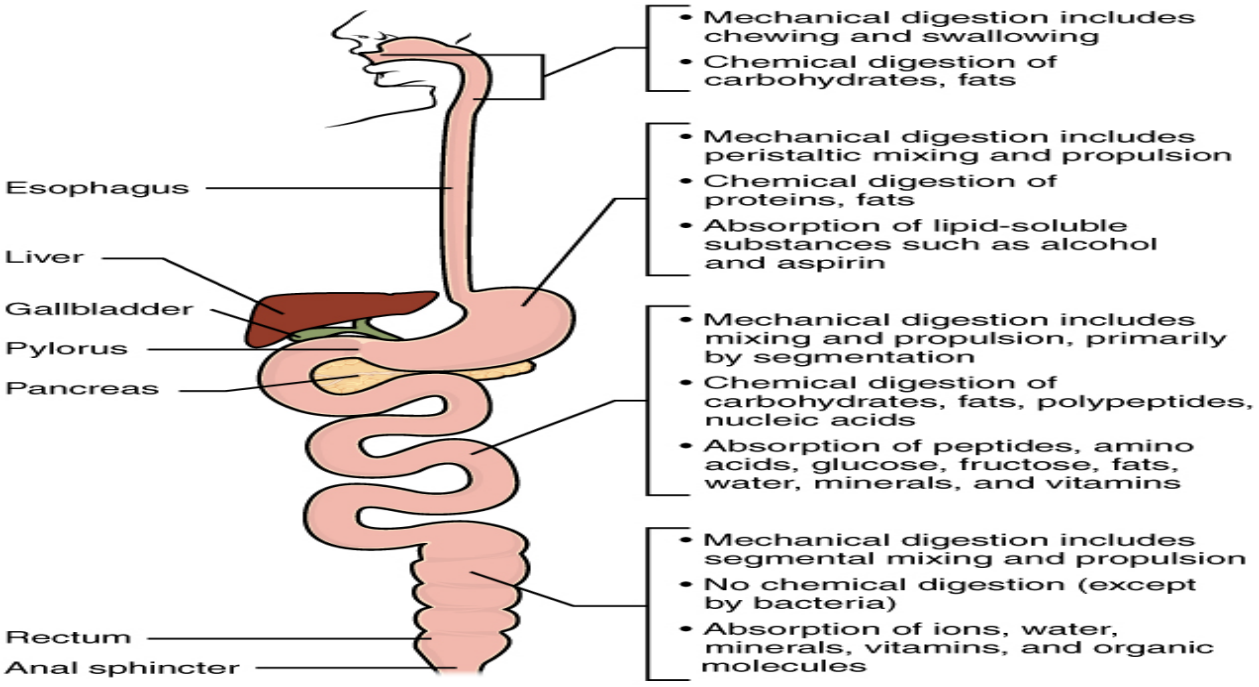


FIG1. Digestion and Absorption Digestion begins in the mouth and continues as food travels through the small intestine. Most absorption occurs in the small intestine.

Chemical Digestion

Large food molecules (for example, proteins, lipids, nucleic acids, and starches) must be broken down into subunits that are small enough to be absorbed by the lining of the alimentary canal. This is accomplished by enzymes through hydrolysis. The many enzymes involved in chemical digestion are summarized in Table 1

The Digestive Enzymes

Enzyme Category	Enzyme Name	Source	Substrate	Product
Salivary Enzymes	Lingual lipase	Lingual glands	Triglycerides	Free fatty acids, and mono- and diglycerides
Salivary Enzymes	Salivary amylase	Salivary glands	Polysaccharides	Disaccharides and trisaccharides
Gastric enzymes	Gastric lipase	Chief cells	Triglycerides	Fatty acids and monoacylglycerides
Gastric enzymes	Pepsin*	Chief cells	Proteins	Peptides
Brush border enzymes	α-Dextrinase	Small intestine	α-Dextrins	Glucose
Brush border enzymes	Enteropeptidase	Small intestine	Trypsinogen	Trypsin
Brush border enzymes	Lactase	Small intestine	Lactose	Glucose and galactose
Brush border enzymes	Maltase	Small intestine	Maltose	Glucose
Brush border enzymes	Nucleosidases and phosphatases	Small intestine	Nucleotides	Phosphates, nitrogenous bases, and pentoses
Brush border enzymes	Peptidases	Small intestine	Aminopeptidase: amino acids at the amino end of peptides Dipeptidase: dipeptides	Aminopeptidase: amino acids and peptides Dipeptidase: amino acids
Brush border enzymes	Sucrase	Small intestine	Sucrose	Glucose and fructose
Pancreatic enzymes	Carboxy-peptidase*	Pancreatic acinar cells	Amino acids at the carboxyl end of peptides	Amino acids and peptides
Pancreatic enzymes	Chymotrypsin*	Pancreatic acinar cells	Proteins	Peptides
Pancreatic enzymes	Elastase*	Pancreatic acinar cells	Proteins	Peptides
Pancreatic enzymes	Nucleases	Pancreatic acinar cells	Ribonuclease: ribonucleic acids Deoxyribonuclease: deoxyribonucleic acids	Nucleotides
Pancreatic enzymes	Pancreatic amylase	Pancreatic acinar cells	Polysaccharides (starches)	α-Dextrins, disaccharides (maltose), trisaccharides (maltotriose)
Pancreatic enzymes	Pancreatic lipase	Pancreatic acinar cells	Triglycerides that have been emulsified by bile salts	Fatty acids and monoacylglycerides
Pancreatic enzymes	Trypsin*	Pancreatic acinar cells	Proteins	Peptides

Table 23.8 *These enzymes have been activated by other substances.

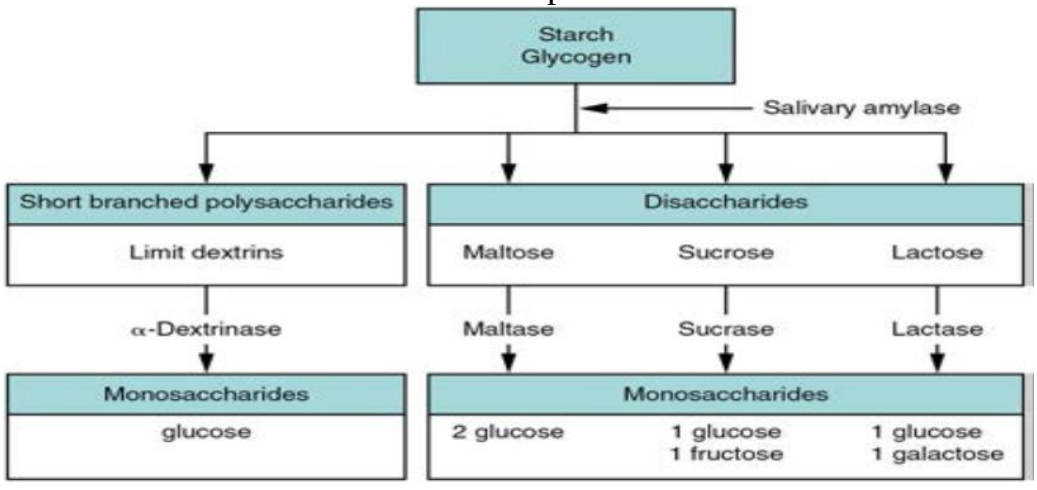
Carbohydrate Digestion

The average American diet is about 50 percent carbohydrates, which may be classified according to the number of monomers they contain of simple sugars (monosaccharides and disaccharides) and/or complex sugars (polysaccharides). Glucose, galactose, and fructose are the three monosaccharides that are commonly consumed and are readily absorbed. Your digestive system is also able to break down the disaccharide sucrose (regular table sugar: glucose + fructose), lactose (milk sugar: glucose + galactose), and maltose (grain sugar: glucose + glucose), and the polysaccharides glycogen and starch (chains of monosaccharides). Your bodies do not produce enzymes that can break down most fibrous polysaccharides, such as cellulose. While indigestible polysaccharides do not provide any nutritional value, they do provide dietary fiber, which

helps propel food through the alimentary canal. The chemical digestion of starches begins in the mouth and has been reviewed above. In the small intestine, **pancreatic amylase** does the 'heavy lifting' for starch and carbohydrate digestion (**Figure 2**).

After amylases break down starch into smaller fragments, the brush border enzyme **α-dextrinase** starts working on **α- dextrin**, breaking off one glucose unit at a time. Three brush border enzymes hydrolyze sucrose, lactose, and maltose into monosaccharides. **Sucrase** splits sucrose into one molecule of fructose and one molecule of glucose; **maltase** breaks down maltose and maltotriose into two and three glucose molecules, respectively; and **lactase** breaks down lactose into one molecule of glucose and one molecule of galactose. Insufficient lactase can lead to lactose intolerance.

Fig 2**: Carbohydrate Digestion Flow Chart** Carbohydrates are broken down into their monomers in a series of steps



Protein Digestion:

Proteins are polymers composed of amino acids linked by peptide bonds to form long chains; The digestion of proteins begins in the stomach. When protein-rich foods enter the stomach, they are greeted by a mixture of the enzyme pepsin and hydrochloric acid (HCl; 0.5 percent). The latter produces an environmental pH of 1.5–3.5 that denatures proteins within food. Pepsin cuts proteins into smaller polypeptides and their constituent amino acids. When the food-gastric juice mixture (chyme) enters the small intestine, the pancreas releases sodium bicarbonate to neutralize the HCl. This helps to protect the lining of the intestine. The small intestine also releases digestive hormones, including secretin and CCK, also, the cells of the brush border of The small intestine secrete enzymes such as aminopeptidase and dipeptidase, which stimulate digestive processes which to break down peptide chains. This results in molecules small enough to enter the bloodstream. Secretin also stimulates the pancreas to release sodium bicarbonate. The pancreas releases most of the digestive enzymes, including the proteases trypsin, chymotrypsin, and elastase, which aid protein digestion. In order to avoid breaking down the proteins that make up the pancreas and small intestine, pancreatic enzymes are released as **inactive proenzymes** that are only activated in the small intestine. In the pancreas, vesicles store **trypsin** and **chymotrypsin** as **trypsinogen** and **chymotrypsinogen**. Once released into the small intestine, an enzyme found in the wall of the small intestine, called **enterokinase**, binds to trypsinogen and converts it into its active form, trypsin. Trypsin then binds to chymotrypsinogen to convert it into the active chymotrypsin. Trypsin and chymotrypsin break down large proteins into smaller peptides, a process called **proteolysis**. All of these enzymes break complex proteins into smaller individual amino acids.

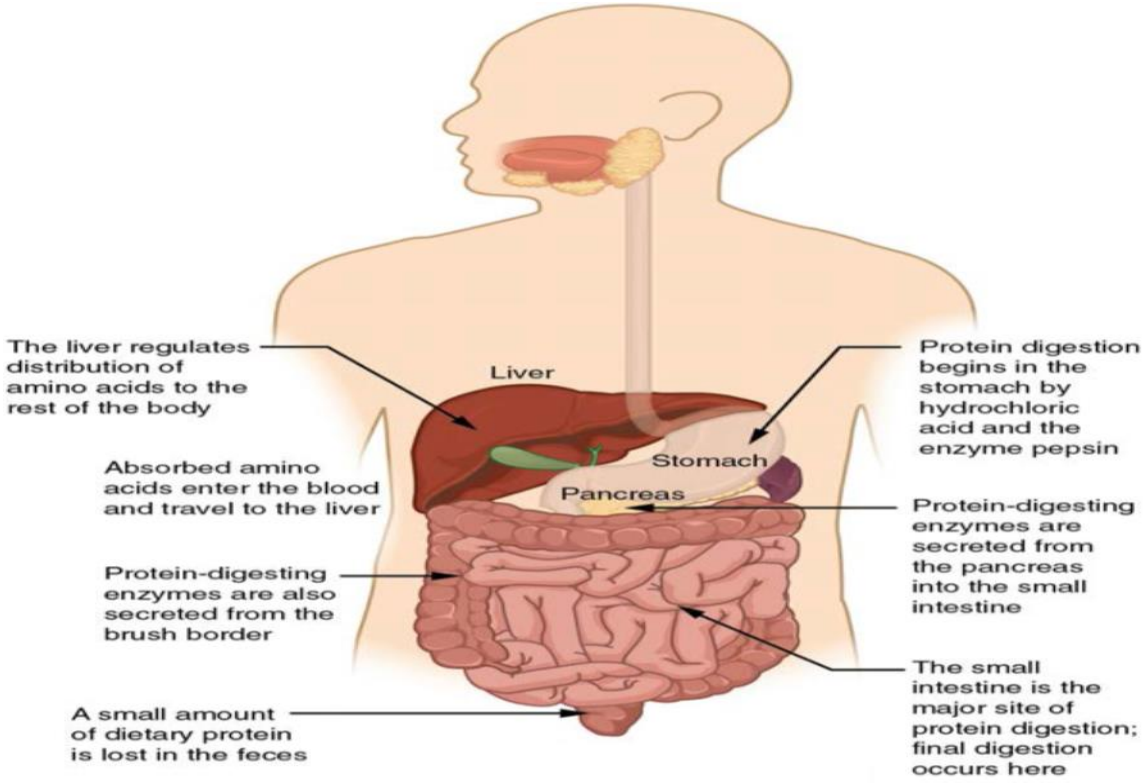


Fig 3**; Digestion of Protein** The digestion of protein begins in the stomach and is completed in the small
Intestine.

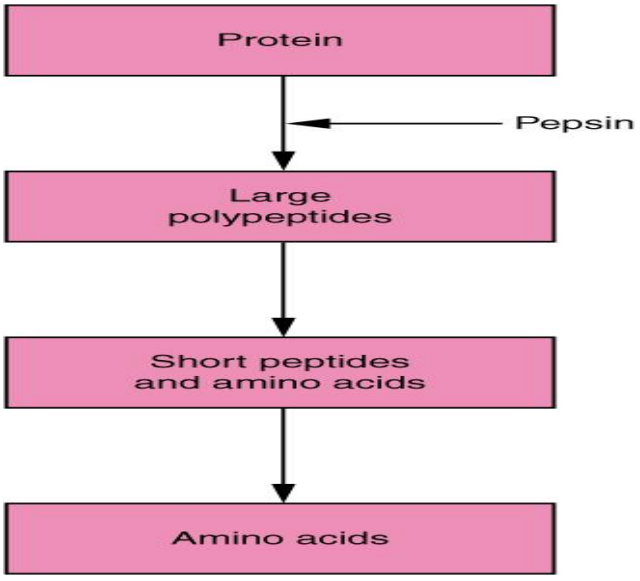


Fig 4: **Digestion of Protein Flow Chart** Proteins are successively broken down into their amino acid components.

Lipid Digestion

A healthy diet limits lipid intake to 35 percent of total calorie intake. The most common dietary lipids are triglycerides, which are made up of a glycerol molecule bound to three fatty acid chains. Small amounts of dietary cholesterol and phospholipids are also consumed. The three lipases responsible for lipid digestion are lingual lipase, gastric lipase, and **pancreatic lipase,** enzymes that break down fats after they are emulsified by bile salts. When food reaches the small intestine in the form of chyme, a digestive hormone called cholecystokinin (CCK) is released by intestinal cells in the intestinal mucosa. CCK stimulates the release of pancreatic lipase from the pancreas and stimulates the contraction of the gallbladder to release stored bile salts into the intestine. CCK also travels to the brain, where it can act as a hunger suppressant.Together, the pancreatic lipases and bile salts break down triglycerides into free fatty acids.. However, because the pancreas is the only consequential source of lipase, virtually all lipid digestion occurs in the small intestine. Pancreatic lipase breaks down each triglyceride into two free fatty acids and a monoglyceride. The fatty acids include both short-chain (less than 10 to 12 carbons) and long-chain fatty acids.

Nucleic Acid Digestion

The nucleic acids DNA and RNA are found in most of the foods you eat. Two types of **pancreatic nuclease** are responsible for their digestion: **deoxyribonuclease**, which digests DNA, and **ribonuclease**, which digests RNA. The nucleotides produced by this digestion are further broken down by two intestinal brush border enzymes (**nucleosidase** and **phosphatase**) into pentoses, phosphates, and nitrogenous bases, which can be absorbed through the alimentary canal wall.

The large food molecules that must be broken down into subunits are summarized **Table 2**

Absorbable Food Substances

Source	Substance
Carbohydrates	Monosaccharides: glucose, galactose, and fructose
Proteins	Single amino acids, dipeptides, and tripeptides
Triglycerides	Monoacylglycerides, glycerol, and free fatty acids
Nucleic acids	Pentose sugars, phosphates, and nitrogenous bases

Absorption

The mechanical and digestive processes have one goal: to convert food into molecules small enough to be absorbed by the epithelial cells of the intestinal villi. The absorptive capacity of the alimentary canal is almost endless. Each day, the alimentary canal processes up to 10 liters of food, liquids, and GI secretions, yet less than one liter enters the large intestine. Almost all ingested food, 80 percent of electrolytes, and 90 percent of water are absorbed in the small intestine. Although the entire small intestine is involved in the absorption of water and lipids, most absorption of carbohydrates an proteins

occurs in the jejunum. Notably, bile salts and vitamin B12 are absorbed in the terminal ileum. By the time chyme passes from the ileum into the large intestine, it is essentially indigestible food residue (mainly plant fibers like cellulose), some water, and millions of bacteria (Figure 5).

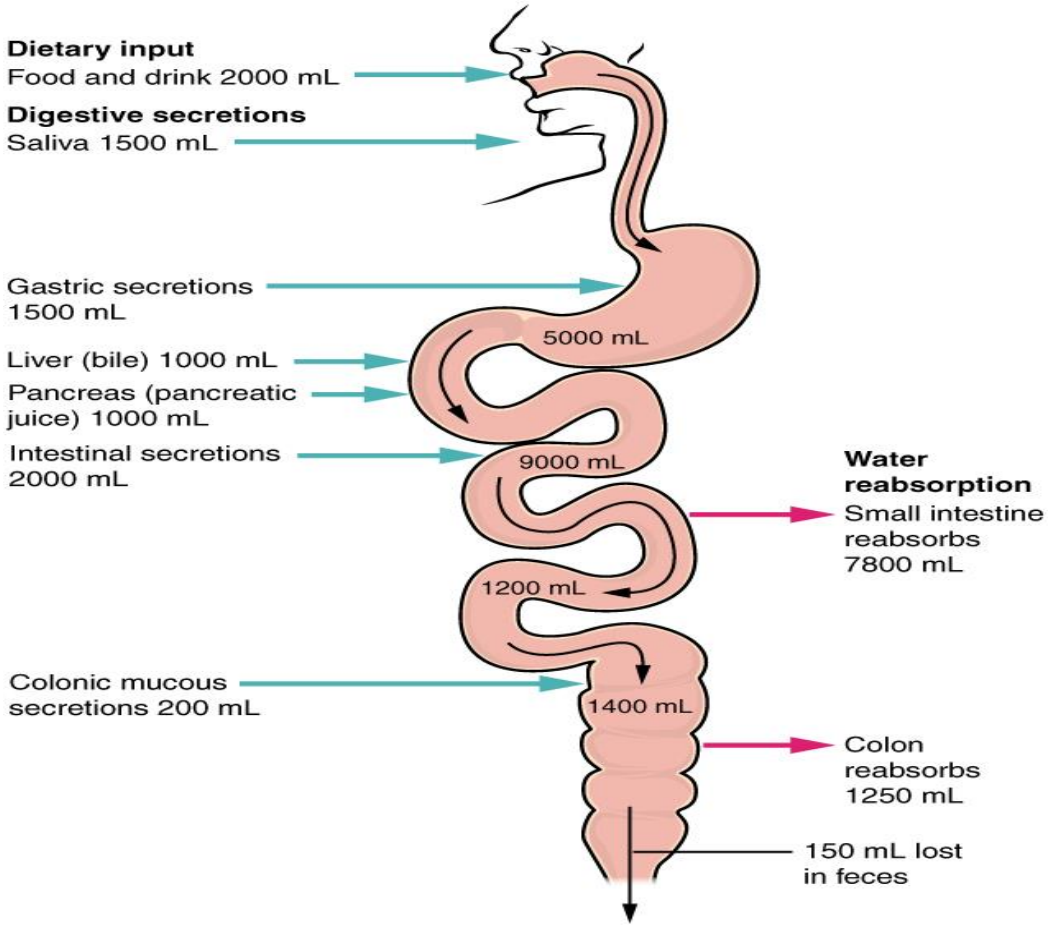


Fig 5: **Digestive Secretions and Absorption of Water** Absorption is a complex process, in which nutrients

from digested food are harvested.

Absorption can occur through five mechanisms: (1) active transport, (2) passive diffusion, (3) facilitated diffusion, (4) cotransport (or secondary active transport), and (5) endocytosis. As you will recall from Chapter 3, active transport refers to the movement of a substance across a cell membrane going from an area of lower concentration to an area of higher concentration (up the concentration gradient). In this type of transport, proteins within the cell membrane act as "pumps, using cellular energy (ATP) to move the substance. Passive diffusion refers to the movement of substances from an area of higher concentration to an area of lower concentration, while facilitated diffusion refers to the movement of substances from an area of higher to an area of lower concentration using a carrier protein in the cell membrane. Co-transport uses the movement of one molecule through the membrane from higher to lower concentration to power the movement of
another from lower to higher. Finally, endocytosis is a transportation process in which the cell membrane engulfs material. It requires energy, generally in the form of ATP. Because the cell's plasma membrane is made up of hydrophobic phospholipids, water-soluble nutrients must use transport molecules embedded in the membrane to enter cells. Moreover, substances cannot pass between the epithelial cells of the intestinal mucosa because these cells are bound together by tight junctions. Thus, substances can only enter blood capillaries by passing through the apical surfaces of epithelial cells and into the interstitial fluid. Water-soluble nutrients enter the capillary blood in the villi and travel to the liver via the hepatic portal vein.

In contrast to the water-soluble nutrients, lipid-soluble nutrients can diffuse through the plasma membrane. Once inside the cell, they are packaged for transport via the base of the cell and then enter the lacteals of the villi to be transported by lymphatic vessels to the systemic circulation via the thoracic duct. The absorption of most nutrients through the mucosa of the intestinal villi requires active transport fueled by ATP. The routes of absorption for each food category are summarized in **Table**3

Absorption in the Alimentary Canal

Food	Breakdown products	Absorption mechanism	Entry to bloodstream	Destination
Carbohydrates	Glucose	Co-transport with sodium ions	Capillary blood in villi	Liver via hepatic portal vein
Carbohydrates	Galactose	Co-transport with sodium ions	Capillary blood in villi	Liver via hepatic portal vein
Carbohydrates	Fructose	Facilitated diffusion	Capillary blood in villi	Liver via hepatic portal vein
Protein	Amino acids	Co-transport with sodium ions	Capillary blood in villi	Liver via hepatic portal vein
Lipids	Long-chain fatty acids	Diffusion into intestinal cells, where they are combined with proteins to create chylomicrons	Lacteals of villi	Systemic circulation via lymph entering thoracic duct
Lipids	Monoacylglycerides	Diffusion into intestinal cells, where they are combined with proteins to create chylomicrons	Lacteals of villi	Systemic circulation via lymph entering thoracic duct
Lipids	Short-chain fatty acids	Simple diffusion	Capillary blood in villi	Liver via hepatic portal vein
Lipids	Glycerol	Simple diffusion	Capillary blood in villi	Liver via hepatic portal vein
Nucleic Acids	Nucleic acid digestion products	Active transport via membrane carriers	Capillary blood in villi	Liver via hepatic portal vein

Carbohydrate Absorption

All carbohydrates are absorbed in the form of monosaccharides. The small intestine is highly efficient at this, absorbing monosaccharides at an estimated rate of 120 grams per hour. All normally digested dietary carbohydrates are absorbed; indigestible fibers are eliminated in the feces. The monosaccharides glucose and galactose are transported into the epithelial cells by common protein carriers via secondary active transport (that is, co-transport with sodium ions). The monosaccharides leave these cells via facilitated diffusion and enter the capillaries through intercellular clefts. The monosaccharide fructose (which is in fruit) is absorbed and transported by facilitated diffusion alone. The monosaccharides combine with the transport proteins immediately after the disaccharides are broken down.

Protein Absorption

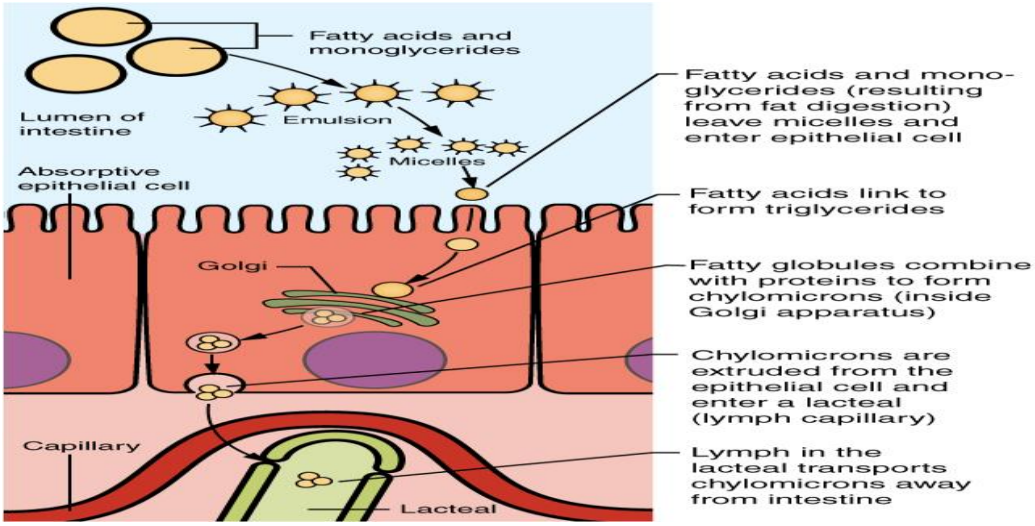
Active transport mechanisms, primarily in the duodenum and jejunum, absorb most proteins as their breakdown products, amino acids. Almost all (95 to 98 percent) protein is digested and absorbed in the small intestine. The type of carrier that transports an amino acid varies. Most carriers are linked to the active transport of sodium. Short chains of two amino epithelial cells, they are broken down into their amino acids before leaving the cell and entering the capillary blood via diffusion.

Lipid Absorption

About 95 percent of lipids are absorbed in the small intestine. Bile salts not only speed up lipid digestion, they are also essential to the absorption of the end products of lipid digestion. Short-chain fatty acids are relatively water soluble and can enter the absorptive cells (enterocytes) directly. The small size of short-chain fatty acids enables them to be absorbed by enterocytes via simple diffusion, and then take the same path as monosaccharides and amino acids into the blood capillary of a villus.

The large and hydrophobic long-chain fatty acids and monoacylglycerides are not so easily suspended in the watery intestinal chyme. However, bile salts and lecithin resolve this issue by enclosing them in a **micelle**, which is a tiny sphere with polar (hydrophilic) ends facing the watery environment and hydrophobic tails turned to the interior, creating a receptive environment for the long-chain fatty acids. The core also includes cholesterol and fat-soluble vitamins. Without micelles, lipids would sit on the surface of chyme and never come in contact with the absorptive surfaces of the epithelial cells. Micelles can easily squeeze between microvilli and get very near the luminal cell surface. At this point, lipid substances exit the micelle and are absorbed via simple diffusion.

The free fatty acids and monoacylglycerides that enter the epithelial cells are reincorporated into triglycerides. The triglycerides are mixed with phospholipids and cholesterol, and surrounded with a protein coat. This new complex, called a **chylomicron**, is a water-soluble lipoprotein. After being processed by the Golgi apparatus, chylomicrons are released from the cell (**Figure 23.33**). Too big to pass through the basement membranes of blood capillaries, chylomicrons instead enter the large pores of lacteals. The lacteals come together to form the lymphatic vessels. The chylomicrons are transported in the lymphatic vessels and empty through the thoracic duct into the subclavian vein of the circulatory system. Once in the bloodstream, the enzyme **lipoprotein lipase** breaks down the triglycerides of the chylomicrons into free fatty acids and glycerol. These breakdown products then pass through capillary walls to be used for energy by cells or stored in adipose tissue as fat. Liver cells combine the remaining chylomicron remnants with proteins, forming lipoproteins that transport cholesterol in the blood.



Lipid Absorption Unlike amino acids and simple sugars, lipids are transformed as they are absorbed through epithelial cells.

Nucleic Acid Absorption

The products of nucleic acid digestion—pentose sugars, nitrogenous bases, and phosphate ions—are transported by carriers
across the villus epithelium via active transport. These products then enter the bloodstream.

Mineral Absorption

The electrolytes absorbed by the small intestine are from both GI secretions and ingested foods. Since electrolytes dissociate into ions in water, most are absorbed via active transport throughout the entire small intestine. During absorption, co-transport mechanisms result in the accumulation of sodium ions inside the cells, whereas anti-port mechanisms reduce the potassium ion concentration inside the cells. To restore the sodium-potassium gradient across the cell membrane, a sodium – potassium pump requiring ATP pumps sodium out and potassium in.

In general, all minerals that enter the intestine are absorbed, whether you need them or not. Iron and calcium are exceptions;
they are absorbed in the duodenum in amounts that meet the body's current requirements, as follows:

Iron—The ionic iron needed for the production of hemoglobin is absorbed into mucosal cells via active transport. Once inside mucosal cells, ionic iron binds to the protein ferritin, creating iron-ferritin complexes that store iron until needed. When the body has enough iron, most of the stored iron is lost when worn-out epithelial cells slough off. When the body needs iron because, for example, it is lost during acute or chronic bleeding, there is increased uptake of iron from the intestine and accelerated release of iron into the bloodstream. Since women experience significant iron loss during

menstruation, they have around four times as many iron transport proteins in their intestinal epithelial cells as do men.

Calcium—Blood levels of ionic calcium determine the absorption of dietary calcium. When blood levels of ionic calcium drop, parathyroid hormone (PTH) secreted by the parathyroid glands stimulates the release of calcium ions from bone matrices and increases the reabsorption of calcium by the kidneys. PTH also upregulates the activation of vitamin D in the kidney, which then facilitates intestinal calcium ion absorption.

Vitamin Absorption

The small intestine absorbs the vitamins that occur naturally in food and supplements. Fat-soluble vitamins (A, D, E, and K) are absorbed along with dietary lipids in micelles via simple diffusion. This is why you are advised to eat some fatty foods when you take fat-soluble vitamin supplements. Most water-soluble vitamins (including most B vitamins and vitamin C) also are absorbed by simple diffusion. An exception is vitamin B12, which is a very large molecule. Intrinsic factor secreted in the stomach binds to vitamin B12, preventing its digestion and creating a complex that binds to mucosal receptors in the terminal ileum, where it is taken up by endocytosis.

Water Absorption

Each day, about nine liters of fluid enter the small intestine. About 2.3 liters are ingested in foods and beverages, and the rest is from GI secretions. About 90 percent of this water is absorbed in the small intestine. Water absorption is driven by the concentration gradient of the water: The concentration of water is higher in chyme than it is in epithelial cells. Thus, water moves down its concentration gradient from the chyme into cells. As noted earlier, much of the remaining water is
then absorbed in the colon.

METABOLISM AND NUTRITION:

Eating is essential to life. Many of us look to eating as not only a necessity, but also a pleasure. You may have been told since childhood to start the day with a good breakfast to give you the energy to get through most of the day. You most likely have heard about the importance of a balanced diet, with plenty of fruits and vegetables. But what does this all mean to your body and the physiological processes it carries out each day? You need to absorb a range of nutrients so that your cells have the building blocks for metabolic processes that release the energy for the cells to carry out their daily jobs, to manufacture new proteins, cells, and body parts, and to recycle materials in the cell. This chapter will take you through some of the chemical reactions essential to life, the sum of which is referred to as metabolism. The focus of these discussions will be anabolic reactions and catabolic reactions. You will examine the various chemical reactions that are important to sustain life, including why you must have oxygen, how

mitochondria transfer energy, and the importance of certain "metabolic" hormones and vitamins. Metabolism varies, depending on age, gender, activity level, fuel consumption, and lean body mass. Your own metabolic
rate fluctuates throughout life. By modifying your diet and exercise regimen, you can increase both lean body mass and metabolic rate. Factors affecting metabolism also play important roles in controlling muscle mass. Aging is known to decrease the metabolic rate by as much as 5 percent per year. Additionally, because men tend have more lean muscle mass then women, their basal metabolic rate (metabolic rate at rest) is higher; therefore, men tend to burn more calories than women do. Lastly, an individual's inherent metabolic rate is a function of the proteins and enzymes derived from their genetic background. Thus, your genes play a big role in your metabolism. Nonetheless, each person's body engages in the same overall metabolic processes.
Metabolic processes are constantly taking place in the body. **Metabolism** is the sum of all of the chemical reactions that are involved in catabolism and anabolism. The reactions governing the breakdown of food to obtain energy are called catabolic reactions. Conversely, anabolic reactions use the energy produced by catabolic reactions to synthesize larger molecules from smaller ones, such as when the body forms proteins by stringing together amino acids. Both sets of reactions are critical to maintaining life. Because catabolic reactions produce energy and anabolic reactions use energy

Catabolic Reactions
Catabolic reactions break down large organic molecules into smaller molecules, releasing the energy contained in the chemical bonds. These energy releases (conversions) are not 100 percent efficient. The amount of energy released is less than the total amount contained in the molecule. Approximately 40 percent of energy yielded from catabolic reactions is directly transferred to the high-energy molecule adenosine triphosphate (ATP).

Anabolic Reactions
In contrast to catabolic reactions, **anabolic reactions** involve the joining of smaller molecules into larger ones. Anabolic reactions combine monosaccharides to form polysaccharides, fatty acids to form triglycerides, amino acids to form proteins, and nucleotides to form nucleic acids. These processes require energy in the form of ATP molecules generated by catabolic reactions.

Hormonal Regulation of Metabolism

Catabolic and anabolic hormones in the body help regulate metabolic processes. **Catabolic hormones** stimulate the breakdown of molecules and the production of energy. These include cortisol, glucagon, adrenaline/epinephrine, and cytokines. All of these hormones are mobilized at specific times to meet the needs of the body. **Anabolic**

hormones are required for the synthesis of molecules and include growth hormone, insulin-like growth factor, insulin, testosterone, and
estrogen. **Table 24.1** summarizes the function of each of the catabolic hormones and **Table 24.2** summarizes the functions of the anabolic hormones.

Catabolic Hormones

Hormone	Function
Cortisol	Released from the adrenal gland in response to stress; its main role is to increase blood glucose levels by gluconeogenesis (breaking down fats and proteins)
Glucagon	Released from alpha cells in the pancreas either when starving or when the body needs to generate additional energy; it stimulates the breakdown of glycogen in the liver to increase blood glucose levels; its effect is the opposite of insulin; glucagon and insulin are a part of a negative-feedback system that stabilizes blood glucose levels
Adrenaline/ epinephrine	Released in response to the activation of the sympathetic nervous system; increases heart rate and heart contractility, constricts blood vessels, is a bronchodilator that opens (dilates) the bronchi of the lungs to increase air volume in the lungs, and stimulates gluconeogenesis

Anabolic Hormones

Hormone	Function
Growth hormone (GH)	Synthesized and released from the pituitary gland; stimulates the growth of cells, tissues, and bones
Insulin-like growth factor (IGF)	Stimulates the growth of muscle and bone while also inhibiting cell death (apoptosis)
Insulin	Produced by the beta cells of the pancreas; plays an essential role in carbohydrate and fat metabolism, controls blood glucose levels, and promotes the uptake of glucose into body cells; causes cells in muscle, adipose tissue, and liver to take up glucose from the blood and store it in the liver and muscle as glucagon; its effect is the opposite of glucagon; glucagon and insulin are a part of a negative-feedback system that stabilizes blood glucose levels
Testosterone	Produced by the testes in males and the ovaries in females; stimulates an increase in muscle mass and strength as well as the growth and strengthening of bone
Estrogen	Produced primarily by the ovaries, it is also produced by the liver and adrenal glands; its anabolic functions include increasing metabolism and fat deposition

carbohydrate metabolism

During digestion, carbohydrates are broken down into simple, soluble sugars that can be transported across the intestinal wall into the circulatory system to be transported throughout the body. Once the absorbed monosaccharides are transported to the tissues, the process of cellular respiration begins. This section will focus first on glycolysis, a process where the monosaccharide glucose is oxidized, releasing the energy stored in its bonds to produce ATP.

Glycolysis

Glucose is the body's most readily available source of energy. After digestive processes break polysaccharides down into monosaccharides, including glucose, the monosaccharides are transported across the wall of the small intestine and into the circulatory system, which transports them to the liver. In the liver, hepatocytes either pass the glucose on through the circulatory system or store excess glucose as glycogen. Cells in the body take up the circulating glucose in response to insulin and, through a series of reactions called **glycolysis**, transfer some of the energy in glucose to ADP to form ATP. The last step in glycolysis produces the product **pyruvate**. Glycolysis begins with the phosphorylation of glucose by hexokinase to form glucose-6-phosphate. This step uses one ATP, which is the donor of the phosphate group. In a series of reactions leading to pyruvate, the two phosphate groups are then transferred to two ADPs to form two ATPs. Thus, glycolysis uses two ATPs but generates four ATPs, yielding a net gain of two ATPs and two molecules of pyruvate. In the presence of oxygen, pyruvate continues on to the Krebs cycle (also called the **citric acid cycle** or **tricarboxylic acid cycle (TCA)**, where additional energy is extracted and passed on. Glycolysis can be expressed as the following equation:

Glucose + 2ATP + 2NAD + + 4ADP + 2P*i* → 2 Pyruvate + 4ATP + 2NADH + 2H+

Gluconeogenesis

Gluconeogenesis is the synthesis of new glucose molecules from pyruvate, lactate, glycerol, or the amino acids alanine or glutamine. This process takes place primarily in the liver during periods of low glucose, that is, under conditions of fasting, starvation, and low carbohydrate diets. So, the question can be raised as to why the body would create something it has just spent a fair amount of effort to break down? Certain key organs, including the brain, can use only glucose as an energy source; therefore, it is essential that the body maintain a minimum blood glucose concentration. When the blood glucose concentration falls below that certain point, new glucose is synthesized by the liver to raise the blood concentration to normal.

Gluconeogenesis is not simply the reverse of glycolysis. There are some important differences. Pyruvate is a common starting material for gluconeogenesis. First, the pyruvate is converted into oxaloacetate**.**

Lipid Metabolism.

Fats (or triglycerides) within the body are ingested as food or synthesized by adipocytes or hepatocytes from carbohydrate precursors. Lipid metabolism entails the oxidation of fatty acids to either generate energy or synthesize new lipids from smaller constituent

molecules. Lipid metabolism is associated with carbohydrate metabolism, as products of glucose (such as acetyl CoA) can be converted into lipids.

Lipid metabolism begins in the intestine where ingested **triglycerides** are broken down into free fatty acids. These fatty acids can be transported across the intestinal membrane. However, once they cross the membrane, they are recombined to again form triglyceride molecules. Within the intestinal cells, these triglycerides are packaged along with cholesterol molecules in phospholipid vesicles called **chylomicrons** (contain triglycerides, cholesterol molecules, and other apolipoproteins (protein molecules). They function to carry these water-insoluble molecules from the intestine, through the lymphatic system, and into the bloodstream, which carries the lipids to adipose tissue for storage.). The chylomicrons enable fats and cholesterol to move within the aqueous environment of your lymphatic and circulatory systems. Chylomicrons leave the enterocytes by exocytosis and enter the lymphatic system via lacteals in the villi of the intestine. From the lymphatic system, the chylomicrons are transported to the circulatory system. Once in the circulation, they can either go to the liver or be stored in fat cells (adipocytes) that comprise adipose (fat) tissue found throughout the body.

Lipolysis

To obtain energy from fat, triglycerides must first be broken down by hydrolysis into their two principal components, fatty acids and glycerol. This process, called **lipolysis**, takes place in the cytoplasm. The resulting fatty acids are oxidized by β- oxidation into acetyl CoA, which is used by the Krebs cycle. The glycerol that is released from triglycerides after lipolysis directly enters the glycolysis pathway as DHAP. Because one triglyceride molecule yields three fatty acid molecules with as much as 16 or more carbons in each one, fat molecules yield more energy than carbohydrates and are an important source of energy for the human body. Triglycerides yield more than twice the energy per unit mass when compared to carbohydrates and proteins. Therefore, when glucose levels are low, triglycerides can be converted into acetyl CoA molecules and used to

generate ATP through aerobic respiration. The breakdown of fatty acids, called **fatty acid oxidation** or **beta (β)-oxidation**, begins in the cytoplasm, where fatty acids are converted into fatty acyl CoA molecules. This fatty acyl CoA combines with carnitine to create a fatty acyl carnitine molecule, which helps to transport the fatty acid across the mitochondrial membrane. Once inside the mitochondrial matrix, the fatty acyl carnitine molecule is converted back into fatty acyl CoA and then into acetyl CoA. The newly formed acetyl CoA enters the Krebs cycle and is used to produce ATP in the same way as acetyl CoA derived from pyruvate.

Lipogenesis

When glucose levels are plentiful, the excess acetyl CoA generated by glycolysis can be converted into fatty acids, triglycerides, cholesterol, steroids, and bile salts. This

process, called **lipogenesis**, creates lipids (fat) from the acetyl CoA and takes place in the cytoplasm of adipocytes (fat cells) and hepatocytes (liver cells). When you eat more glucose or carbohydrates than your body needs, your system uses acetyl CoA to turn the excess into fat. Although there are several metabolic sources of acetyl CoA, it is most commonly derived from glycolysis. Acetyl CoA availability is significant, because it initiates lipogenesis. Lipogenesis begins with acetyl CoA and advances by the subsequent addition of two carbon, atoms from another acetyl CoA; this process is repeated until fatty acids are the appropriate length. Because this is a bond creating anabolic process, ATP is consumed. However, the creation of triglycerides and lipids is an efficient way of storing the energy available in carbohydrates. Triglycerides and lipids, high-energy molecules, are stored in adipose tissue until they are needed. Although lipogenesis occurs in the cytoplasm, the necessary acetyl CoA is created in the mitochondria and cannot be transported across the mitochondrial membrane. To solve this problem, pyruvate is converted into both oxaloacetate and acetyl CoA. Two different enzymes are required for these conversions. Oxaloacetate forms via the action of pyruvate carboxylase, whereas the action of pyruvate dehydrogenase creates acetyl CoA. Oxaloacetate and acetyl CoA combine to form citrate, which can cross the mitochondrial membrane and enter the cytoplasm. In the cytoplasm, citrate is converted back into oxaloacetate and acetyl CoA. Oxaloacetate is converted into malate and then into pyruvate. Pyruvate crosses back across the mitochondrial membrane to wait for the next cycle of lipogenesis. The acetyl CoA is converted into malonyl CoA that is used to synthesize fatty acids.

Protein Metabolism:

When the amino acids transported across the intestinal mucosa to be used to create new proteins, or to be converted into fats or acetyl CoA and used in the Krebs cycle.

smaller peptides are catabolized into their constituent amino acids, which are transported across the apical surface of the intestinal mucosa in a process that is mediated by sodium-amino acid transporters. These transporters bind sodium and then bind the amino acid to transport it across the membrane. At the basal surface of the mucosal cells, the sodium and amino acid are released. The sodium can be reused in the transporter, whereas the amino acids are transferred into the bloodstream to be transported to the liver and cells throughout the body for protein synthesis. Freely available amino acids are used to create proteins. If amino acids exist in excess, the body has no capacity or mechanism for their storage; thus, they are converted into glucose or ketones, or they are decomposed. Amino acid decomposition results in hydrocarbons and nitrogenous waste. However, high concentrations of nitrogen are toxic. The urea cycle processes nitrogen and facilitates its excretion from the body.

Urea Cycle

The **urea cycle** is a set of biochemical reactions that produces urea from ammonium ions in order to prevent a toxic level of ammonium in the body. It occurs primarily in the liver and, to a lesser extent, in the kidney. Prior to the urea cycle, ammonium ions are produced from the breakdown of amino acids. In these reactions, an amine group, or ammonium ion, from the amino acid is exchanged with a keto group on another molecule. This **transamination** event creates a molecule that is necessary for the Krebs cycle and an ammonium ion that enters into the urea cycle to be eliminated. In the urea cycle, ammonium is combined with CO2, resulting in urea and water. The urea is eliminated through the kidneys in the urine. Amino acids can also be used as a source of energy, especially in times of starvation. Because the processing of amino acids results in the creation of metabolic intermediates, including pyruvate, acetyl CoA, acetoacyl CoA, oxaloacetate, and α-ketoglutarate, amino acids can serve as a source of energy production through the Krebs cycle.

Food and Metabolism

The amount of energy that is needed or ingested per day is measured in calories. The nutritional **Calorie** (C) is the amount of heat it takes to raise 1 kg (1000 g) of water by 1 °C. This is different from the calorie (c) used in the physical sciences, which is the amount of heat it takes to raise 1 g of water by 1 °C. When we refer to "calorie," we are referring to the nutritional Calorie. On average, a person needs 1500 to 2000 calories per day to sustain (or carry out) daily activities. The total number of calories needed by one person is dependent on their body mass, age, height, gender, activity level, and the amount of exercise per day. If exercise is regular part of one's day, more calories are required. As a rule, people underestimate the number of calories ingested and overestimate the amount they burn through exercise. This can lead to ingestion of too many calories per day. The accumulation of an extra 3500 calories adds one pound of weight. If an excess of 200 calories per day is ingested, one extra pound of body weight will be gained every 18 days. At that rate, an extra 20 pounds can be gained over the course of a year. Of course, this increase in calories could be offset by increased exercise. Running or jogging one mile burns almost 100 calories.

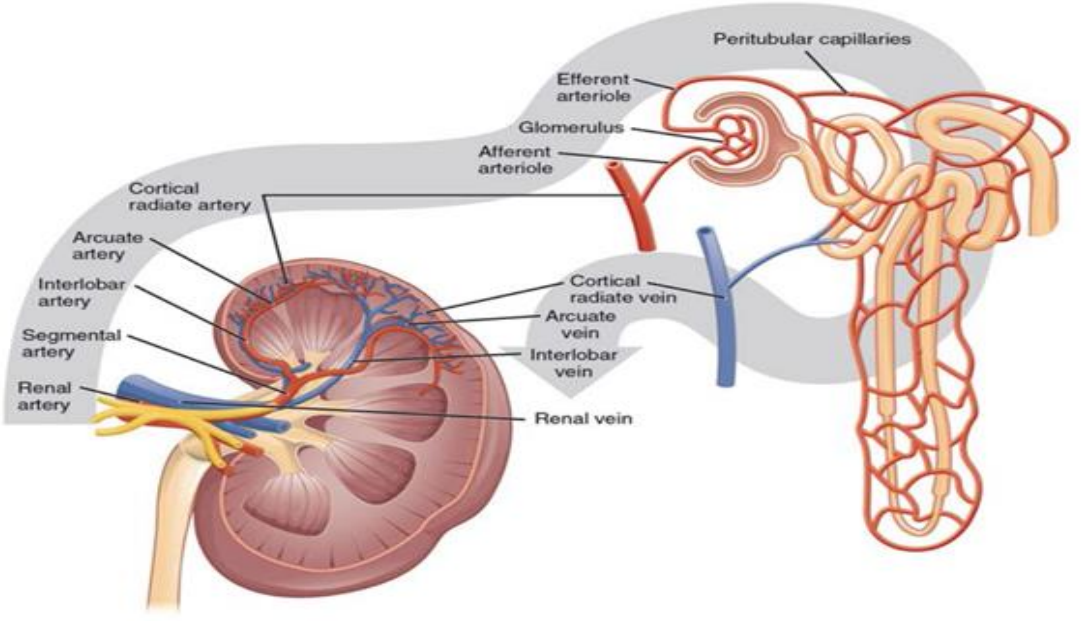
The type of food ingested also affects the body's metabolic rate. Processing of carbohydrates requires less energy than processing of proteins. In fact, the breakdown of carbohydrates requires the least amount of energy, whereas the processing of proteins demands the most energy. In general, the number of calories ingested and the number of calories burned determines the overall weight. To lose weight, the number of calories burned per day must exceed the number ingested. Calories are in almost everything you ingest, so when considering calorie intake, beverages must also be considered. To help

provide guidelines regarding the types and quantities of food that should be eaten every day, the USDA has updated their food guidelines from MyPyramid to MyPlate. They have put the recommended elements of a healthy meal into the context of a place setting of food. MyPlate categorizes food into the standard six food groups: fruits, vegetables, grains, protein foods, dairy, and oils. The accompanying website gives clear recommendations regarding quantity and type of each food that you should consume each day, as well as identifying which foods belong in each category. The accompanying graphic gives a clear visual with general recommendations for a healthy and balanced meal. The guidelines recommend to "Make half your plate fruits and vegetables." The other half is grains and protein, with a slightly higher quantity of grains than protein. Dairy products are represented by a drink, but the quantity can be applied to other dairy products as well.

2- The Urinary System

The urinary system has roles you may be well aware of: cleansing the blood and ridding the body of wastes probably come to mind. However, there are additional, equally important functions played by the system. Take for example, regulation of pH, a function shared with the lungs and the buffers in the blood. Additionally, the regulation of blood pressure is a role shared with the heart and blood vessels. What about regulating the concentration of solutes in the blood? Did you know that the kidney is important in determining the concentration of red blood cells? Eighty-five percent of the erythropoietin (EPO) produced to stimulate red blood cell production is produced in the kidneys. The kidneys also perform the final synthesis step of vitamin D production, converting calcidiol to calcitriol, the active form of vitamin D.

The urinary system's ability to filter the blood resides in about 2 to 3 million tufts of specialized capillaries—the glomeruli—distributed more or less equally between the two kidneys. Because the glomeruli filter the blood based mostly on particle size, large elements like blood cells, platelets, antibodies, and albumen are excluded. The glomerulus is the first part of the nephron, which then continues as a highly specialized tubular structure responsible for creating the final urine composition. All other solutes, such as ions, amino acids, vitamins, and wastes, are filtered to create a filtrate composition very similar to plasma. The glomeruli create about 200 liters (189 quarts) of this filtrate every day, yet you excrete less than two liters of waste.



Nephrons: The Functional Unit

Normal Urine Characteristics

Characteristic	Normal values
Color	Pale yellow to deep amber
Odor	Odorless
Volume	750–2000 mL/24 hour
pH	4.5–8.0
Specific gravity	1.003–1.032
Osmolarity	40–1350 mOsmol/kg
Urobilinogen	0.2–1.0 mg/100 mL
White blood cells	0–2 HPF (per high-power field of microscope)
Leukocyte esterase	None
Protein	None or trace
Bilirubin	<0.3 mg/100 mL
Ketones	None
Nitrites	None
Blood	None
Glucose	None

Physiology of Urine Formation

Having reviewed the anatomy and microanatomy of the urinary system, now is the time to focus on the physiology. You will discover that different parts of the nephron utilize specific processes to produce urine: filtration, reabsorption, and secretion. You will learn how each of these processes works and where they occur along the nephron and collecting ducts. The physiologic goal is to modify the composition of the plasma and, in doing so, produce the waste product urine.

Glomerular Filtration Rate (GFR)

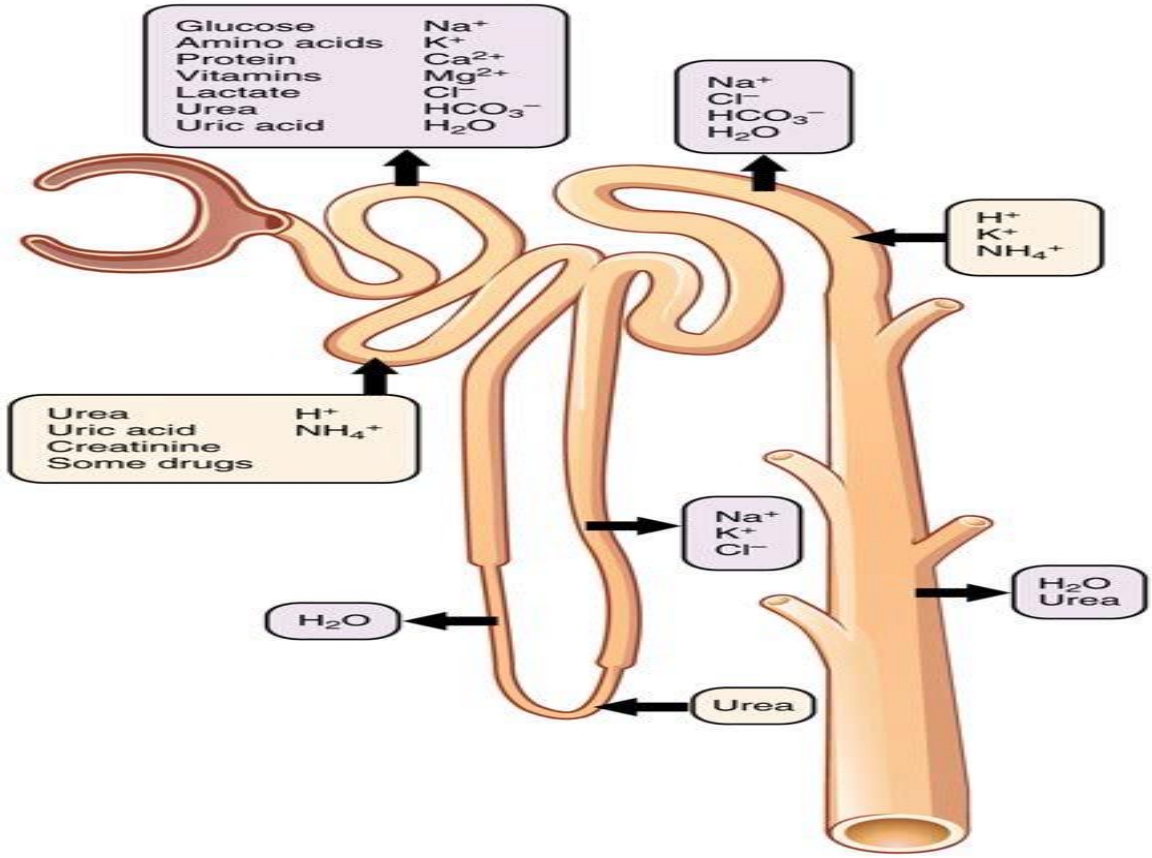
The volume of filtrate formed by both kidneys per minute is termed the **glomerular filtration rate (GFR)**. The heart pumps about 5 L blood per min under resting conditions. Approximately 20 percent or one liter enters the kidneys to be filtered. On average, this liter results in the production of about 125 mL/min filtrate produced in men (range of 90 to 140 mL/min) and 105 mL/min filtrate produced in women (range of 80 to 125 mL/min). This amount equates to a volume of about 180 L/day in men and 150 L/day in women. Ninety-nine percent of this filtrate is returned to the circulation by reabsorption so that only about 1–2 liters of urine are produced per day. GFR is

influenced by the hydrostatic pressure and colloid osmotic pressure on either side of the capillary membrane of the glomerulus. Recall that filtration occurs as pressure forces fluid and solutes through a semipermeable barrier with the solute movement constrained by particle size.

Hydrostatic pressure is the pressure produced by a fluid against a surface. If you have a fluid on both sides of a barrier, both fluids exert a pressure in opposing directions. Net fluid movement will be in the direction of the lower pressure. Osmosis is the movement of solvent (water) across a membrane that is impermeable to a solute in the solution. This creates a pressure, osmotic pressure, which will exist until the solute concentration is the same on both sides of a semipermeable membrane. As long as the concentration differs, water will move. Glomerular filtration occurs when glomerular hydrostatic pressure exceeds the luminal hydrostatic pressure of Bowman's capsule. There is also an opposing force, the osmotic pressure, which is typically higher in the glomerular capillary. To understand why this is so, look more closely at the microenvironment on either side of the filtration membrane. You will find osmotic pressure exerted by the solutes inside the lumen of the capillary as well as inside of Bowman's capsule. Since the filtration membrane limits the size of particles crossing the membrane, the osmotic pressure inside the glomerular capillary is higher than the osmotic pressure in Bowman's capsule. Recall that cells and the medium-to-large proteins cannot pass between the podocyte processes or through the fenestrations of the capillary endothelial cells. This means that red and white blood cells, platelets, albumins, and other proteins too large to pass through the filter remain in the capillary, creating an average colloid osmotic pressure of 30 mm Hg within the capillary. The absence of proteins in Bowman's space (the lumen within Bowman's capsule) results in an osmotic pressure near zero. Thus, the only pressure moving fluid across the capillary wall into the lumen of Bowman's space is hydrostatic pressure. Hydrostatic (fluid) pressure is sufficient to push water through the membrane despite the osmotic pressure working against it.

Tubular Reabsorption

With up to 180 liters per day passing through the nephrons of the kidney, it is quite obvious that most of that fluid and its contents must be reabsorbed. That recovery occurs in the PCT, loop of Henle, DCT, and the collecting ducts (**Table 25.5** and **Figure 25.17**). Various portions of the nephron differ in their capacity to reabsorb water and specific solutes. While much of the reabsorption and secretion occur passively based on concentration gradients, the amount of water that is reabsorbed or lost is tightly regulated. This control is exerted directly by ADH and aldosterone, and indirectly by renin. Most water is recovered in the PCT, loop of Henle, and DCT. About 10 percent (about 18 L) reaches the collecting ducts. The collecting ducts, under the influence of ADH, can recover almost all of the water passing through them, in cases of dehydration, or almost none of the water, in cases of over-hydration.



Substances Secreted or Reabsorbed in the Nephron and Their Locations

Substance	PCT	Loop of Henle	DCT	Collecting ducts
Glucose	Almost 100 percent reabsorbed; secondary active transport with Na^+			
Oligopeptides, proteins, amino acids	Almost 100 percent reabsorbed; symport with Na^+			
Vitamins	Reabsorbed			
Lactate	Reabsorbed			
Creatinine	Secreted			

Substances Secreted or Reabsorbed in the Nephron and Their Locations

Substance	PCT	Loop of Henle	DCT	Collecting ducts
Urea	50 percent reabsorbed by diffusion; also secreted	Secretion, diffusion in descending limb		Reabsorption in medullary collecting ducts; diffusion
Sodium	65 percent actively reabsorbed	25 percent reabsorbed in thick ascending limb; active transport	5 percent reabsorbed; active	5 percent reabsorbed stimulated by aldosterone; active
Chloride	Reabsorbed, symport with Na^+, diffusion	Reabsorbed in thin and thick ascending limb; diffusion in ascending limb	Reabsorbed; diffusion	Reabsorbed; symport
Water	67 percent reabsorbed osmotically with solutes	15 percent reabsorbed in descending limb; osmosis	8 percent reabsorbed if ADH; osmosis	Variable amounts reabsorbed, controlled by ADH, osmosis
Bicarbonate	80–90 percent symport reabsorption with Na^+	Reabsorbed, symport with Na^+ and antiport with Cl^-; in ascending limb		Reabsorbed antiport with Cl^-
H^+	Secreted; diffusion		Secreted; active	Secreted; active
NH_4^+	Secreted; diffusion		Secreted; diffusion	Secreted; diffusion
HCO_3^-	Reabsorbed; diffusion	Reabsorbed; diffusion in ascending limb	Reabsorbed; diffusion	Reabsorbed; antiport with Na^+
Some drugs	Secreted		Secreted; active	Secreted; active
Potassium	65 percent reabsorbed; diffusion	20 percent reabsorbed in thick ascending limb; symport	Secreted; active	Secretion controlled by aldosterone; active
Calcium	Reabsorbed; diffusion	Reabsorbed in thick ascending limb; diffusion		Reabsorbed if parathyroid hormone present; active
Magnesium	Reabsorbed; diffusion	Reabsorbed in thick ascending limb; diffusion	Reabsorbed	
Phosphate	85 percent reabsorbed, inhibited by parathyroid hormone, diffusion		Reabsorbed; diffusion	

Endocrine Regulation of Kidney Function

Renin–Angiotensin–Aldosterone

Renin is an enzyme that is produced by the granular cells of the afferent arteriole at the JGA. It enzymatically converts angiotensinogen (made by the liver, freely circulating) into angiotensin I. Its release is stimulated by prostaglandins and NO from the JGA in response to decreased extracellular fluid volume.

ACE is not a hormone but it is functionally important in regulating systemic blood pressure and kidney function. It is produced in the lungs but binds to the surfaces of endothelial cells in the afferent arterioles and glomerulus. It enzymatically converts inactive angiotensin I into active angiotensin II. ACE is important in raising blood pressure. People with high blood pressure are sometimes prescribed ACE inhibitors to lower their blood pressure. Angiotensin II is a potent vasoconstrictor that plays an immediate role in the regulation of blood pressure. It acts systemically to cause vasoconstriction as well as constriction of both the afferent and efferent arterioles of the glomerulus. In instances of blood loss or dehydration, it reduces both GFR and renal blood flow, thereby limiting fluid loss and preserving blood volume. Its release is usually stimulated by decreases in blood pressure, and so the preservation of adequate blood pressure is its primary role.

Aldosterone, often called the "salt-retaining hormone," is released from the adrenal cortex in response to angiotensin II or directly in response to increased plasma K+. It promotes Na+ reabsorption by the nephron, promoting the retention of water. It is also important in regulating K+, promoting its excretion. (This dual effect on two minerals and its origin in the adrenal cortex explains its designation as a mineralocorticoid.) As a result, renin has an immediate effect on blood pressure due to angiotensin II–stimulated vasoconstriction and a prolonged effect through Na+ recovery due to aldosterone. At the same time that aldosterone causes increased recovery of Na+, it also causes greater loss of K+. Progesterone is a steroid that is structurally similar to aldosterone. It binds to the aldosterone receptor and weakly stimulates Na+ reabsorption and
increased water recovery. This process is unimportant in men due to low levels of circulating progesterone. It may cause increased retention of water during some periods of the menstrual cycle in women when progesterone levels increase.

Antidiuretic Hormone (ADH)

Diuretics are drugs that can increase water loss by interfering with the recapture of solutes and water from the forming urine. They are often prescribed to lower blood pressure. Coffee, tea, and alcoholic beverages are familiar diuretics. ADH, a 9-amino acid peptide released by the posterior pituitary, works to do the exact opposite. It promotes the recovery of water, decreases urine volume, and maintains plasma osmolarity and blood pressure. It does so by stimulating the movement of aquaporin proteins into the apical cell membrane of principal cells of the collecting ducts to form

water channels, allowing the transcellular movement of water from the lumen of the collecting duct into the interstitial space in the medulla of the kidney by osmosis. From there, it enters the vasa recta capillaries to return to the circulation. Water is attracted by the high osmotic environment of the deep kidney medulla.

Diuretics and Fluid Volume

A **diuretic** is a compound that increases urine volume. Three familiar drinks contain diuretic compounds: coffee, tea, and alcohol. The caffeine in coffee and tea works by promoting vasodilation in the nephron, which increases GFR. Alcohol increases GFR by inhibiting ADH release from the posterior pituitary, resulting in less water recovery by the collecting duct. In cases of high blood pressure, diuretics may be prescribed to reduce blood volume and, thereby, reduce blood pressure. The most frequently prescribed anti-hypertensive diuretic is hydrochlorothiazide. It inhibits the Na+/ Cl– symporter in the DCT and collecting duct. The result is a loss of Na+ with water following passively by osmosis. Osmotic diuretics promote water loss by osmosis. An example is the indigestible sugar mannitol, which is most often administered to reduce brain swelling after head injury. However, it is not the only sugar that can produce a diuretic effect. In cases of poorly controlled diabetes mellitus, glucose levels exceed the capacity of the tubular glucose symporters, resulting in glucose in the urine. The unrecovered glucose becomes a powerful osmotic diuretic. Classically, in the days before glucose could be detected in the blood and urine, clinicians identified diabetes mellitus by the three Ps: polyuria (diuresis), polydipsia (increased thirst), and polyphagia (increased hunger).

The Urinary System and Homeostasis

Vitamin D Synthesis

In order for vitamin D to become active, it must undergo a hydroxylation reaction in the kidney, that is, an –OH group must be added to calcidiol to make calcitriol (1,25-dihydroxycholecalciferol). Activated vitamin D is important for absorption of Ca++ in the digestive tract, its reabsorption in the kidney, and the maintenance of normal serum concentrations of Ca++ and phosphate. Calcium is vitally important in bone health, muscle contraction, hormone secretion, and neurotransmitter release. Inadequate Ca++ leads to disorders like osteoporosis and **osteomalacia** in adults and rickets in children. Deficits may also result in problems with cell proliferation, neuromuscular function, blood clotting, and the inflammatory response. Recent research has confirmed that vitamin D receptors are present in most, if not all, cells of the body, reflecting the systemic importance of vitamin D. Many scientists have suggested it be referred to as a hormone rather than a vitamin.

Erythropoiesis

EPO is a 193-amino acid protein that stimulates the formation of red blood cells in the bone marrow. The kidney produces 85 percent of circulating EPO; the liver, the remainder. If you move to a higher altitude, the partial pressure of oxygen is lower, meaning there is less pressure to push oxygen across the alveolar membrane and into the red blood cell. One way the body compensates is to manufacture more red blood cells by increasing EPO production. If you start an aerobic exercise program, your tissues will need more oxygen to cope, and the kidney will respond with more EPO. If erythrocytes are lost due to severe or prolonged bleeding, or under produced due to disease or severe malnutrition, the kidneys come to the rescue by producing more EPO. Renal failure (loss of EPO production) is associated with anemia, which makes it difficult for the body to cope with increased oxygen demands or to supply oxygen adequately even under normal conditions. Anemia diminishes performance and can be life threatening.

Blood Pressure Regulation

Due to osmosis, water follows where Na+ leads. Much of the water the kidneys recover from the forming urine follows the reabsorption of Na+. ADH stimulation of aquaporin channels allows for regulation of water recovery in the collecting ducts. Normally, all of the glucose is recovered, but loss of glucose control (diabetes mellitus) may result in an osmotic dieresis severe enough to produce severe dehydration and death. A loss of renal function means a loss of effective vascular volume control, leading to hypotension (low blood pressure) or hypertension (high blood pressure), which can lead to stroke, heart attack, and aneurysm formation. The kidneys cooperate with the lungs, liver, and adrenal cortex through the renin–angiotensin–aldosterone system (see **Figure 25.14**). The liver synthesizes and secretes the inactive precursor angiotensinogen. When the blood pressure is low, the kidney synthesizes and releases renin. Renin converts angiotensinogen into angiotensin I, and ACE produced in the lung converts angiotensin I into biologically active angiotensin II (**Figure 25.23**). The immediate and short-term effect of angiotensin II is to raise blood pressure by causing widespread vasoconstriction. angiotensin II also stimulates the adrenal cortex to release the steroid hormone aldosterone, which results in renal reabsorption of Na+ and its associated osmotic recovery of water. The reabsorption of Na+ helps to raise and maintain blood pressure over a longer term.

Regulation of Osmolarity

Blood pressure and osmolarity are regulated in a similar fashion. Severe hypo-osmolarity can cause problems like lysis (rupture) of blood cells or widespread edema, which is due to a solute imbalance. Inadequate solute concentration (such as protein) in the plasma results in water moving toward an area of greater solute concentration, in

this case, the interstitial space and cell cytoplasm. If the kidney glomeruli are damaged by an autoimmune illness, large quantities of protein may be lost in the urine. The resultant drop in serum osmolarity leads to widespread edema that, if severe, may lead to damaging or fatal brain swelling. Severe hypertonic conditions may arise with severe dehydration from lack of water intake, severe vomiting, or uncontrolled diarrhea. When the kidney is unable to recover sufficient water from the forming urine, the consequences may be severe (lethargy, confusion, muscle cramps, and finally, death).

Recovery of Electrolytes

Sodium, calcium, and potassium must be closely regulated. The role of Na^+ and Ca^{++} homeostasis has been discussed at length. Failure of K^+ regulation can have serious consequences on nerve conduction, skeletal muscle function, and most significantly, on cardiac muscle contraction and rhythm.

pH Regulation

Recall that enzymes lose their three-dimensional conformation and, therefore, their function if the pH is too acidic or basic.This loss of conformation may be a consequence of the breaking of hydrogen bonds. Move the pH away from the optimum for a specific enzyme and you may severely hamper its function throughout the body, including hormone binding, central nervous system signaling, or myocardial contraction. Proper kidney function is essential for pH homeostasis.

3-THE CARDIOVASCULAR SYSTEM

Recall that blood is a connective tissue. Like all connective tissues, it is made up of cellular elements and an extracellular matrix. The cellular elements—referred to as the formed elements—include red blood cells (RBCs), white blood cells (WBCs), and cell fragments called platelets. The extracellular matrix, called plasma, makes blood unique among connective tissues because it is fluid. This fluid, which is mostly water, perpetually suspends the formed elements and enables them to circulate throughout the body within the cardiovascular system.

Functions of Blood

The primary function of blood is to deliver oxygen and nutrients to and remove wastes from body cells, but that is only the beginning of the story. The specific functions of blood also include defense, distribution of heat, and maintenance of homeostasis.

Transportation

Nutrients from the foods you eat are absorbed in the digestive tract. Most of these travel in the bloodstream directly to the liver, where they are processed and released back into the bloodstream for delivery to body cells. Oxygen from the air you breathe diffuses into the blood, which moves from the lungs to the heart, which then pumps it out to the rest of the body. Moreover, endocrine glands scattered throughout the body release their products, called hormones, into the bloodstream, which carries them to distant target cells. Blood also picks up cellular wastes and byproducts, and transports them to various organs for removal. For instance, blood moves carbon dioxide to the lungs for exhalation from the body, and various waste products are transported to the kidneys and liver for excretion from the body in the form of urine or bile.

Defense

Many types of WBCs protect the body from external threats, such as disease-causing bacteria that have entered the bloodstream in a wound. Other WBCs seek out and destroy internal threats, such as cells with mutated DNA that could multiply to become cancerous, or body cells infected with viruses. When damage to the vessels results in bleeding, blood platelets and certain proteins dissolved in the plasma, the fluid portion of the blood, interact to block the ruptured areas of the blood vessels involved. This protects the body from further blood loss.

Maintenance of Homeostasis

Recall that body temperature is regulated via a classic negative-feedback loop. If you were exercising on a warm day, your rising core body temperature would

trigger several homeostatic mechanisms, including increased transport of blood from your core to your body periphery, which is typically cooler. As blood passes through the vessels of the skin, heat would be dissipated to the environment, and the blood returning to your body core would be cooler. In contrast, on a cold day, blood is diverted away from the skin to maintain a warmer body core. In extreme cases, this may result in frostbite. Blood also helps to maintain the chemical balance of the body. Proteins and other compounds in blood act as buffers, which thereby help to regulate the pH of body tissues. Blood also helps to regulate the water content of body cells.

Composition of Blood

You have probably had blood drawn from a superficial vein in your arm, which was then sent to a lab for analysis. Some of the most common blood tests—for instance, those measuring lipid or glucose levels in plasma—determine which substances are present within blood and in what quantities. Other blood tests check for the composition of the blood itself, including
the quantities and types of formed elements. One such test, called a hematocrit, measures the percentage of RBCs, clinically known as erythrocytes, in a blood sample. It is performed by spinning the blood sample in a specialized centrifuge, a process that causes the heavier elements suspended within the blood sample to separate from the lightweight, liquid plasma (Figure 18.2). Because the heaviest elements in blood are the erythrocytes, these settle at the very bottom of the hematocrit tube. Located above the erythrocytes is a pale, thin layer composed of the remaining formed elements of blood. These are the WBCs, clinically known as leukocytes, and
the platelets, cell fragments also called thrombocytes. This layer is referred to as the buffy coat because of its color; it normally constitutes less than 1 percent of a blood sample. Above the buffy coat is the blood plasma, normally a pale, straw-colored fluid, which constitutes the remainder of the sample. The volume of erythrocytes after centrifugation is also commonly referred to as packed cell volume (PCV). In normal blood, about 45 percent of a sample is erythrocytes. The hematocrit of any one sample can vary significantly, however, about 36–50 percent, according to gender and other factors. Normal hematocrit values for females range from 37 to 47,
with a mean value of 41; for males, hematocrit ranges from 42 to 52, with a mean of 47. The percentage of other formed elements, the WBCs and platelets, is extremely small so it is not normally considered with the hematocrit. So the mean plasma percentage is the percent of blood that is not erythrocytes: for females, it is approximately 59 (or 100 minus 41), and
for males, it is approximately 53 (or 100 minus 47).

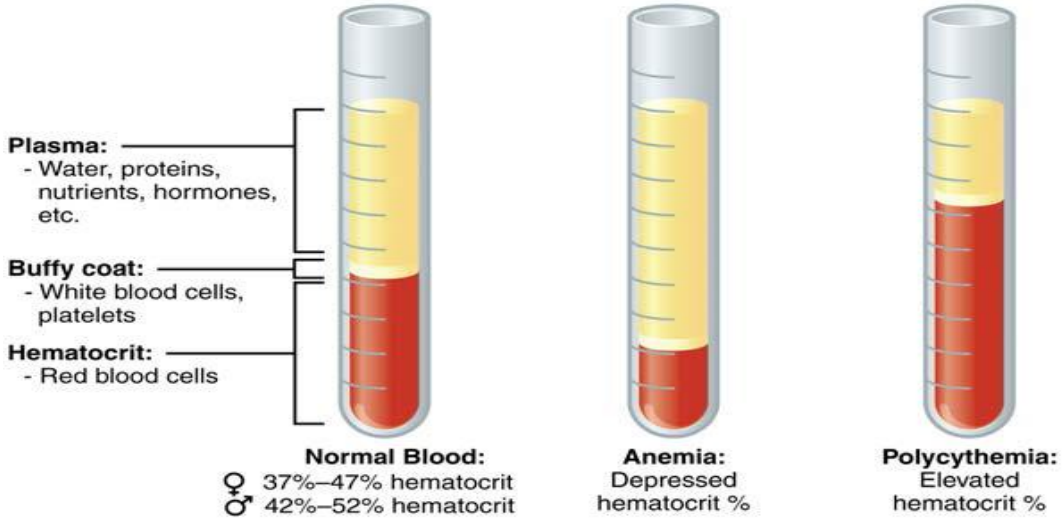


Figure 18.2 Composition of Blood

Characteristics of Blood

When you think about blood, the first characteristic that probably comes to mind is its color. Blood that has just taken up oxygen in the lungs is bright red, and blood that has released oxygen in the tissues is a more dusky red. This is because hemoglobin is a pigment that changes color, depending upon the degree of oxygen saturation. Blood is viscous and somewhat sticky to the touch. It has a viscosity approximately five times greater than water. Viscosity is a measure of a fluid's thickness or resistance to flow, and is influenced by the presence of the plasma proteins and formed elements within the blood. The viscosity of blood has a dramatic impact on blood pressure and flow. Consider the difference in flow between water and honey. The more viscous honey would demonstrate a greater resistance to flow than the less viscous water. The same principle applies to blood. The normal temperature of blood is slightly higher than normal body temperature—about 38 °C (or 100.4 °F), compared to 37 °C (or 98.6 °F) for an internal body temperature reading, although daily variations of 0.5 °C are normal. Although the surface of blood vessels is relatively smooth, as blood flows through them, it experiences some friction and resistance, especially as vessels age and lose their elasticity, thereby producing heat. This accounts for its slightly higher temperature. The pH of blood averages about 7.4; however, it can range from 7.35 to 7.45 in a healthy person. Blood is therefore somewhat more basic (alkaline) on a chemical scale than pure water, which has a pH of 7.0. Blood contains numerous buffers that actually help to regulate pH. Blood constitutes approximately 8 percent of adult body weight. Adult males typically average about 5 to 6 liters of blood.
Females average 4–5 liters.

Blood Plasma

Like other fluids in the body, plasma is composed primarily of water: In fact, it is about 92 percent water. Dissolved or suspended within this water is a mixture of substances, most of which are proteins. There are literally hundreds of substances dissolved or suspended in the plasma, although many of them are found only in very small quantities.

Plasma Proteins

About 7 percent of the volume of plasma—nearly all that is not water—is made of proteins. These include several plasma proteins (proteins that are unique to the plasma), plus a much smaller number of regulatory proteins, including enzymes and some hormones. The major components of plasma are summarized in **Figure 18.3**.

The three major groups of plasma proteins are as follows:

• **Albumin** is the most abundant of the plasma proteins. Manufactured by the liver, albumin molecules serve as binding proteins—transport vehicles for fatty acids and steroid hormones. Recall that lipids are hydrophobic; however, their binding to albumin enables their transport in the watery plasma. Albumin is also the most significant contributor to the osmotic pressure of blood; that is, its presence holds water inside the blood vessels and draws water from the tissues, across blood vessel walls, and into the bloodstream. This in turn helps to maintain both blood volume and blood pressure. Albumin normally accounts for approximately 54 percent of the total plasma protein content, in clinical levels of 3.5–5.0 g/dL blood.

• The second most common plasma proteins are the **globulins**. A heterogeneous group, there are three main subgroups known as alpha, beta, and gamma globulins. The alpha and beta globulins transport iron, lipids, and the fat-soluble vitamins A, D, E, and K to the cells; like albumin, they also contribute to osmotic pressure. The gamma globulins are proteins involved in immunity and are better known as an **antibodies** or **immunoglobulins**. Although other plasma proteins are produced by the liver, immunoglobulins are produced by specialized leukocytes known as plasma cells. (Seek additional content for more information about immunoglobulins.) Globulins make up approximately 38 percent of the total plasma protein volume, in clinical levels of 1.0–1.5 g/dL blood.

• The least abundant plasma protein is **fibrinogen**. Like albumin and the alpha and beta globulins, fibrinogen is produced by the liver. It is essential for blood clotting, a process described later in this chapter. Fibrinogen accounts for about 7 percent of the total plasma protein volume, in clinical levels of 0.2–0.45 g/dL blood.

Other Plasma Solutes

In addition to proteins, plasma contains a wide variety of other substances. These include various electrolytes, such as sodium, potassium, and calcium ions; dissolved gases, such as oxygen, carbon dioxide, and nitrogen; various organic nutrients, such as vitamins, lipids, glucose, and amino acids; and metabolic wastes. All of these nonprotein solutes combined contribute approximately 1 percent to the total volume of plasma.

Component and % of blood	Subcomponent and % of component	Type and % (where appropriate)	Site of production	Major function(s)
Plasma 46–63 percent	Water 92 percent	Fluid	Absorbed by intestinal tract or produced by metabolism	Transport medium
	Plasma proteins 7 percent	Albumin 54–60 percent	Liver	Maintain osmotic concentration, transport lipid molecules
		Globulins 35–38 percent	Alpha globulins—liver	Transport, maintain osmotic concentration
			Beta globulins—liver	Transport, maintain osmotic concentration
			Gamma globulins (immunoglobulins)—plasma cells	Immune responses
		Fibrinogen 4–7 percent	Liver	Blood clotting in hemostasis
	Regulatory proteins <1 percent	Hormones and enzymes	Various sources	Regulate various body functions
	Other solutes 1 percent	Nutrients, gases, and wastes	Absorbed by intestinal tract, exchanged in respiratory system, or produced by cells	Numerous and varied
Formed elements 37–54 percent	Erythrocytes 99 percent	Erythrocytes	Red bone marrow	Transport gases, primarily oxygen and some carbon dioxide
	Leukocytes <1 percent Platelets <1 percent	Granular leukocytes: neutrophils eosinophils basophils	Red bone marrow	Nonspecific immunity
		Agranular leukocytes: lymphocytes monocytes	Lymphocytes: bone marrow and lymphatic tissue	Lymphocytes: specific immunity
			Monocytes: red bone marrow	Monocytes: nonspecific immunity
	Platelets <1 percent		Megakaryocytes: red bone marrow	Hemostasis

Production of the Formed Elements:

The lifespan of the formed elements is very brief. Although one type of leukocyte called memory cells can survive for years, most erythrocytes,

leukocytes, and platelets normally live only a few hours to a few weeks. Thus, the body must form new blood cells and platelets quickly and continuously. When you donate a unit of blood during a blood drive (approximately 475 mL, or about 1 pint), your body typically replaces the donated plasma within 24 hours, but it takes about 4 to 6 weeks to replace the blood cells. This restricts the frequency with which donors can contribute their blood. The process by which this replacement occurs is called **hemopoiesis**, or hematopoiesis (from the Greek root haima- = "blood"; -poiesis = "production").

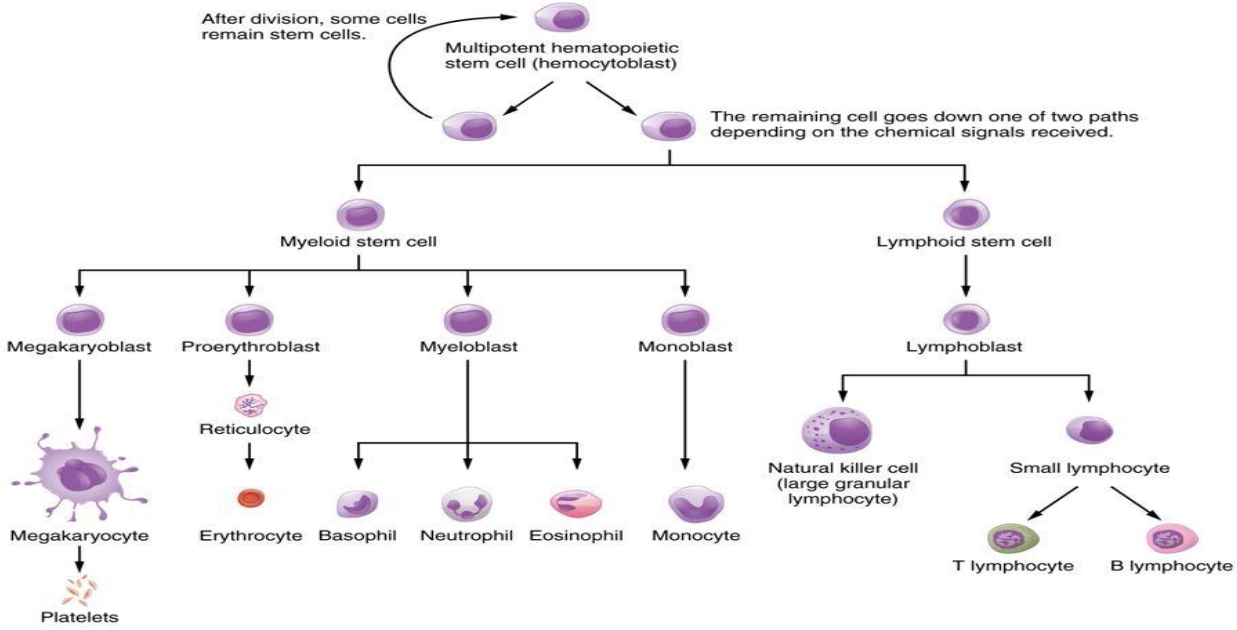
Sites of Hemopoiesis

Prior to birth, hemopoiesis occurs in a number of tissues, beginning with the yolk sac of the developing embryo, and continuing in the fetal liver, spleen, lymphatic tissue, and eventually the red bone marrow. Following birth, most hemopoiesis occurs in the red marrow, a connective tissue within the spaces of spongy (cancellous) bone tissue. In children, hemopoiesis can occur in the medullary cavity of long bones; in adults, the process is largely restricted to the cranial and

pelvic bones, the vertebrae, the sternum, and the proximal epiphyses of the femur and humerus.

Throughout adulthood, the liver and spleen maintain their ability to generate the formed elements. This process is referred to as extramedullary hemopoiesis (meaning hemopoiesis outside the medullary cavity of adult bones). When a disease such as bone cancer destroys the bone marrow, causing hemopoiesis to fail, extramedullary hemopoiesis may be initiated.

(**Figure 18.4**):



Hemopoietic Growth Factors

Development from stem cells to precursor cells to mature cells is again initiated

by hemopoietic growth factors. These include the following:

• **Erythropoietin (EPO)** is a glycoprotein hormone secreted by the interstitial fibroblast cells of the kidneys in response to low oxygen levels. It prompts the production of erythrocytes. Some athletes use synthetic EPO as a performance enhancing drug (called blood doping) to increase RBC counts and subsequently increase oxygen delivery to tissues throughout the body. EPO is a banned substance in most organized sports, but it is also used medically in the treatment of certain anemia, specifically those triggered by certain types of cancer, and other disorders in which increased erythrocyte counts and oxygen levels are desirable.

• **Thrombopoietin**, another glycoprotein hormone, is produced by the liver and kidneys. It triggers the development of megakaryocytes into platelets.

• **Cytokines** are glycoproteins secreted by a wide variety of cells, including red bone marrow, leukocytes, macrophages, fibroblasts, and endothelial cells. They act locally as autocrine or paracrine factors, stimulating the proliferation of progenitor cells and helping to stimulate both nonspecific and specific resistance to disease.

Erythrocytes

The **erythrocyte**, commonly known as a red blood cell (or RBC), is by far the most common formed element: A single drop of blood contains millions of erythrocytes and just thousands of leukocytes. Specifically, males have about 5.4 million erythrocytes per microliter (μL) of blood, and females have approximately 4.8 million per μL. In fact, erythrocytes are estimated to make up about 25 percent of the total cells in the body. As you can imagine, they are quite small cells, with a mean diameter of only about 7–8 micrometers (μm) (**Figure 18.5**). The primary functions of erythrocytes are to pick up inhaled oxygen from the lungs and transport it to the body's tissues, and to pick up some (about 24 percent) carbon dioxide waste at the tissues and transport it to the lungs for exhalation. Erythrocytes remain within the vascular network. Although leukocytes typically leave the blood vessels to perform their defensive functions, movement of erythrocytes from the blood vessels is abnormal.

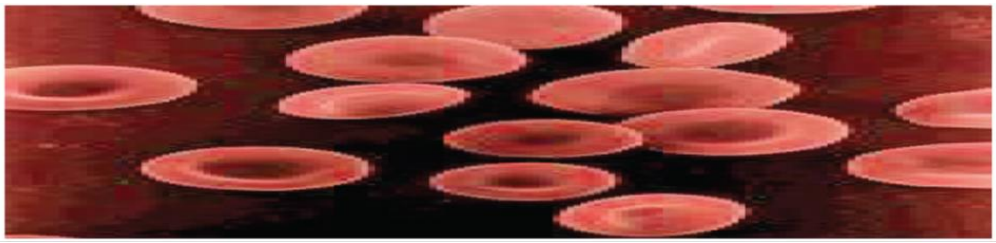
Formed element	Major subtypes	Numbers present per microliter (μL) and mean (range)	Appearance in a standard blood smear	Summary of functions	Comments
Erythrocytes (red blood cells)		5.2 million (4.4–6.0 million)	Flattened biconcave disk; no nucleus; pale red color	Transport oxygen and some carbon dioxide between tissues and lungs	Lifespan of approximately 120 days
Leukocytes (white blood cells)		7000 (5000–10,000)	Obvious dark-staining nucleus	All function in body defenses	Exit capillaries and move into tissues; lifespan of usually a few hours or days
	Granulocytes including neutrophils, eosinophils, and basophils	4360 (1800–9950)	Abundant granules in cytoplasm; nucleus normally lobed	Nonspecific (innate) resistance to disease	Classified according to membrane-bound granules in cytoplasm
	Neutrophils	4150 (1800–7300)	Nuclear lobes increase with age; pale lilac granules	Phagocytic; particularly effective against bacteria. Release cytotoxic chemicals from granules	Most common leukocyte; lifespan of minutes to days
	Eosinophils	165 (0–700)	Nucleus generally two-lobed; bright red-orange granules	Phagocytic cells; particularly effective with antigen- antibody complexes. Release antihistamines. Increase in allergies and parasitic infections	Lifespan of minutes to days
	Basophils	44 (0–150)	Nucleus generally two-lobed but difficult to see due to presence of heavy, dense, dark purple granules	Promotes inflammation	Least common leukocyte; lifespan unknown
	Agranulocytes including lymphocytes and monocytes	2640 (1700–4950)	Lack abundant granules in cytoplasm; have a simple-shaped nucleus that may be indented	Body defenses	Group consists of two major cell types from different lineages
	Lymphocytes	2185 (1500–4000)	Spherical cells with a single often large nucleus occupying much of the cell's volume; stains purple; seen in large (natural killer cells) and small (B and T cells) variants	Primarily specific (adaptive) immunity: T cells directly attack other cells (cellular immunity); B cells release antibodies (humoral immunity); natural killer cells are similar to T cells but nonspecific	Initial cells originate in bone marrow, but secondary production occurs in lymphatic tissue; several distinct subtypes; memory cells form after exposure to a pathogen and rapidly increase responses to subsequent exposure; lifespan of many years
	Monocytes	455 (200–950)	Largest leukocyte with an indented or horseshoe-shaped nucleus	Very effective phagocytic cells engulfing pathogens or worn out cells; also serve as antigen-presenting cells (APCs) for other components of the immune system	Produced in red bone marrow; referred to as macrophages after leaving circulation
Platelets		350,000 (150,000–500,000)	Cellular fragments surrounded by a plasma membrane and containing granules; purple stain	Hemostasis plus release growth factors for repair and healing of tissue	Formed from megakaryocytes that remain in the red bone marrow and shed platelets into circulation

Shape and Structure of Erythrocytes

As an erythrocyte matures in the red bone marrow, it extrudes its nucleus and most of its other organelles. During the first day or two that it is in the circulation, an immature erythrocyte, known as a **reticulocyte**, will still typically contain remnants of organelles. Reticulocytes should comprise approximately 1–2 percent of the erythrocyte count and provide a rough estimate of the rate of RBC production, with abnormally low or high rates indicating deviations in the production of these cells. These remnants, primarily of networks (reticulum) of ribosomes, are quickly shed, however, and mature, circulating erythrocytes have few internal cellular structural components. Lacking mitochondria, for example, they rely on anaerobic respiration. This means that they do not utilize any of the oxygen they are transporting, so they can deliver it all to the tissues. They also lack endoplasmic reticula and do not synthesize proteins. Erythrocytes do, however, contain some
structural proteins that help the blood cells maintain their unique structure and enable them to change their shape to squeeze through capillaries. This includes the protein spectrin, a cytoskeletal protein element.

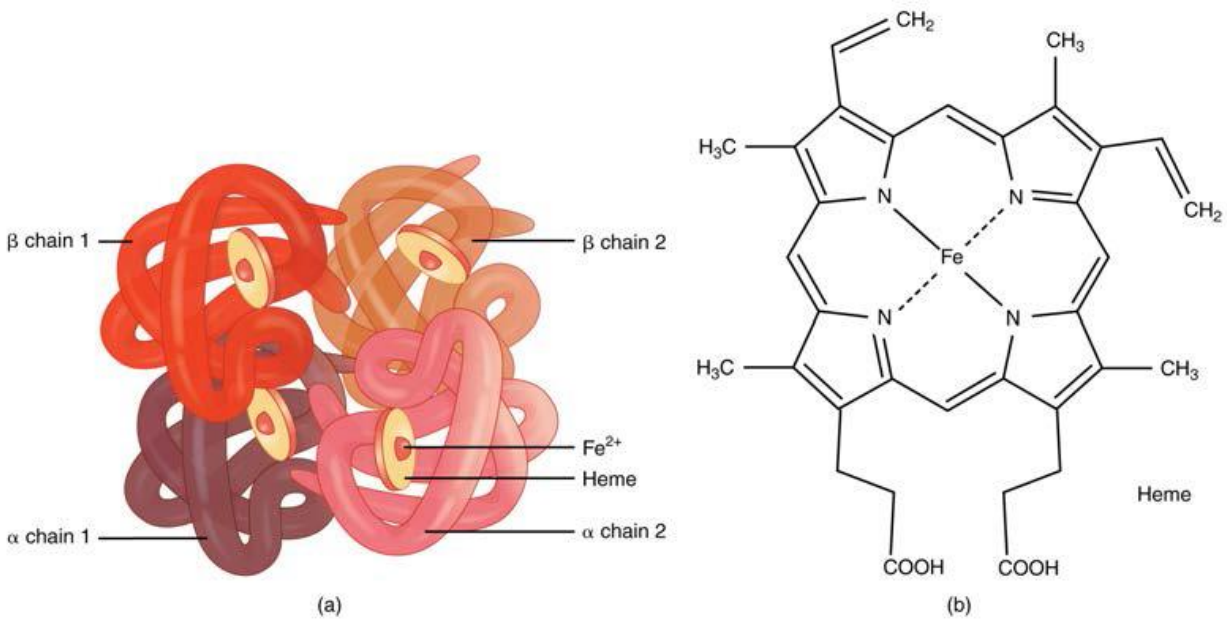
Erythrocytes are biconcave disks; that is, they are plump at their periphery and very thin in the center (**Figure 18.6**). Since they lack most organelles, there is more interior space for the presence of the hemoglobin molecules that, as you will see shortly, transport gases. The biconcave shape also provides a greater surface area across which gas exchange can occur, relative to its volume; a sphere of a similar diameter would have a lower surface area-to-volume ratio. In the capillaries, the oxygen carried by the erythrocytes can diffuse into the plasma and then through the capillary walls to reach the cells, whereas some of the carbon dioxide produced by the cells as a waste product diffuses into the capillaries to be picked up by
the erythrocytes. Capillary beds are extremely narrow, slowing the passage of the erythrocytes and providing an extended opportunity for gas exchange to occur. However, the space within capillaries can be so minute that, despite their own small size, erythrocytes may have to fold in on themselves if they are to make their way through. Fortunately, their structural proteins like spectrin are flexible, allowing them to bend over themselves to a surprising degree, then spring back again when they enter a wider vessel. In wider vessels, erythrocytes may stack up much like a roll of coins, forming a rouleaux, from the French word for “roll.”

Figure 18.6 Shape of Red Blood Cells



Hemoglobin

Hemoglobin is a large molecule made up of proteins and iron. It consists of four folde chains of a protein called **globin**, designated alpha 1 and 2, and beta 1 and 2 (**Figure 18.7a**). Each of these globin molecules is bound to a red pigmentmolecule called **heme**, which contains an ion of iron (Fe2+) (**Figure 18.7b**).



Each iron ion in the heme can bind to one oxygen molecule; therefore, each hemoglobin molecule can transport four oxygen molecules. An individual erythrocyte may contain about 300 million hemoglobin molecules, and therefore can bind to and transport up to 1.2 billion oxygen molecules (see **Figure 18.7b**). In the lungs, hemoglobin picks up oxygen, which binds to the iron ions, forming **oxyhemoglobin**. The bright red, oxygenated hemoglobin travels to the body tissues, where it releases some of the oxygen molecules, becoming darker red **deoxyhemoglobin**, sometimes referred to as reduced hemoglobin. Oxygen release depends on the need for oxygen in the surrounding tissues, so

hemoglobin rarely if ever leaves all of its oxygen behind. In the capillaries, carbon dioxide enters the bloodstream. About 76 percent dissolves in the plasma, some of it remaining as dissolved CO_2, and the remainder forming bicarbonate ion. About 23–24 percent of it binds to the amino acids in hemoglobin, forming a molecule known as **carbaminohemoglobin**. From the capillaries, the hemoglobin carries carbon dioxide back to the lungs, where it releases it
for exchange of oxygen. Changes in the levels of RBCs can have significant effects on the body's ability to effectively deliver oxygen to the tissues. Ineffective hematopoiesis results in insufficient numbers of RBCs and results in one of several forms of anemia.

An overproduction of RBCs produces a condition called polycythemia. The primary drawback with polycythemia is not a failure to directly deliver enough oxygen to the tissues, but rather the increased viscosity of the blood, which makes it more difficult for the heart to circulate the blood. In patients with insufficient hemoglobin, the tissues may not receive sufficient oxygen, resulting in another form of anemia. In determining oxygenation of tissues, the value of greatest interest in healthcare is the percent saturation; that is, the percentage of hemoglobin sites occupied by oxygen in a patient's blood. Clinically this value is commonly referred to simply as "percent sat." Percent saturation is normally monitored using a device known as a pulse oximeter, which is applied to a thin part of the body, typically the tip of the patient's finger. The device works by sending two different wavelengths of light (one red, the other infrared) through the finger and measuring the light with a photodetector as it exits. Hemoglobin absorbs
light differentially depending upon its saturation with oxygen. The machine calibrates the amount of light received by the photodetector against the amount absorbed by the partially oxygenated hemoglobin and presents the data as percent saturation. Normal pulse oximeter readings range from 95–100 percent. Lower percentages reflect **hypoxemia**, or low blood oxygen. The term hypoxia is more generic and simply refers to low oxygen levels. Oxygen levels are also directly monitored from free oxygen in the plasma typically following an arterial stick. When this method is applied, the amount of oxygen present is expressed in terms of partial pressure of oxygen or simply pO_2 and is typically recorded in units of millimeters of mercury, mm Hg. The kidneys filter about 180 liters (~380 pints) of blood in an average adult each day, or about 20 percent of the total resting volume, and thus serve as ideal sites for receptors that determine oxygen saturation. In response to hypoxemia, less oxygen will exit the vessels supplying the kidney, resulting in hypoxia (low oxygen concentration) in the tissue fluid of increasing erythrocyte production and restoring oxygen levels. In a classic negative-feedback loop, as oxygen

saturation rises, EPO secretion falls, and vice versa, thereby maintaining homeostasis. Populations dwelling at high elevations, with inherently lower levels of oxygen in the atmosphere, naturally maintain a hematocrit higher than people living at sea level. Consequently, people traveling to high elevations may experience symptoms of hypoxemia, such as fatigue, headache, and shortness of breath, for a few days after their arrival. In response to the hypoxemia, the kidneys secrete EPO to step up the production of erythrocytes until homeostasis is achieved once again. To avoid the symptoms of hypoxemia, or altitude sickness, mountain climbers typically rest for several days to a week or more at a series of camps situated at increasing elevations to allow EPO levels and, consequently, erythrocyte counts to rise. When climbing the tallest peaks, such as Mt. Everest and K2 in the Himalayas, many mountain climbers rely upon bottled oxygen as they near the summit.

Lifecycle of Erythrocytes

Production of erythrocytes in the marrow occurs at the staggering rate of more than 2 million cells per second. For this production to occur, a number of raw materials must be present in adequate amounts. These include the same nutrients that are essential to the production and maintenance of any cell, such as glucose, lipids, and amino acids. However, erythrocyte production also requires several trace elements:

• Iron. We have said that each heme group in a hemoglobin molecule contains an ion of the trace mineral iron. On average, less than 20 percent of the iron we consume is absorbed. Heme iron, from animal foods such as meat, poultry, and fish, is absorbed more efficiently than non-heme iron from plant foods. Upon absorption, iron becomes part of the body's total iron pool. The bone marrow, liver, and spleen can store iron in the protein compounds **ferritin** and **hemosiderin**. Ferroportin transports the iron across the intestinal cell plasma membranes and from its storage sites into tissue fluid where it enters the blood. When EPO stimulates the production of erythrocytes, iron is released from storage, bound to transferrin, and carried to the red marrow where it attaches to erythrocyte precursors.

• Copper. A trace mineral, copper is a component of two plasma proteins, hephaestin and ceruloplasmin. Without these, hemoglobin could not be adequately produced. Located in intestinal villi, hephaestin enables iron to be absorbed by intestinal cells. Ceruloplasmin transports copper. Both enable the oxidation of iron from Fe^{2+} to Fe^{3+}, a form in which
it can be bound to its transport protein, **transferrin**, for transport to body cells. In a state of copper deficiency, the transport of iron for heme synthesis decreases, and iron can accumulate in tissues, where it can eventually lead to organ damage.

• Zinc. The trace mineral zinc functions as a co-enzyme that facilitates the

synthesis of the heme portion of hemoglobin.

• B vitamins. The B vitamins folate and vitamin B12 function as co-enzymes that facilitate DNA synthesis. Thus, both are critical for the synthesis of new cells, including erythrocytes.

Erythrocytes live up to 120 days in the circulation, after which the worn-out cells are removed by a type of myeloid phagocytic cell called a **macrophage**, located primarily within the bone marrow, liver, and spleen. The components of the degraded erythrocytes' hemoglobin are further processed as follows:

• Globin, the protein portion of hemoglobin, is broken down into amino acids, which can be sent back to the bone marrow to be used in the production of new erythrocytes. Hemoglobin that is not phagocytized is broken down in the circulation, releasing alpha and beta chains that are removed from circulation by the kidneys.

• The iron contained in the heme portion of hemoglobin may be stored in the liver or spleen, primarily in the form of ferritin or hemosiderin, or carried through the bloodstream by transferrin to the red bone marrow for recycling into new erythrocytes.

• The non-iron portion of heme is degraded into the waste product **biliverdin**, a green pigment, and then into another waste product, **bilirubin**, a yellow pigment. Bilirubin binds to albumin and travels in the blood to the liver, which uses it in the manufacture of bile, a compound released into the intestines to help emulsify dietary fats. In the large intestine, bacteria break the bilirubin apart from the bile and converts it to urobilinogen and then into stercobilin. It is then eliminated from the body in the feces. Broad-spectrum antibiotics typically eliminate these bacteria as well and may alter the color of feces. The kidneys also remove any circulating bilirubin and other related metabolic byproducts such as urobilins and secrete them into the urine.

The breakdown pigments formed from the destruction of hemoglobin can be seen in a variety of situations. At the site of an injury, biliverdin from damaged RBCs produces some of the dramatic colors associated with bruising. With a failing liver,

bilirubin cannot be removed effectively from circulation and causes the body to assume a yellowish tinge associated with jaundice. Stercobilins within the feces produce the typical brown color associated with this waste. And the yellow of urine is associated with the urobilins.

The erythrocyte lifecycle is summarized in **Figure 18.8**.

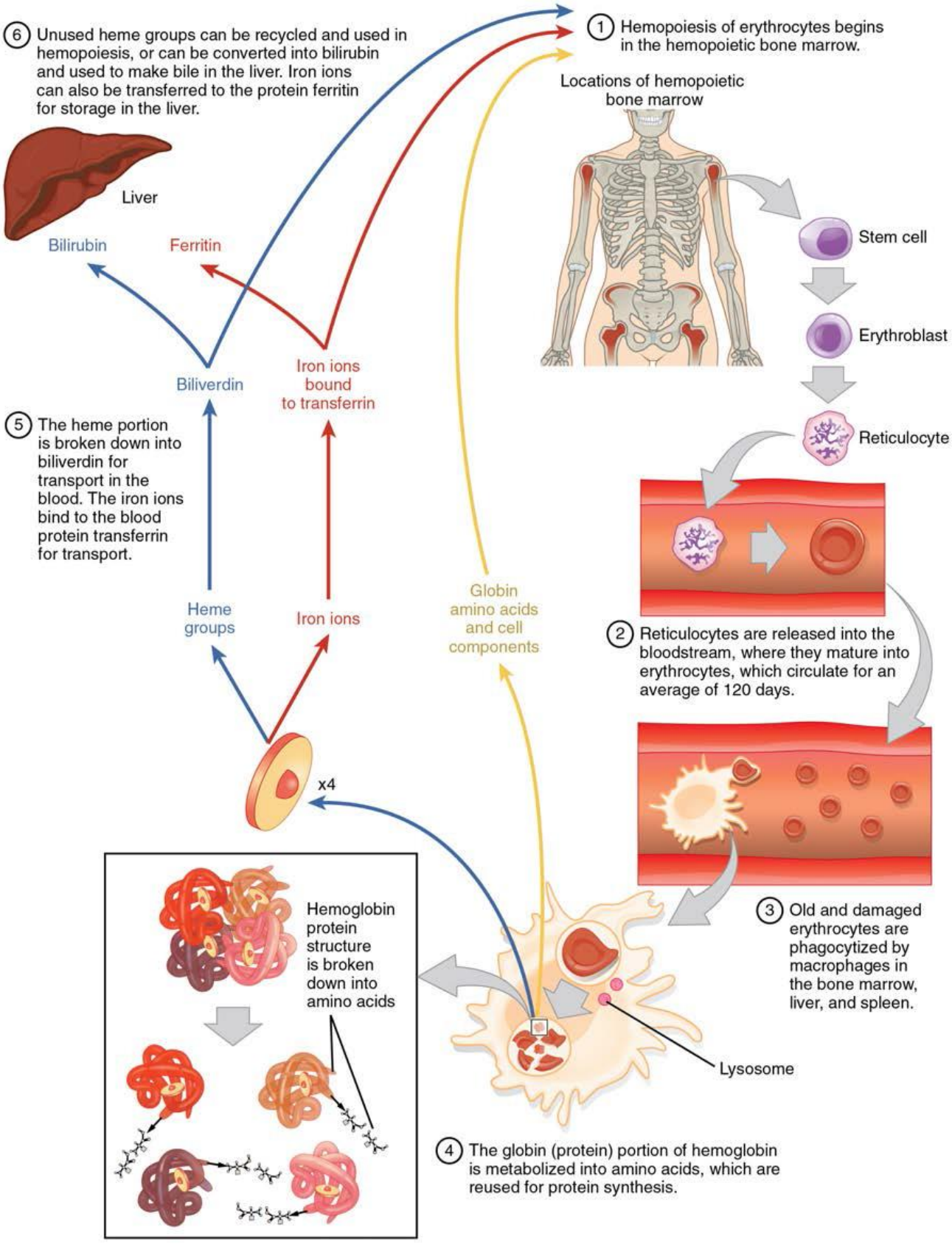

6 Unused heme groups can be recycled and used in hemopoiesis, or can be converted into bilirubin and used to make bile in the liver. Iron ions can also be transferred to the protein ferritin for storage in the liver.
Liver
Bilirubin
Ferritin
Biliverdin
Iron ions bound to transferrin
5 The heme portion is broken down into biliverdin for transport in the blood. The iron ions bind to the blood protein transferrin for transport.
Heme groups
Iron ions
x4
1 Hemopoiesis of erythrocytes begins in the hemopoietic bone marrow.
Locations of hemopoietic bone marrow
Stem cell
Erythroblast
Reticulocyte
Globin amino acids and cell components
2 Reticulocytes are released into the bloodstream, where they mature into erythrocytes, which circulate for an average of 120 days.
3 Old and damaged erythrocytes are phagocytized by macrophages in the bone marrow, liver, and spleen.
Lysosome
Hemoglobin protein structure is broken down into amino acids
4 The globin (protein) portion of hemoglobin is metabolized into amino acids, which are reused for protein synthesis.

Fig. **18.8**.

Disorders of Erythrocytes

The size, shape, and number of erythrocytes, and the number of hemoglobin molecules can have a major impact on a person's health. When the number of RBCs or hemoglobin is deficient, the general condition is called **anemia**. There are more than 400 types of anemia and more than 3.5 million Americans suffer from this condition. Anemia can be broken down into three major groups: those caused by blood loss, those caused by faulty or decreased RBC production, and
those caused by excessive destruction of RBCs. Clinicians often use two groupings in diagnosis: The kinetic approach focuses on evaluating the production, destruction, and removal of RBCs, whereas the morphological approach examines the RBCs themselves, paying particular emphasis to their size. A common test is the mean corpuscle volume (MCV), which measures size. Normal-sized cells are referred to as normocytic, smaller-than-normal cells are referred to as microcytic, and larger-than-normal cells are referred to as macrocytic. Reticulocyte counts are also important and may reveal inadequate production of RBCs. The effects of the various anemias are widespread, because reduced numbers of RBCs or hemoglobin will result in lower levels of oxygen being delivered to body tissues. Since oxygen is required for tissue functioning, anemia
produces fatigue, lethargy, and an increased risk for infection. An oxygen deficit in the brain impairs the ability to think clearly, and may prompt headaches and irritability. Lack of oxygen leaves the patient short of breath, even as the heart and lungs work harder in response to the deficit. Blood loss anemias are fairly straightforward. In addition to bleeding from wounds or other lesions, these forms of anemia may be due to ulcers, hemorrhoids, inflammation of the stomach (gastritis), and some cancers of the gastrointestinal tract. The excessive use of aspirin or other nonsteroidal anti-inflammatory drugs such as ibuprofen can trigger ulceration and gastritis. Excessive menstruation and loss of blood during childbirth are also potential causes.
Anemias caused by faulty or decreased RBC production include sickle cell anemia, iron deficiency anemia, vitamin deficiency anemia, and diseases of the bone marrow and stem cells.

• A characteristic change in the shape of erythrocytes is seen in **sickle cell disease** (also referred to as sickle cell anemia). A genetic disorder, it is caused by production of an abnormal type of hemoglobin, called hemoglobin S, which delivers less oxygen to tissues and causes erythrocytes to assume a sickle (or crescent) shape, especially at low oxygen concentrations (**Figure 18.9**). These abnormally shaped cells can then become lodged in narrow capillaries because they are unable to fold in on themselves to squeeze through, blocking blood flow to tissues and causing a variety of serious problems from painful joints to delayed growth and even blindness and cerebrovascular accidents (strokes). Sickle cell anemia is a genetic condition particularly found in individuals of African descent.

. Iron deficiency anemia is the most common type and results when the amount of

available iron is insufficient to allow production of sufficient heme. This condition can occur in individuals with a deficiency of iron in the diet and is especially common in teens and children as well as in vegans and vegetarians. Additionally, iron deficiency anemia may be caused by either an inability to absorb and transport iron or slow, chronic bleeding.

• Vitamin-deficient anemias generally involve insufficient vitamin B12 and folate.

◦ **Megaloblastic anemia** involves a deficiency of vitamin B12 and/or folate, and often involves diets deficient in these essential nutrients. Lack of meat or a viable alternate source, and overcooking or eating insufficient amounts of vegetables may lead to a lack of folate.

◦ **Pernicious anemia** is caused by poor absorption of vitamin B12 and is often seen in patients with Crohn's disease (a severe intestinal disorder often treated by surgery), surgical removal of the intestines or stomach (common in some weight loss surgeries), intestinal parasites, and AIDS.

◦ Pregnancies, some medications, excessive alcohol consumption, and some diseases such as celiac disease are also associated with vitamin deficiencies. It is essential to provide sufficient folic acid during the early stages of pregnancy to reduce the risk of neurological defects, including spina bifida, a failure of the neural tube to close.

• Assorted disease processes can also interfere with the production and formation of RBCs and hemoglobin. If myeloid stem cells are defective or replaced by cancer cells, there will be insufficient quantities of RBCs produced.

◦ **Aplastic anemia** is the condition in which there are deficient numbers of RBC stem cells. Aplastic anemia is often inherited, or it may be triggered by radiation, medication, chemotherapy, or infection.

◦ **Thalassemia** is an inherited condition typically occurring in individuals from the Middle East, the Mediterranean, African, and Southeast Asia, in which maturation of the RBCs does not proceed normally. The most severe form is called Cooley's anemia.

◦ **Lead exposure** from industrial sources or even dust from paint chips of iron-containing paints or pottery that has
not been properly glazed may also lead to destruction of the red marrow.

• Various disease processes also can lead to anemias. These include chronic kidney diseases often associated with a decreased production of EPO, hypothyroidism, some forms of cancer, lupus, and rheumatoid arthritis.

In contrast to anemia, an elevated RBC count is called **polycythemia** and is detected in a patient's elevated hematocrit. It can occur transiently in a person who is dehydrated; when water intake is inadequate or water losses are excessive, the plasma volume falls. As a result, the hematocrit rises. For reasons mentioned earlier, a mild form of polycythemia is chronic but normal in people living at high altitudes. Some elite athletes train at high elevations specifically to induce this
phenomenon. Finally, a type of bone marrow disease called polycythemia vera (from the Greek vera = "true") causes an excessive production of immature erythrocytes.

Polycythemia vera can dangerously elevate the viscosity of blood, raising blood pressure and making it more difficult for the heart to pump blood throughout the body. It is a relatively rare disease that occurs more often in men than women, and is more likely to be present in elderly patients those over 60 years of age.

Leukocytes and Platelets

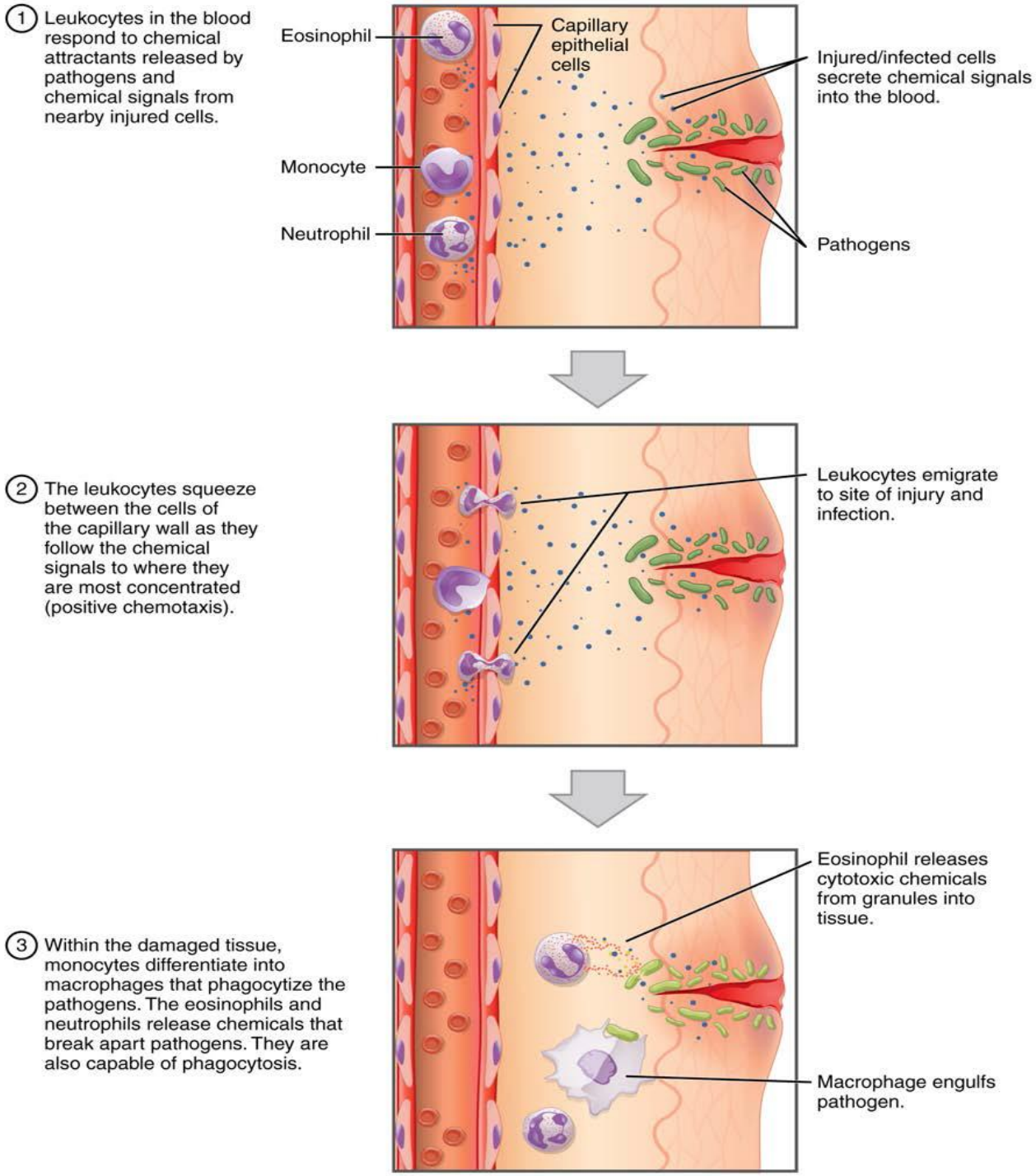
The **leukocyte**, commonly known as a white blood cell (or WBC), is a major component of the body's defenses against disease. Leukocytes protect the body against invading microorganisms and body cells with mutated DNA, and they clean up debris. Platelets are essential for the repair of blood vessels when damage to them has occurred; they also provide growth factors for healing and repair. See **Figure 18.5** for a summary of leukocytes and platelets.

Characteristics of Leukocytes

Although leukocytes and erythrocytes both originate from hematopoietic stem cells in the bone marrow, they are very different from each other in many significant ways. For instance, leukocytes are far less numerous than erythrocytes: Typically there are only 5000 to 10,000 per μL. They are also larger than erythrocytes and are the only formed elements that are complete cells, possessing a nucleus and organelles. And although there is just one type of erythrocyte, there are many
types of leukocytes. Most of these types have a much shorter lifespan than that of erythrocytes, some as short as a few hours or even a few minutes in the case of acute infection.

One of the most distinctive characteristics of leukocytes is their movement. Whereas erythrocytes spend their days circulating within the blood vessels, leukocytes routinely leave the bloodstream to perform their defensive functions in the body's tissues. For leukocytes, the vascular network is simply a highway they travel and soon exit to reach their true destination. When they arrive, they are often given distinct names, such as macrophage or microglia, depending on their function. As shown in **Figure 18.10**, they leave the capillaries—the smallest blood vessels—or other small vessels through a process known as **emigration** (from the Latin for "removal") or **diapedesis** (dia- = "through"; -pedan = "to leap") in which they squeeze through adjacent cells in a blood vessel wall. Once they have exited the capillaries, some leukocytes will take up fixed positions in lymphatic tissue, bone marrow, the spleen, the thymus, or other organs. Others will move about through the tissue spaces very much like amoebas, continuously extending their plasma membranes, sometimes wandering freely, and sometimes moving toward the direction in which they are drawn by chemical signals. This attracting of leukocytes occurs because of **positive chemotaxis** (literally "movement in response to chemicals"), a phenomenon in which injured or infected cells and nearby

leukocytes emit the equivalent of a chemical “911” call, attracting more leukocytes to the site. In clinical medicine, the differential counts of the types and percentages of leukocytes present are often key indicators in making a diagnosis and selecting a treatment.



Classification of Leukocytes

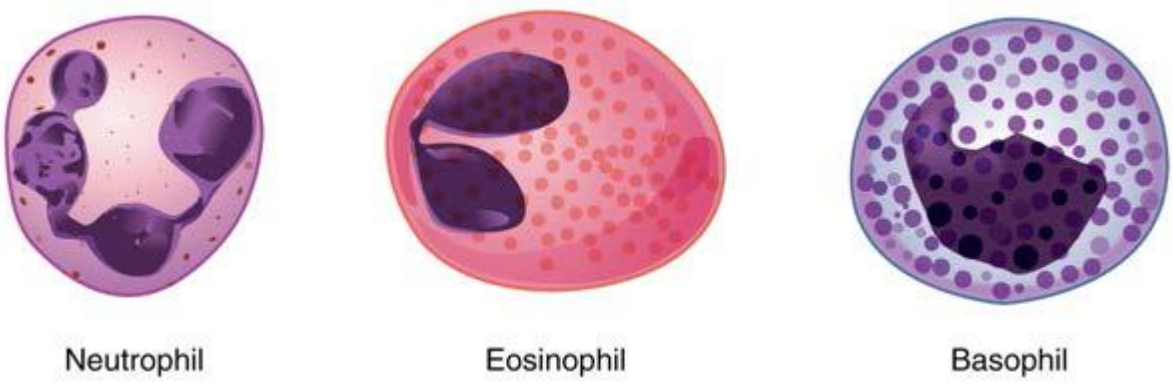
When scientists first began to observe stained blood slides, it quickly became evident that leukocytes could be divided into two groups, according to whether their cytoplasm contained highly visible granules:

Granular leukocytes contain abundant granules within the cytoplasm. They include neutrophils, eosinophils, and basophils (you can view their lineage from myeloid stem cells in **Figure 18.4**).

• While granules are not totally lacking in **agranular leukocytes**, they are far fewer and less obvious. Agranular leukocytes include monocytes, which mature into macrophages that are phagocytic, and lymphocytes, which arise from the lymphoid stem cell line.

Granular Leukocytes

We will consider the granular leukocytes in order from most common to least common. All of these are produced in the red bone marrow and have a short lifespan of hours to days. They typically have a lobed nucleus and are classified according to which type of stain best highlights their granules (**Figure 18.11**).



The most common of all the leukocytes, **neutrophils** will normally comprise 50–70 percent of total leukocyte count. They are 10–12 μm in diameter, significantly larger than erythrocytes. They are called neutrophils because their granules show up most clearly with stains that are chemically neutral (neither acidic nor basic). The granules are numerous but quite fine and normally appear light lilac. The nucleus has a distinct lobed appearance and may have two to five lobes, the number increasing with the age of the cell. Older neutrophils have increasing numbers of lobes and are often referred to as **polymorphonuclear** (a nucleus with many forms), or simply "polys." Younger and immature neutrophils begin to develop lobes and are known as "bands."

Neutrophils are rapid responders to the site of infection and are efficient phagocytes with a preference for bacteria. Their granules include **lysozyme**, an enzyme capable of lysing, or breaking down, bacterial cell walls; oxidants such as hydrogen peroxide; and **defensins**, proteins that bind to and puncture bacterial and fungal plasma membranes, so that the cell contents leak out. Abnormally high counts of neutrophils indicate infection

and/or inflammation, particularly triggered by bacteria but are also found in burn patients and others experiencing unusual stress. A burn injury increases the proliferation of neutrophils in order to fight off infection that can result from the destruction of the barrier of the skin. Low counts may be caused by drug toxicity and other disorders, and may increase an individual's susceptibility to infection. **Eosinophils** typically represent 2–4 percent of total leukocyte count. They are also 10–12 μm in diameter. The granules of eosinophils stain best with an acidic stain known as eosin. The nucleus of the eosinophil will typically have two to three lobes and, if stained properly, the granules will have a distinct red to orange color. The granules of eosinophils include antihistamine molecules, which counteract the activities of histamines, inflammatory chemicals produced by basophils and mast cells. Some eosinophil granules contain molecules toxic to parasitic worms, which can enter the body through the integument, or when an individual consumes raw or undercooked fish or meat.

Eosinophils are also capable of phagocytosis and are particularly effective when antibodies bind to the target and form an antigen-antibody complex. High counts of eosinophils are typical of patients experiencing allergies, parasitic worm infestations, and some autoimmune diseases. Low counts may be due to drug toxicity and stress. **Basophils** are the least common leukocytes, typically comprising less than one percent of the total leukocyte count. They are slightly smaller than neutrophils and eosinophils at 8–10 μm in diameter. The granules of basophils stain best with

basic (alkaline) stains. Basophils contain large granules that pick up a dark blue stain and are so common they may make it difficult to see the two-lobed nucleus. In general, basophils intensify the inflammatory response. They share this trait with mast cells. In the past, mast cells were

considered to be basophils that left the circulation. However, this appears not to be the case, as the two cell types develop from different lineages. The granules of basophils release histamines, which contribute to inflammation, and heparin, which opposes blood clotting. High counts of basophils are associated with allergies, parasitic infections, and hypothyroidism. Low counts are associated with pregnancy, stress, and hyperthyroidism.

Agranular Leukocytes

Agranular leukocytes contain smaller, less-visible granules in their cytoplasm than do granular leukocytes. The nucleus is simple in shape, sometimes with an indentation but without distinct lobes. There are two major types of agranulocytes: lymphocytes and monocytes (see **Figure 18.4**).

Lymphocytes are the only formed element of blood that arises from lymphoid stem cells. Although they form initially in the bone marrow, much of their subsequent development and reproduction occurs in the lymphatic tissues. Lymphocytes are the second most common type of leukocyte, accounting for about 20–30 percent of all leukocytes, and are essential for the immune response. The size range of lymphocytes is quite extensive, with some authorities recognizing two size classes and others three.

Typically, the large cells are 10–14 μm and have a smaller nucleus-to-cytoplasm ratio and more granules. The smaller cells are typically 6–9 μm with a larger volume of nucleus to cytoplasm, creating a "halo" effect. A few cells may fall outside these ranges, at 14–17 μm. This finding has led to the three size range classification. The three major groups of lymphocytes include natural killer cells, B cells, and T cells. **Natural killer (NK) cells** are capable of recognizing cells that do not express "self" proteins on their plasma membrane or that contain foreign or abnormal markers. These "nonself" cells include cancer cells, cells infected with a virus, and other cells with atypical surface proteins. Thus, they provide generalized, nonspecific immunity. The larger lymphocytes are typically NK cells.

B cells and T cells, also called **B lymphocytes** and **T lymphocytes**, play prominent roles in defending the body against specific pathogens (disease-causing microorganisms) and are involved in specific immunity. One form of B cells (plasma cells) produces the antibodies or immunoglobulins that bind to specific foreign or abnormal components of plasma membranes. This is also referred to as humoral (body fluid) immunity. T cells provide cellular-level immunity by physically attacking foreign or diseased cells.

A **memory cell** is a variety of both B and T cells that forms after exposure to a pathogen and mounts rapid responses upon subsequent exposures. Unlike other leukocytes, memory cells live for many years. B cells undergo a maturation process in the bone marrow, whereas T cells undergo maturation in the thymus. This site of the maturation process gives rise to the name B and T cells. The functions of lymphocytes are complex and will be covered in detail in the chapter covering the lymphatic system and immunity. Smaller lymphocytes are either B or T cells, although they cannot be differentiated in a normal blood smear. Abnormally high lymphocyte counts are characteristic of viral infections as well as some types of cancer. Abnormally low lymphocyte counts are characteristic of prolonged (chronic) illness or immunosuppression, including that caused by HIV infection and drug therapies that often involve steroids.

Monocytes originate from myeloid stem cells. They normally represent 2–8 percent of the total leukocyte count. They are typically easily recognized by their large size of 12–20 μm and indented or horseshoe-shaped nuclei. Macrophages are monocytes that have left the circulation and phagocytize debris, foreign pathogens, worn-out erythrocytes, and many other dead, worn out, or damaged cells. Macrophages also release antimicrobial defensins and chemotactic chemicals that attract other leukocytes to the site of an infection. Some macrophages occupy fixed locations, whereas others wander through the tissue fluid.

Abnormally high counts of monocytes are associated with viral or fungal infections, tuberculosis, and some forms of leukemia and other chronic diseases. Abnormally low counts are typically caused by suppression of the bone marrow.

Lifecycle of Leukocytes

Most leukocytes have a relatively short lifespan, typically measured in hours or days. Production of all leukocytes begins in the bone marrow under the influence of CSFs and interleukins. Secondary production and maturation of lymphocytes occurs in specific regions of lymphatic tissue known as germinal centers. Lymphocytes are fully capable of mitosis and may produce clones of cells with identical properties. This capacity enables an individual to maintain immunity throughout life to many threats that have been encountered in the past.

Disorders of Leukocytes

Leukopenia is a condition in which too few leukocytes are produced. If this condition is pronounced, the individual may be unable to ward off disease. Excessive leukocyte proliferation is known as **leukocytosis**. Although leukocyte counts are high, the cells themselves are often nonfunctional, leaving the individual at increased risk for disease.

Leukemia is a cancer involving an abundance of leukocytes. It may involve only one specific type of leukocyte from either the myeloid line (myelocytic leukemia) or the lymphoid line (lymphocytic leukemia). In chronic leukemia, mature leukocytes accumulate and fail to die. In acute leukemia, there is an overproduction of young, immature leukocytes. In both conditions the cells do not function properly.

Lymphoma is a form of cancer in which masses of malignant T and/or B lymphocytes collect in lymph nodes, the spleen, the liver, and other tissues. As in leukemia, the malignant leukocytes do not function properly, and the patient is vulnerable to infection. Some forms of lymphoma tend to progress slowly and respond well to treatment. Others tend to progress quickly and require aggressive treatment, without which they are rapidly fatal.

Platelets

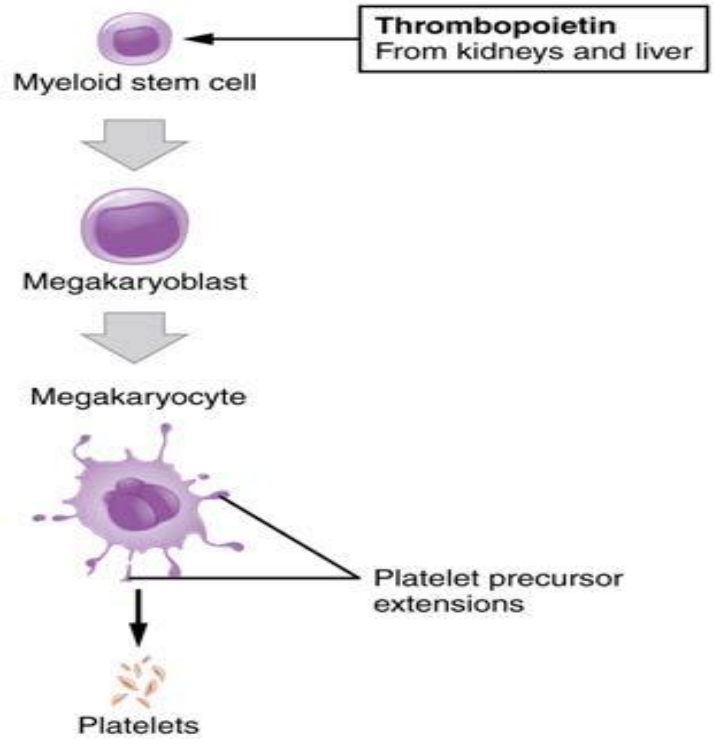
You may occasionally see platelets referred to as **thrombocytes**, but because this name suggests they are a type of cell, it is not accurate. A platelet is not a cell but rather a fragment of the cytoplasm of a cell called a **megakaryocyte** that is surrounded by a plasma membrane. Megakaryocytes are descended from myeloid stem cells (see **Figure 18.4**) and are large, typically 50–100 μm in diameter, and contain an enlarged, lobed nucleus. As noted earlier, thrombopoietin, a glycoprotein secreted by the kidneys and liver, stimulates the proliferation of megakaryoblasts, which mature into megakaryocytes. These remain within bone marrow tissue (**Figure 18.12**) and ultimately form platelet-precursor extensions that extend through the walls of bone marrow capillaries to release into the circulation thousands of cytoplasmic fragments, each enclosed by a bit of plasma membrane. These enclosed fragments are platelets. Each megakarocyte releases 2000–3000 platelets during its lifespan. Following platelet release, megakaryocyte remnants, which are little more than a cell nucleus, are

consumed by macrophages. Platelets are relatively small, 2–4 μm in diameter, but numerous, with typically 150,000–160,000 per μL of blood. After
entering the circulation, approximately one-third migrate to the spleen for storage for later release in response to any rupture in a blood vessel. They then become activated to perform their primary function, which is to limit blood loss. Platelets remain only about 10 days, then are phagocytized by macrophages. Platelets are critical to hemostasis, the stoppage of blood flow following damage to a vessel. They also secrete a variety of growth factors essential for growth and repair of tissue, particularly connective tissue. Infusions of concentrated platelets are now being used in some therapies to stimulate healing.

Disorders of Platelets

Thrombocytosis is a condition in which there are too many platelets. This may trigger formation of unwanted blood clots
(thrombosis), a potentially fatal disorder. If there is an insufficient number of platelets, called **thrombocytopenia**, blood
may not clot properly, and excessive bleeding may result.

Figure 18.12 Platelets Platelets are derived from cells called megakaryocytes



Hemostasis

Platelets are key players in **hemostasis**, the process by which the body seals a ruptured blood vessel and prevents further loss of blood. Although rupture of larger vessels usually requires medical intervention, hemostasis is quite effective in dealing with small, simple wounds. There are three steps to the process: vascular spasm, the formation of a platelet plug, and coagulation (blood clotting). Failure of any of these steps will result in **hemorrhage**—excessive bleeding.

Vascular Spasm

When a vessel is severed or punctured, or when the wall of a vessel is damaged, vascular spasm occurs. In **vascular spasm**, the smooth muscle in the walls of the vessel contracts dramatically. This smooth muscle has both circular layers; larger vessels also have longitudinal layers. The circular layers tend to constrict the flow of blood, whereas the longitudinal layers, when present, draw the vessel back into the surrounding tissue, often making it more difficult for a surgeon to locate, clamp, and tie off a severed vessel. The vascular spasm response is believed to be triggered by several chemicals called endothelins that are released by vessel-lining cells and by pain receptors in response to vessel injury. This phenomenon typically lasts for up to 30 minutes, although it can last for hours.

Formation of the Platelet Plug

In the second step, platelets, which normally float free in the plasma, encounter the area of vessel rupture with the exposed underlying connective tissue and collagenous fibers. The platelets begin to clump together, become spiked and sticky, and bind to the exposed collagen and endothelial lining. This process is assisted by a glycoprotein in the blood plasma called von Willebrand factor, which helps stabilize the growing **platelet plug**. As platelets collect, they simultaneously release
chemicals from their granules into the plasma that further contribute to hemostasis. Among the substances released by the platelets are:

- adenosine diphosphate (ADP), which helps additional platelets to adhere to the injury site, reinforcing and expanding the platelet plug
- serotonin, which maintains vasoconstriction
- prostaglandins and phospholipids, which also maintain vasoconstriction and help to activate further clotting chemicals, as discussed next

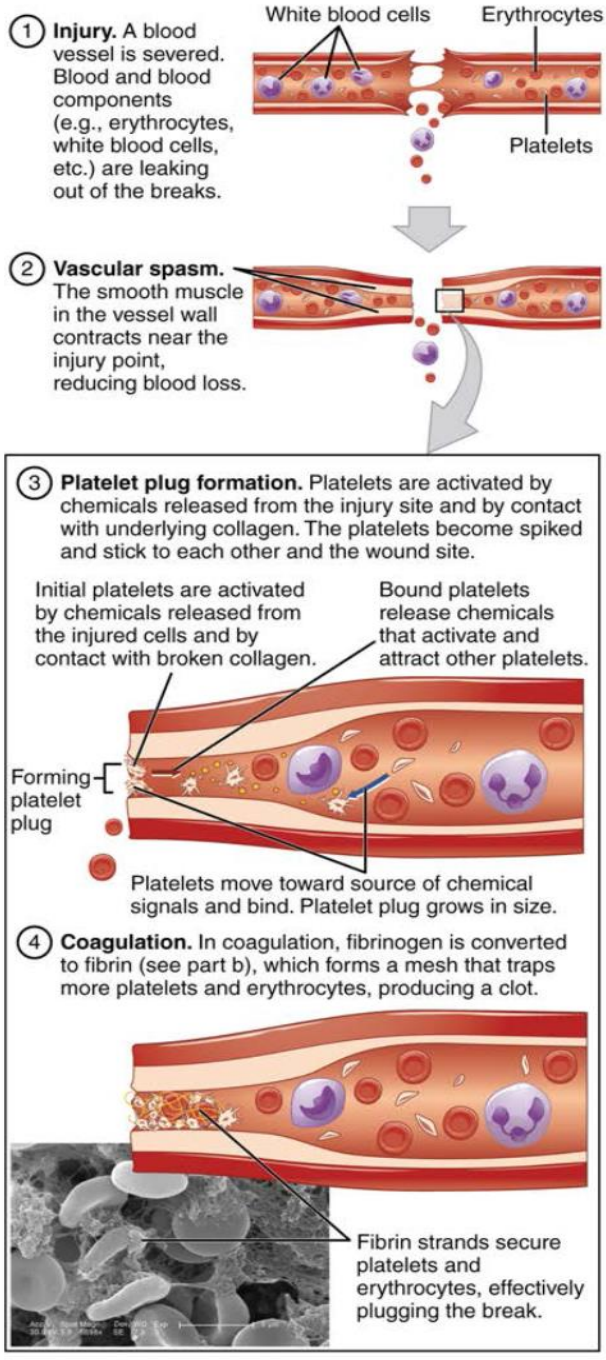
A platelet plug can temporarily seal a small opening in a blood vessel. Plug formation, in essence, buys the body time while more sophisticated and durable repairs are being made. In a similar manner, even modern naval warships still carry an assortment of wooden plugs to temporarily repair small breaches in their hulls until permanent repairs can be made.

Coagulation

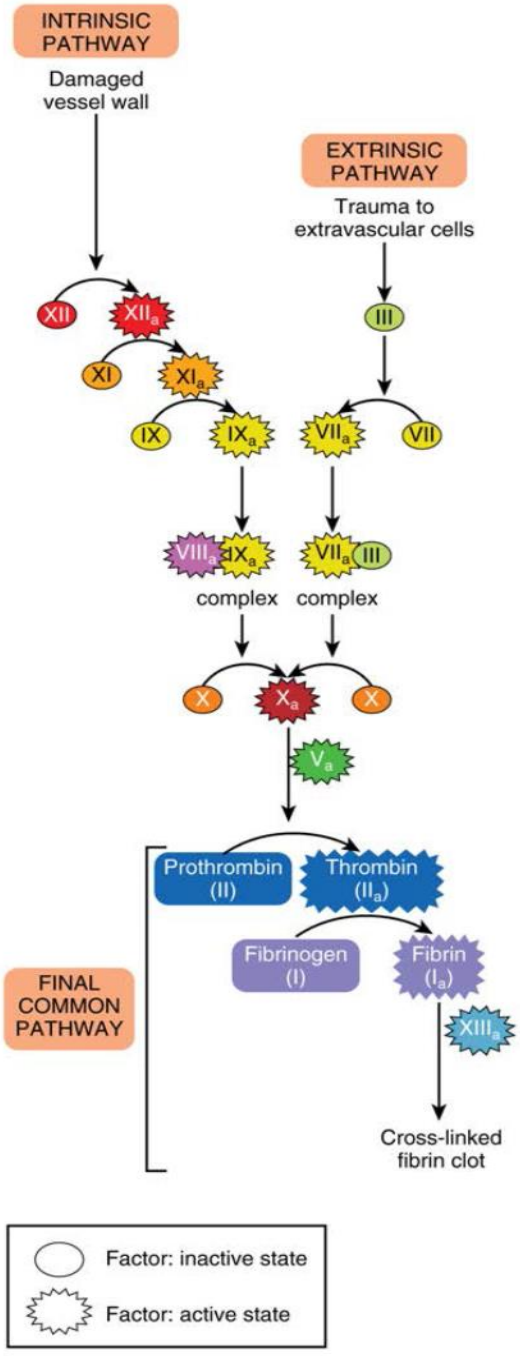
Those more sophisticated and more durable repairs are collectively called **coagulation**, the formation of a blood clot. The process is sometimes characterized as a cascade, because one event prompts the next as in a multi-level waterfall. The result is the

production of a gelatinous but robust clot made up of a mesh of **fibrin**—an insoluble filamentous protein derived from fibrinogen, the plasma protein introduced earlier—in which platelets and blood cells are trapped.

Figure 18.14 summarizes the three steps of hemostasis



(a) The general steps of clotting



(b) Fibrin synthesis cascade

THE CARDIOVASCULAR SYSTEM: THE HEART

In this chapter, you will explore the remarkable pump that propels the blood into the vessels. There is no single better word to describe the function of the heart other than "pump," since its contraction develops the pressure that ejects blood into the major vessels: the aorta and pulmonary trunk. From these vessels, the blood is distributed to the remainder of the body. Although the connotation of the term "pump" suggests a mechanical device made of steel and plastic, the anatomical structure is a living, sophisticated muscle. As you read this chapter, try to keep these twin concepts in mind: pump and muscle. Although the term "heart" is an English word, cardiac (heart-related) terminology can be traced back to the Latin term, "kardia." Cardiology is the study of the heart, and cardiologists are the physicians who deal primarily with the heart.

Functional anatomy of the heart

The adult heart is enclosed in a double walled sac, the pericardium that attaches it to the mediastinum. The apex is rounded and formed by the left ventricle and located behind the sixth rib, about 3 inches to the left of the midline of the body.

The myocardium is about half of the tissue of the heart, the other half is connective tissue, the fibrous skeleton, valves, tendons, blood vessels, lymphatics and nerves. The chambers of the heart are lined by endothelium, a thin smooth layer of cells. The main conducting system of the heart is made up of modified cardiac muscle fibers situated in the interventricular septum and radiating out into the walls of the ventricles. This tissue has lost contractile elements and become specialized for the rapid conduction of electrical impulses. Two nodes/areas, the sinoatrial node, and the atrioventricular node discharge rhythmic impulses that are transmitted through the heart. In humans, the heart and vessels form a closed circulation that assures all the circulating blood returning to the heart. The fluid and proteins that leak out in the tissues are brought back to the blood through the lymphatic circulation.

Blood Vessels of the Heart: Heart has its delivery system for the cardiac muscle fibers; it cannot be nourished by blood flowing through its chambers but are supplied by a specialized 'coronary circulation'.

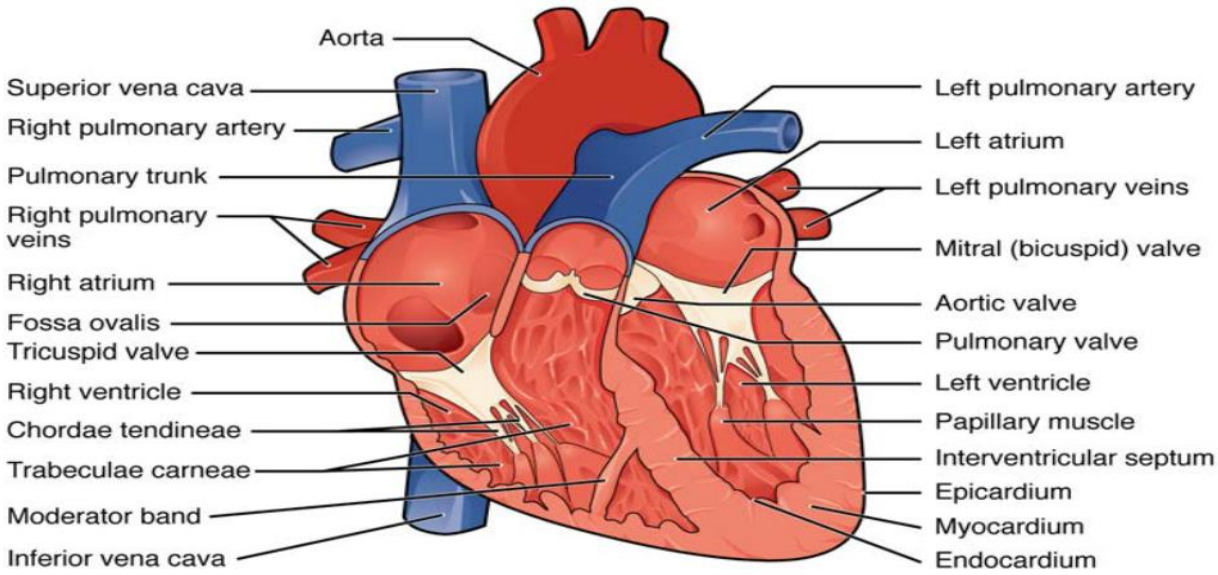
Heart Valves: The blood flow through the heart is from the large veins into the atria, from the atria to the ventricles, and from the ventricles into elastic, thick-walled arteries. This one-way/unidirectional flow is achieved through the atrioventricular valves that guard entrance to the ventricles and the semilunar valves that guard the arterial openings. These valves are regulated by pressure gradient across them (see figure 43).

Atrioventricular (AV) Valves

Tricuspid is between the right atrium and right ventricle, getting its name from three cusps/ flaps around the opening to the ventricle. The AV valve is the bicuspid or mitral valve. Both valves are fastened to small conical 'papillary muscles, on the ventricular walls through several tendinous, the 'chordae tendinae'. The papillary muscle and the ventricles contract at the same time to prevent valve's excursion into the atrium.

Aortic and Pulmonary (Semilunar) Valves

Both large arteries are guarded by the semilunar valves at the exit of the two ventricles. Each valve is made up of three half-moon cusps; the cusps are thin but very strong, fitting very closely, enabling them to withstand very high pressures that cause the valves to open and to snap shut during ventricular contraction and at the end of systole. The semilunar valves close during the ventricular relaxation (diastole).



Anterior view

4- RESPIRATORY SYSTEM

Introduction

The major functions of the respiratory system can be divided in two categories: respiratory and non-respiratory. The first function is to carry out gas exchange. Metabolizing tissues utilize oxygen and produce carbondioxide. The respiratory system must obtain oxygen from the environment and must eliminate carbondioxide produced by cellular metabolism. These processes must be coordinated so that the demand for oxygen is met and so that the carbondioxide that is produced is eliminated. The respiratory system is well designed to carry out gas exchange in an expeditious manner.

The respiratory system is also involved in non-respiratory functions. It participates in maintaining acid-base balance, since increase in Co_2 in the body lead to increased H^+ the lungs also metabolize naturally occurring compounds such as angiotensin I, prostaglandins and epinephrine. The lungs are also responsible for protecting the body from inhaled particles.

Function of the respiratory system:

Function of the respiratory system is the exchange of O_2 and CO_2 between the external environment and cells of the body.

Functional anatomy of the respiratory system

Functionally, the respiratory air passages are divided into two zones: a conductive zone and a respiratory zone. The airway tree consists of a series of highly branched hollow tubes that decrease in diameter and become more numerous at each branching. Trachea, the main airway in turn branches into two bronchi, one of which enters each lung. Within each lung, these bronchi branch many times into progressively smaller bronchi, which in turn branch into terminal bronchioles analogous to twigs of a tree. The terminal bronchioles redivide to form respiratory bronchioles, which end as alveoli, analogous to leaves on a tree. (See fig. 59)

Conducting zone

The conducting zone includes all of the anatomical structures through which air passes before reaching the respiratory zone. The conducting zone includes all of the anatomical structures through which air passes before reaching the respiratory zone. The conducting zone carries gas to and from the alveoli, i.e., it exchanges air between the alveoli and atmosphere. The conducting zone of the respiratory system, in summary consists of the following parts:

Mouth→ nose→ pharynx→ larynx→ trachea→ primary bronchi→ all successive branches of bronchioles including terminal bronchioles

Functions

1 Warming and humidification of the inspired air

Regardless of the temperature and humidity of the atmosphere, when the inspired air reaches the respiratory zone, it is at a body temperature of 37^{o} C (body temperature) and it is saturated with water vapor. This ensures that a constant internal body temperature will be maintained and that delicate lung tissue will be protected from desiccation.

2. Filtration and cleaning: Mucous secreted by the cells of the conducting zone serves to trap small particles in the inspired air and thereby performs a filtration function. This mucus is moved along at a rate of 1-2cm/min by cilia projecting from the tops of the epithelial cells that line the Conducting zone. There are about 300 cilia per cell that bend in a coordinated fashion to move mucus toward the pharynx, where it can either be swallowed or expectorated. As a result of this filtration function, particles larger than about 6 m do not enter the respiratory zone of the lungs. The importance of this disease is evidenced by the disease called black lung, which occurs in miners who inhale too much carbon dust and therefore develop pulmonary fibrosis. The cleansing action of cilia and macrophages in the lungs is diminished by cigarette smoke.

3. Distribute air to the gas exchange surface of the lung.

Respiratory zone

The respiratory zone includes the respiratory bronchioles (because they contain separate out pouching of alveoli) and the alveoli. Alveoli are tiny air sacs, having a diameter of 0.25-0.50mm. There are about 300-500 million alveoli in a lung. The numerous numbers of these structures provide a large surface area (60-80m^2 or 760ft^2) for diffusion of gases.

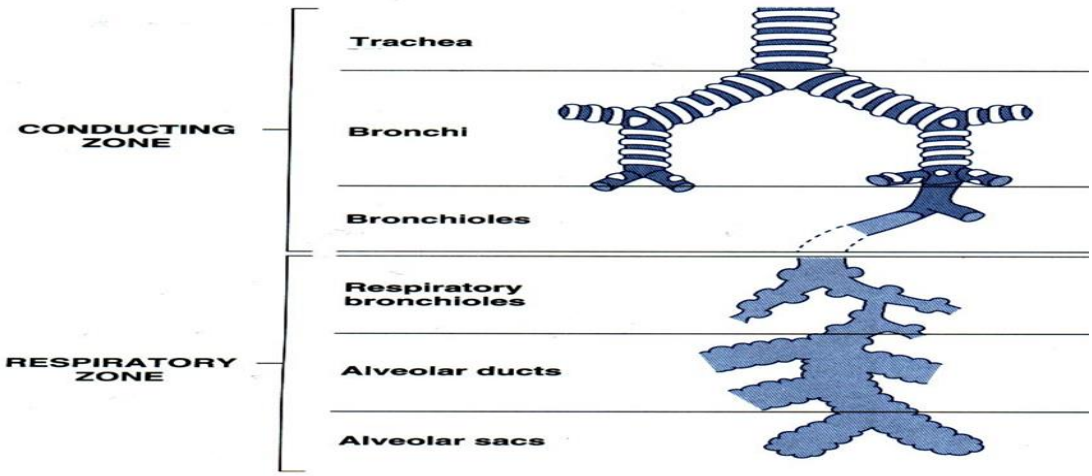


Figure 59. Structure of the airway

Lung Volumes and Capacities Lung Volumes. (See figure 60)

Tidal volume (TV) - volume expired or inspired with each breath at rest

Normal TV is 350-500 ml and includes volume that fills alveoli plus the volume that fills airways

Inspiratory reserve volume (IRV)-additional volume of air inspired on maximal forced inspiration at the end of normal tidal inspiration.

Normal IRV-3000ml

Expiratory reserve volume (ERV): Volume of air still be expired by forceful expiration after the end of normal tidal expiration.

Normal value= 1100ml

Residual volume (RV): Volume that remains in the lungs after maximum expiration, normal=1200ml.

RV cannot be measured with spirometer

Lung capacities- addition of 2 or more volumes

Inspiratory capacity (IC)=TV+ IRV= 3500ml

Functional residual capacity (FRC) =ERV+RV =2400ml

Vital capacity (VC) =IRV+ERV=4700ml

Total lung capacity (TLC) =includes all lung volumes and capacity

=VC+RV=590ml

Helium dilution and body plethysmograph methods are used to measure FRC

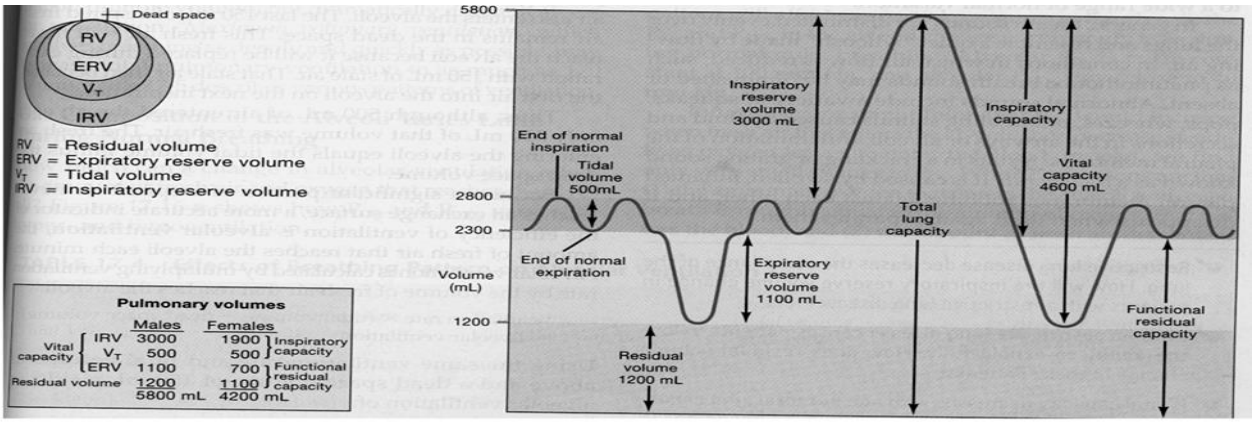


Figure 60. Lung volumes and capacities

Mechanics of breathing:

Muscles used for breathing:

Muscles of inspiration: The diaphragm is the most important inspiratory muscle. When diaphragm contracts, abdominal contents are pushed downward and the ribs are lifted upward and outward. These changes increase intrathoracic volume and lowers intrathoracic pressure. These initiates flow of air into the lungs. During exercise, when breathing frequency and TV increases, external intercostals muscles and accessory muscles are used for more vigorous inspiration.

Muscles of expiration: Expiration is normally passive. During exercise or in diseases, in which airway resistance is increased (e.g. asthma) expiratory muscles are used such as abdominal muscles which compress abdominal cavity and push diaphragm up. Internal intercostals muscles pull ribs downward and inward.

Compliance and elastance.

Definition: Change of volume per unit change of pressure ($\Delta V/\Delta P$). Compliance describes distensibility. In respiration, compliance of the lungs and chest wall are important. Compliance of lung and chest wall are inversely correlated with their elastic properties (elastance)

Changes in lung compliance: Increase in lung compliance may occur due to loss of elastic fibers (e.g., emphysema, old age). Decrease in lung compliance increases the tendency of lung to collapse, e.g., in fibrosis

Surface tension of alveoli and surfactant:

Small size of alveoli is difficult to keep them open because of surface tension. Surfactant line alveoli and reduce surface tension. Thus, surfactant keeps alveoli open. Atelectasis- collapsed alveoli due to reduced surfactant.

Surfactant is synthesized by Type II alveolar cell. Surfactant is lacking in premature infants, causing neonatal respiratory distress syndrome.

Inspiration. The diaphragm contracts, causing volume of thorax to increase. Both airway and alveolar pressure becomes negative (i.e., less than atmospheric). Now pressure gradient is created between atmosphere, airways and alveoli. Air flows into the lungs until the pressure
gradient is dissipated. Intrapleural pressure becomes even more negative than at rest. The reason is as lung volume increases, elastic recoil strength of lungs increases.
Airway an alveolar pressure becomes negative as volume of thorax increase.
The two effects together cause intrapleural pressure to be more negative (~ -8cmH_2O).
Expiration: Expiration is normally passive. Alveolar pressure becomes positive (higher than atmospheric) because the elastic forces of the lung compress air in the alveoli. When alveolar pressure is greater than atmospheric, air flows out of lungs. Following expiration, volume in the lung decreases and intrapleural pressure returns to its resting volume (i.e.-5cmH_2O). Pneumothorax occurs when air is introduced into intrapleural space (e.g. hole by sharp object). In such a case there is no counterbalancing expanding force, thus lung collapses.

Work of breathing.

Refers to energy expended to:

- Expand elastic tissues of chest wall and lungs (compliance work)
- Overcome viscosity of inelastic structures of chest wall and lungs (tissue resistance work).
- Move air against resistance of airways. (airway resistance work) Work of breathing accounts 2-3% of body's total energy expenditure.

Alveolar gas exchange

Gas exchange in the respiratory system refers to diffusion of oxygen and carbon dioxide in the lungs and in the peripheral tissues. Oxygen is transferred from alveolar gas into pulmonary capillary blood and, ultimately it is delivered to the tissues, where it diffuses from systemic capillary blood into the cells. Carbon dioxide is delivered from the tissues to venous blood, (to pulmonary capillary blood), and is transferred to alveolar gas to be expired.

5-THE NERVOUS SYSTEM

Basic Structure and Function of the Nervous System

the nervous system probably includes the brain, the nervous tissue contained within the cranium, and the spinal cord, the extension of nervous tissue within the vertebral column. That suggests it is made of two organs—and you may not even think of the spinal cord as an organ—but the nervous system is a very complex structure. Within the brain, many different and separate regions are responsible for many different and separate functions. It is as if the nervous system is composed of many organs that all look similar and can only be differentiated using tools such as the microscope or electrophysiology**.**

The Central and Peripheral Nervous Systems

The nervous system can be divided into two major regions: the central and peripheral nervous systems. The central nervous system (CNS) is the brain and spinal cord, and the peripheral nervous system (PNS) are referred to as ganglia and Nerves. The brain is contained within the cranial cavity of the skull, and the spinal cord is contained within the vertebral cavity of the vertebral column.

Nervous tissue, present in both the CNS and PNS, contains two basic types of cells: neurons and glial cells. A **glial cell** is one of a variety of cells that provide a framework of tissue that supports the neurons and their activities. The **neuron** is the more functionally important of the two, in terms of the communicative function of the nervous system. To describe the functional divisions of the nervous system, it is important to understand the structure of a neuron. Neurons are cells and therefore have a **soma**, or cell body, but they also have extensions of the cell; each extension is generally referred to as a **process**. There is one important process that every neuron has called an **axon**, which is the fiber that connects a neuron with its target. Another type of process that branches off from the soma is the **dendrite**. Dendrites are responsible for receiving most of the input from other neurons. Looking at nervous tissue, there are regions that predominantly contain cell bodies and regions that are largely composed of just axons. These two regions within nervous system structures are often referred to as gray matter (the regions with many cell bodies and dendrites) or white matter (the regions with many axons).

Basic Functions of the Nervous System

The nervous system is involved in receiving information about the environment around us (sensation) and generating responses to that information (motor responses). The nervous system can be divided into regions that are responsible

for **sensation** (sensory functions) and for the **response** (motor functions). But there is a third function that needs to be included. Sensory input needs to be integrated with other sensations, as well as with memories, emotional state, or learning (cognition). Some regions of the nervous system are termed **integration** or association areas. The process of integration combines sensory perceptions and higher cognitive functions such as memories, learning, and emotion to produce a response.

Sensation. The first major function of the nervous system is sensation−receiving information about the environment to gain input about what is happening outside the body (or, sometimes, within the body). The sensory functions of the nervous system register the presence of a change from homeostasis or a particular event in the environment, known as a **stimulus**. The senses we think of most are the "big five": taste, smell, touch, sight, and hearing.

Response. The nervous system produces a response on the basis of the stimuli perceived by sensory structures. An obvious response would be the movement of muscles, such as withdrawing a hand from a hot stove, but there are broader uses of the term. The nervous system can cause the contraction of all three types of muscle tissue. For example, skeletal muscle contracts to move the skeleton, cardiac muscle is influenced as heart rate increases during exercise, and smooth muscle contracts as the digestive system moves food along the digestive tract. Responses also include the neural control of glands in the body as well, such as the production and secretion of sweat by the eccrine and merocrine sweat glands found in the skin to lower body temperature.

Controlling the Body

The nervous system can be divided into two parts mostly on the basis of a functional difference in responses. The **somatic nervous system (SNS)** is responsible for conscious perception and voluntary motor responses. Voluntary motor response means the contraction of skeletal muscle, but those contractions are not always voluntary in the sense that you have to want to perform them. Some somatic motor responses are reflexes, and often happen without a conscious decision to perform them. If your friend jumps out from behind a corner and yells "Boo!" you will be startled and you might scream or leap back. You didn't decide to do that, and you may not have wanted to give your friend a reason to laugh at your expense, but it is a reflex involving skeletal muscle contractions. Other motor responses become automatic (in other words, unconscious) as a person learns motor skills (referred to as "habit learning" or "procedural memory"). The **autonomic nervous system (ANS)** is responsible for involuntary control of the body, usually for the sake of homeostasis (regulation of the internal environment). Sensory input for autonomic functions can be from sensory structures tuned to external or internal environmental stimuli.

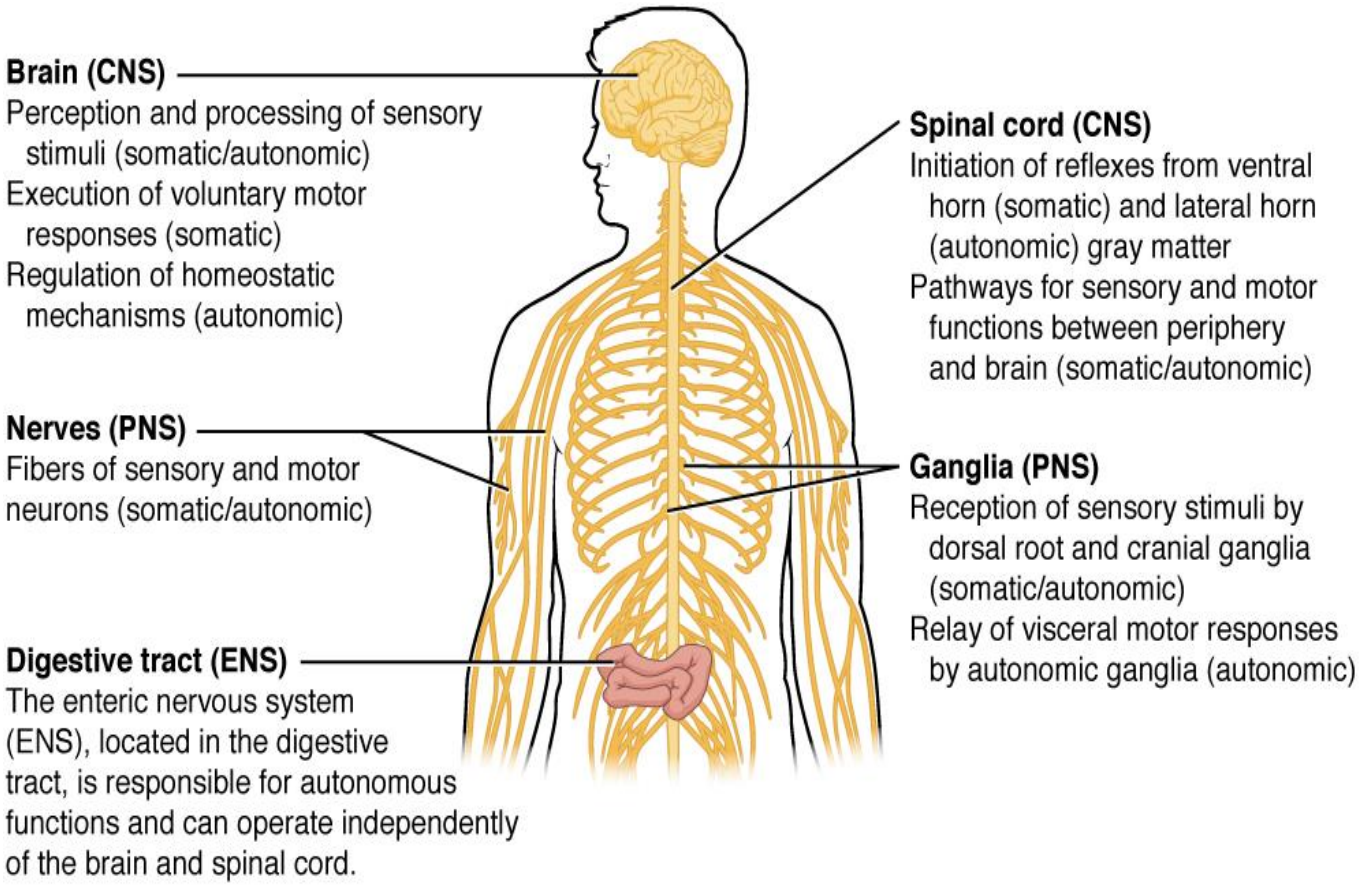


Figure: Somatic, Autonomic, and Enteric Structures of the Nervous System Somatic structures include the spinal nerves, both motor and sensory fibers, as well as the sensory ganglia (posterior root ganglia and cranial nerve ganglia). Autonomic structures are found in the nerves also, but include the sympathetic and parasympathetic ganglia. The enteric nervous system includes the nervous tissue within the organs of the digestive tract.

Nervous Tissue:

Nervous tissue is composed of two types of cells, neurons and glial cells. Neurons are the primary type of cell that most anyone associates with the nervous system. They are responsible for the computation and communication that the nervous system provides.

Neurons

Neurons are the cells considered to be the basis of nervous tissue. They are responsible for the electrical signals that communicate information about sensations, and that produce movements in response to those stimuli, along with inducing thought processes within the brain. An important part of the function of neurons is in their structure, or shape. The threedimensional shape of these cells makes the immense

numbers of connections within the nervous system possible.

Parts of a Neuron

As you learned in the first section, the main part of a neuron is the cell body, which is also known as the soma (soma = "body"). The cell body contains the nucleus and most of the major organelles. But what makes neurons special is that they have many extensions of their cell membranes, which are generally referred to as processes. Neurons are usually described as having one, and only one, axon−a fiber that emerges from the cell body and projects to target cells. That single axon can branch repeatedly to communicate with many target cells. It is the axon that propagates the nerve impulse, which is communicated to one or more cells. The other processes of the neuron are dendrites, which receive information from other neurons at specialized areas of contact called **synapses**. The dendrites are usually highly branched processes, providing locations for other neurons to communicate with the cell body. Information flows through a neuron from the dendrites, across the cell body, and down the axon. This gives the neuron a polarity−meaning that information flows in this one direction. **Figure 12.8** shows the relationship of these parts to one another.

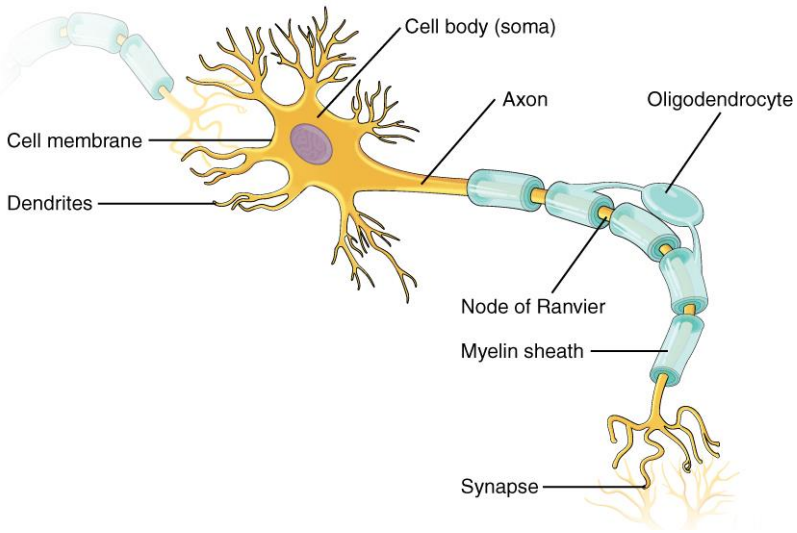
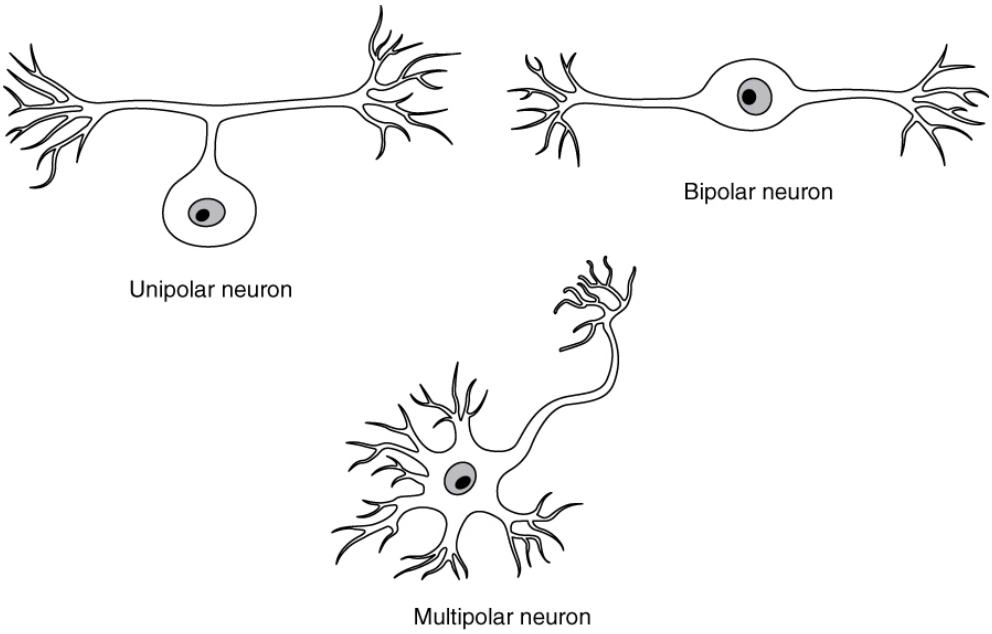


Figure : Parts of a Neuron The major parts of the neuron are labeled on a multipolar neuron from the CNS. Where the axon emerges from the cell body, there is a special region referred to as the **axon hillock**. This is a tapering of the cell body toward the axon fiber. Within the axon hillock, the cytoplasm changes to a solution of limited components called **axoplasm**. Because the axon hillock represents the beginning of the axon, it is also referred to as the **initial segment**.

Types of Neurons

There are many neurons in the nervous system—a number in the trillions. And there are many different types of neurons. They can be classified by many different criteria. The first way to classify them is by the number of processes attached to the cell body. Using the standard model of neurons, one of these processes is the axon, and the rest are dendrites. Because information flows through the neuron from dendrites or cell bodies toward the axon, these names are based on the neuron's polarity.



Unipolar cells have only one process emerging from the cell. True unipolar cells are only found in invertebrate animals, so the unipolar cells in humans are more appropriately called "pseudo-unipolar" cells. Invertebrate unipolar cells do not have dendrites. Human unipolar cells have an axon that emerges from the cell body, but it splits so that the axon can extend along a very long distance. At one end of the axon are dendrites, and at the other end, the axon forms synaptic connections with a target. Unipolar cells are exclusively sensory neurons and have two unique characteristics. First, their dendrites are receiving sensory information, sometimes directly from the stimulus itself. Secondly, the cell bodies of unipolar neurons are always found in ganglia. Sensory reception is a peripheral function (those dendrites are in the periphery, perhaps in the skin) so the cell body is in the periphery, though closer to the CNS in a ganglion. The axon projects from the dendrite endings, past the cell body in a ganglion, and into the central nervous system.

Bipolar cells have two processes, which extend from each end of the cell body, opposite to each other. One is the axon and one the dendrite. Bipolar cells are not very common. They are found mainly in the olfactory epithelium (where smell stimuli are sensed), and as part of the retina.

Multipolar neurons are all of the neurons that are not unipolar or bipolar. They have one axon and two or more dendrites (usually many more).With the exception of the unipolar sensory ganglion cells, and the two specific bipolar cells mentioned above, all other neurons are multipolar. Some cutting edge research suggests that certain neurons in the CNS do not conform to the standard model of "one, and only one" axon. Some sources describe a fourth type of neuron, called an anaxonic neuron. The name suggests that it has no axon (an- = "without"), but this is not accurate. Anaxonic neurons are very small, and if you look through a microscope at the standard resolution used in histology (approximately 400X to 1000X total magnification), you will not be able to distinguish any process specifically as an axon or a dendrite. Any of those processes can function as an axon depending on the conditions at any given time. Nevertheless, even if they cannot be easily seen, and one specific process is definitively the axon, these neurons have multiple processes and are therefore multipolar.

Glial Cells

Glial cells, or neuroglia or simply glia, are the other type of cell found in nervous tissue. They are considered to be supporting cells, and many functions are directed at helping neurons complete their function for communication. The name glia comes from the Greek word that means "glue," and was coined by the German pathologist Rudolph Virchow, who wrote in 1856: "This connective substance, which is in the brain, the spinal cord, and the special sense nerves, is a kind of glue (neuroglia) in which the nervous elements are planted.

Synapses

There are two types of connections between electrically active cells, chemical synapses and electrical synapses **chemical synapse**, a chemical signal−namely, a neurotransmitter −is released from one cell and it affects the other cell.

In an **electrical synapse**, there is a direct connection between the two cells so that ions can pass directly from one cell to the next. If one cell is depolarized in an electrical synapse, the joined cell also depolarizes because the ions pass between the cells. Chemical synapses involve the transmission of chemical information from one cell to the next. This section will concentrate on the chemical type of synapse.

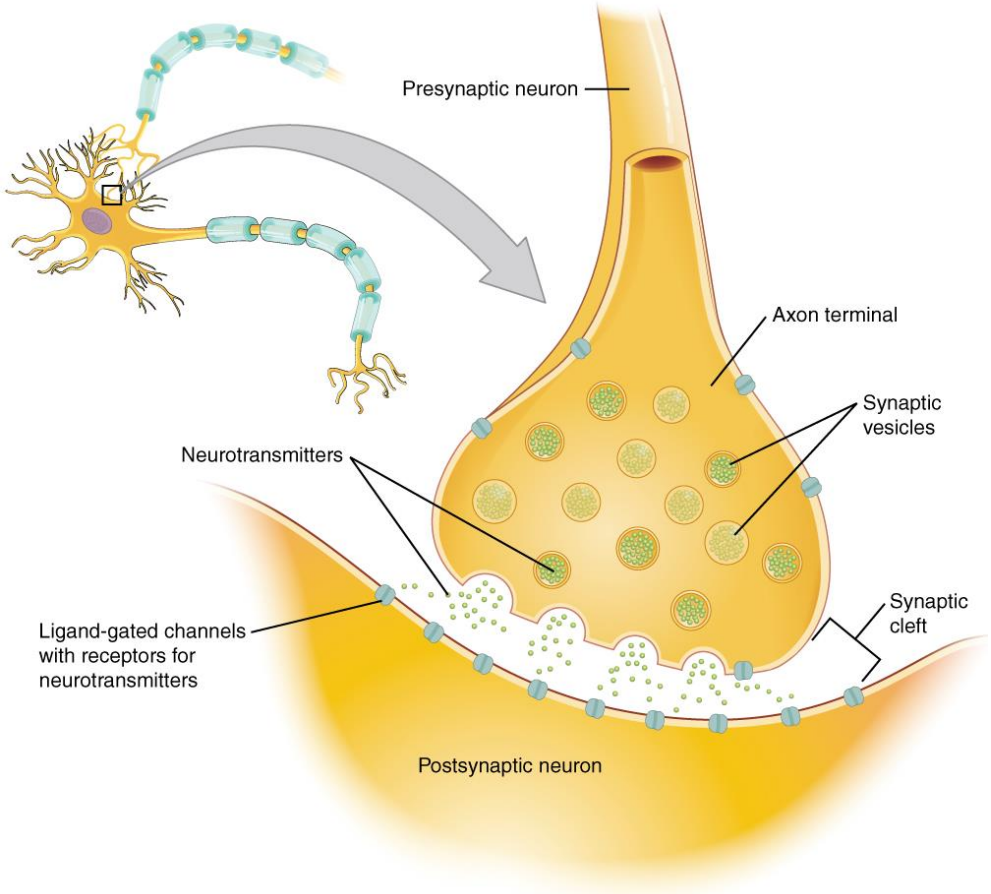


Figure 12.27 The Synapse The synapse is a connection between a neuron and its target cell (which is not necessarily a neuron). The presynaptic element is the synaptic end bulb of the axon where Ca2+ enters the bulb to cause vesicle fusion and neurotransmitter release. The neurotransmitter diffuses across the synaptic cleft to bind to its receptor. The neurotransmitter is cleared from the synapse either by enzymatic degradation, neuronal reuptake, or glial reuptake.

6- Sensation

Sensation is the process by which we receive information from the environment.

A. What kind of information? A stimulus is a detectable input from the environment:

1- Light—vision
2 -Sound—hearing
3- Chemicals—taste and smell
4- Pressure, temperature, pain—sense of touch
4- Orientation, balance—kinesthetic senses

B. Environmental information (stimuli) exists in many forms:

1- A physical stimulus must first be introduced. For example: air vibrations, gases, chemicals, tactile pressures
2-Our senses respond to a limited range of environmental stimuli
. For example, we cannot hear sound of frequenc above 20,000 Hz, even though dogs can hear them

C. Some physical stimuli that our bodies are sensitive to:

1- Light as experienced through vision
a. Visible light is part of the electromagnetic spectrum.
b. Properties of light
    i. Intensity (experienced as brightness(
    ii. Wavelength (experienced as hue(
    iii. Complexity or purity (experienced as saturation
2- Sound as experienced through audition
Properties of sound
    i. Intensity (influences mainly loudness(
    ii. Frequency (influences mainly pitch(
    iii. Wave form (influences mainly timbre(
    iv. As noted above, there is not a one-to-one

relationship between physical properties and perceptual experience. For example, intensity can also influence perception of pitch.

D. Sensory processes are the initial steps to perception.

1- Transduction is the process of converting energy of a stimulus into neural activity. The stimulus is recoded as a neural pattern.
2- Transduction can be affected by our experiences, such as through adaptation; a constant level of stimulus results in a decreased response over time. With continued exposure, the neural response to the stimulus may change. Adaption is also perceptual, not just sensory.

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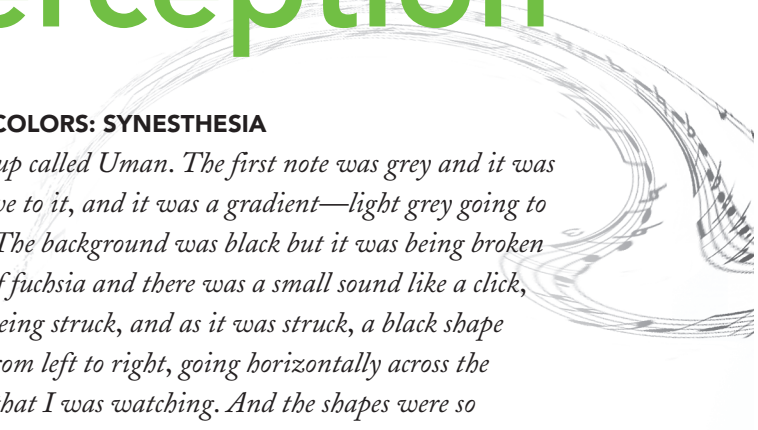
3 sensation and perception



SEEING SOUNDS AND HEARING COLORS: SYNESTHESIA

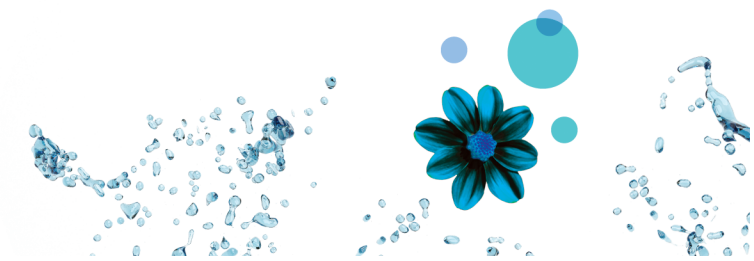
"There was a piece of music by a group called Uman. The first note was grey and it was like a band of grey with a slight curve to it, and it was a gradient—light grey going to dark grey—it had gold specks on it. The background was black but it was being broken up by other colours, moving shapes of fuchsia and there was a small sound like a click, almost like a drumbeat, something being struck, and as it was struck, a black shape appeared, and the shapes appeared from left to right, going horizontally across the bottom of this—like a movie screen that I was watching. And the shapes were so exquisite, so simple, so pure and so beautiful, I wanted somehow to be able to capture them, but they were moving too quickly and I couldn't remember them all."
—Carol Steen (1996), New York artist and synesthete, quoted from ABC Radio National Transcripts, Health Report with Robin Hughes

Ms. Steen is a most unusual artist because she is able to perceive a world where sounds have colors and shapes, an ability she often turns into unusual and beautiful sculptures. A *synesthete* is a person with **synesthesia**, which literally means "joined sensation." People with this condition are rare—about 1 in 25,000. In the synesthete, the signals that come from the sensory organs, such as the eyes or the ears, go to places in the brain where they weren't originally meant to be, causing those signals to be interpreted as more than one sensation. A fusion of sound and sight is most common, but touch, taste, and even smell can enter into the mix (Cytowic, 1989).

Although research on the physical causes of synesthesia is ongoing, some studies suggest that areas of the left side of the brain deep inside the temporal lobe and nearby in the parietal lobe may be responsible (Ramachandran & Hubbard, 2003; Rouw & Scholte, 2007). LINK to Chapter Two: The Biological Perspective, pp. 75–76.

synesthesia disorder in which the signals from the various sensory organs are processed in the wrong cortical areas, resulting in the sense information being interpreted as more than one sensation.

CHAPTER OUTLINE



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Why study sensation and perception?

Without sensations to tell us what is outside our own mental world, we would live entirely in our own minds, separate from one another and unable to find food or any other basics that sustain life. Sensations are the mind's window to the world that exists around us. Without perception, we would be unable to understand what all those sensations mean—perception is the process of interpreting the sensations we experience so that we can act upon them.

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learning objectives

3.1 How does sensation travel through the central nervous system, and why are some sensations ignored?

3.2 What is light, and how does it travel through the various parts of the eye?

3.3 How do the eyes see, and how do the eyes see different colors?

3.4 What is sound, and how does it travel through the various parts of the ear?

3.5 Why are some people unable to hear, and how can their hearing be improved?

3.6 How do the senses of taste and smell work, and how are they alike?

3.7 What allows people to experience the sense of touch, pain, motion, and balance?

3.8 What are perception and perceptual constancies?

3.9 What are the Gestalt principles of perception?

3.10 What is depth perception and what kind of cues are important for it to occur?

3.11 What are visual illusions and how can they and other factors influence and alter perception?

study tip

As you are reading this chapter, remember to use the SQ3R method discussed on pages I-7–I-8 in *Psychology in Action*. Breaking your reading into small sections will help you get more out of every chapter.

How do we get information from the outside world into our brains?

The ABCs of Sensation

How do we get information from the outside world into our brains?

Information about the world has to have a way to get into the brain, where it can be used to determine actions and responses. The way into the brain is through the sensory organs and the process of sensation.

WHAT IS SENSATION?

3.1 How does sensation travel through the central nervous system, and why are some sensations ignored?

Sensation occurs when special receptors in the sense organs—the eyes, ears, nose, skin, and taste buds—are activated, allowing various forms of outside stimuli to become neural signals in the brain. (This process of converting outside stimuli, such as light, into neural activity is called **transduction**.) Let's take a closer look at these special receptors.

SENSORY RECEPTORS The *sensory receptors* are specialized forms of neurons, the cells that make up the nervous system. Instead of receiving neurotransmitters from other cells, these receptor cells are stimulated by different kinds of energy—for example, the receptors in the eyes are stimulated by light, whereas the receptors in the ears are activated by vibrations. Touch receptors are stimulated by pressure or temperature, and the receptors for taste and smell are triggered by chemical substances.

SENSORY THRESHOLDS

Ernst Weber (1795–1878) did studies trying to determine the smallest difference between two weights that could be detected. His research led to the formulation known as Weber's law of **just noticeable differences (jnd,** or the **difference threshold**). A jnd is the smallest difference between two stimuli that is detectable 50 percent of the time, and Weber's law simply means that whatever the difference between stimuli might be, it is always a *constant*. If to notice a difference the amount of sugar a person would need to add to a cup of coffee that is already sweetened with 5 teaspoons is 1 teaspoon, then the percentage of change needed to detect a just noticeable difference is one-fifth, or 20 percent. So if the coffee has 10 teaspoons of sugar in it, the person would have to add another 20 percent, or 2 teaspoons, to be able to taste the difference half of the time. Most people would not

sensation the process that occurs when special receptors in the sense organs are activated, allowing various forms of outside stimuli to become neural signals in the brain.

transduction the process of converting outside stimuli, such as light, into neural activity.

just noticeable difference (jnd or the **difference threshold)** the smallest difference between two stimuli that is detectable 50 percent of the time.

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typically drink a cup of coffee with 10 teaspoons of sugar in it, let alone 12 teaspoons, but you get the point.

Gustav Fechner (1801–1887) expanded on Weber's work by studying something he called the **absolute threshold** (Fechner, 1860). An absolute threshold is the lowest level of stimulation that a person can consciously detect 50 percent of the time the stimulation is present. (Remember, the jnd is detecting a difference *between two* stimuli.) For example, assuming a very quiet room and normal hearing, how far away can someone sit and you might still hear the tick of their analog watch on half of the trials? For some examples of absolute thresholds for various senses, see Table 3.1.

absolute threshold the lowest level of stimulation that a person can consciously detect 50 percent of the time the stimulation is present.

I've heard about people being influenced by stuff in movies and on television, things that are just below the level of conscious awareness. Is that true?

I've heard about people being influenced by stuff in movies and on television, things that are just below the level of conscious awareness. Is that true?

Stimuli that are below the level of conscious awareness are called *subliminal stimuli*. (The word *limin* means "threshold," so *sublimin* means "below the threshold.") These stimuli are just strong enough to activate the sensory receptors but not strong enough for people to be consciously aware of them. Many people believe that these stimuli act upon the unconscious mind, influencing behavior in a process called *subliminal perception*.

At one time, many people believed that a market researcher named James Vicary had demonstrated the power of subliminal perception in advertising. It was five years before Vicary finally admitted that he had never conducted a real study (Merikle, 2000; Pratkanis, 1992). Furthermore, many researchers have gathered scientific evidence that subliminal perception does not work in advertising (Bargh et al., 1996; Broyles, 2006; Moore, 1988; Pratkanis & Greenwald, 1988; Trappey, 1996; Vokey & Read, 1985).

This is not to say that subliminal perception does not exist—there is a growing body of evidence that we process some stimuli without conscious awareness, especially stimuli that are fearful or threatening (LeDoux & Phelps, 2008; Öhman, 2008). In this effort, researchers have used *event-related potentials* (ERPs) and functional magnetic resonance imaging (fMRI) to verify the existence of subliminal perception and associated learning in the laboratory (Babiloni et al., 2010; Bernat et al., 2001; Fazel-Rezai & Peters, 2005; Sabatini et al., 2009). However, as in about every other case where subliminal perception has reportedly occurred, these studies use stimuli that are *supraliminal*—"above the threshold"—and detectable by our sensory systems. However, they are below the level of conscious perception and participants are not aware or conscious that they have been exposed to the stimuli due to masking or manipulation of attention. Furthermore,

In some parts of the USA, "coffee regular" refers to coffee with two creams and two sugars. How much more sugar would you need to add to taste a difference?

This young woman does not feel the piercings on her ear and nose because sensory adaptation allows her to ignore a constant, unchanging stimulation from the metal rings. What else is she wearing that would cause sensory adaptation?

Table 3.1
Examples of Absolute Thresholds

SENSE	THRESHOLD
Sight	A candle flame at 30 miles on a clear, dark night
Hearing	The tick of a watch 20 feet away in a quiet room
Smell	One drop of perfume diffused throughout a three-room apartment
Taste	1 teaspoon of sugar in 2 gallons of water
Touch	A bee's wing falling on the cheek from 1 centimeter above

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the stimuli typically influence automatic reactions (such as an increase in facial tension) rather than direct voluntary behaviors (such as going to buy something suggested by advertising).

The real world is full of complex motives that are not as easily influenced as one might think (Pratkanis, 1992). Even the so-called hidden pictures that some artists airbrush into the art in advertisements aren't truly subliminal—if someone points one out, it can be seen easily enough.

HABITUATION AND SENSORY ADAPTATION

In Chapter Two it was stated that the lower centers of the brain filter sensory stimulation and "ignore" or prevent conscious attention to stimuli that do not change. The brain is only interested in changes in information. That's why people don't really "hear" the noise of the air conditioner unless it suddenly cuts off or the noise made in some classrooms unless it gets very quiet. Although they actually are *hearing* it, they aren't paying attention to it. This is called **habituation**, and it is the way the brain deals with unchanging information from the environment. LINK to Chapter Two: The Biological Perspective, p. 70.

Sometimes I can smell the odor of the garbage can in the kitchen when I first come home, but after a while the smell seems to go away—is this also habituation?

Sometimes I can smell the odor of the garbage can in the kitchen when I first come home, but after a while the smell seems to go away—is this also habituation?

Although different from habituation, **sensory adaptation** is another process by which constant, unchanging information from the sensory receptors is effectively ignored. In habituation, the sensory receptors are still responding to stimulation but the lower centers of the brain are not sending the signals from those receptors to the cortex. The process of sensory adaptation differs because the receptor cells *themselves* become less responsive to an unchanging stimulus—garbage odors included—and the receptors no longer send signals to the brain.

For example, when you eat, the food that you put in your mouth tastes strong at first, but as you keep eating the same thing, the taste does fade somewhat, doesn't it? Smell, taste, and touch are all subject to sensory adaptation.

You might think, then, that if you stare at something long enough, it would also disappear, but the eyes are a little different. Even though the sensory receptors in the back of the eyes adapt to and become less responsive to a constant visual stimulus, under ordinary circumstances the eyes are never entirely still. There's a constant movement of the eyes, tiny little vibrations called "microsaccades" or "saccadic movements" that people don't consciously notice. These movements keep the eyes from adapting to what they see. (That's a good thing, because otherwise many students would no doubt go blind from staring off into space.)

habituation tendency of the brain to stop attending to constant, unchanging information.

sensory adaptation tendency of sensory receptor cells to become less responsive to a stimulus that is unchanging.

3.1

CONCEPT MAP

The ABCs of Sensation

- **sensation** process by which information from the outside world enters the brain
  - related to the activation of receptors in the various sense organs
  - related to changes in physical stimuli
    - detected by sensory receptors
    - sometimes "ignored" through sensory adaptation or cognitive habituation

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PRACTICE quiz How much do you remember? ANSWERS ON PAGE AK-1.

Pick the best answer.

1. The smallest difference between two stimuli that can be detected 50 percent of the time it is present is called _____.
   a. absolute threshold. **c.** sensation.
   b. just noticeable difference. **d.** sensory adaptation.
2. When receptor cells for the senses are activated, the process called _____ has begun.
   a. perception **c.** adaptation
   b. sublimination **d.** sensation
3. You have a piece of candy that you are holding in your mouth. After a while, the candy doesn't taste as strong as it did when you first tasted it. What has happened?
   a. sensory adaptation **c.** habituation
   b. subliminal perception **d.** perceptual defense
4. While driving down the road looking for the new restaurant you want to try out, not hearing the clicking of the turn signal you forgot to turn off until one of your friends point it out is likely due to _____:
   a. accommodation **c.** sublimation
   b. adaptation **d.** habituation

The Science of Seeing

I've heard that light is waves, but I've also heard that light is made of particles—which is it?

I've heard that light is waves, but I've also heard that light is made of particles—which is it?

Light is a complicated phenomenon. Although scientists have long argued over the nature of light, they finally have agreed that light has the properties of both waves and particles. The following section gives a brief history of how scientists have tried to "shed light" on the mystery of light.

PERCEPTUAL PROPERTIES OF LIGHT: CATCHING THE WAVES

3.2 What is light, and how does it travel through the various parts of the eye?

It was Albert Einstein who first proposed that light is actually tiny "packets" of waves. These "wave packets" are called *photons* and have specific wavelengths associated with them (Lehnert, 2007; van der Merwe & Garuccio, 1994).

When people experience the physical properties of light, they are not really aware of its dual, wavelike and particle-like, nature. With regard to its psychological properties, there are three aspects to our perception of light: *brightness, color*, and *saturation*.

Brightness is determined by the amplitude of the wave—how high or how low the wave actually is. The higher the wave, the brighter the light appears to be. Low waves are dimmer. *Color*, or hue, is largely determined by the length of the wave. Long wavelengths (measured in nanometers) are found at the red end of the *visible spectrum* (the portion of the whole spectrum of light that is visible to the human eye; see Figure 3.1), whereas shorter wavelengths are found at the blue end. (Note that when combining different colors, light behaves differently than pigments or paint. We will look at this distinction when we examine perception of color).

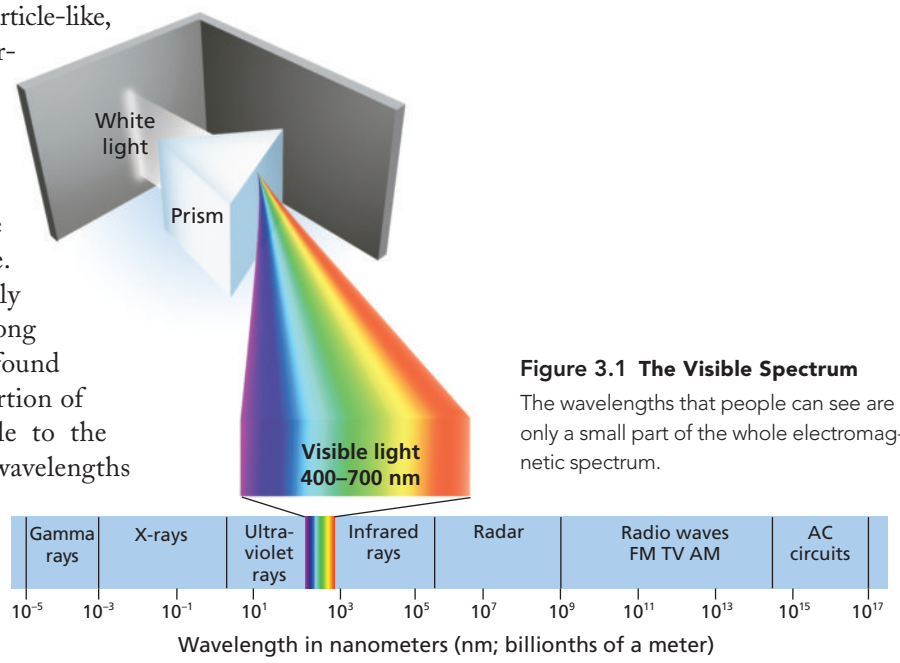

Figure 3.1 The Visible Spectrum
The wavelengths that people can see are only a small part of the whole electromagnetic spectrum.

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Saturation refers to the purity of the color people perceive: A highly saturated red, for example, would contain only red wavelengths, whereas a less-saturated red might contain a mixture of wavelengths. For example, when a child is using the red paint from a set of poster paints, the paint on the paper will look like a pure red, but if the child mixes in some white paint, the paint will look pink. The hue is still red but it will be less of a saturated red because of the presence of white wavelengths. Mixing in black or gray would also lessen the saturation.

THE STRUCTURE OF THE EYE

The best way to talk about how the eye processes light is to talk about what happens to an image being viewed as the photons of light from that image travel through the eye. Refer to Figure 3.2 to follow the path of the image. **Simulate** on **mypsychlab.com**

Simulate the structures of the eye on **mypsychlab.com**

FROM FRONT TO BACK: THE PARTS OF THE EYE Light enters the eye directly from a source (such as the sun) or indirectly by reflecting off of an object. To see clearly, a single point of light from a source or reflected from an object must travel through the structures of the eye and end up on the retina as a single point. Light bends as it passes through substances of different densities, through a process known as refraction. For example, have you ever looked at a drinking straw in a glass of water through the side of the glass? It appears that the straw bends, or is broken, at the surface of the water. That optical illusion is due to the refraction of light. The structures of the eye play a vital role in both collecting and focusing of light so we can see clearly.

The surface of the eye is covered in a clear membrane called the *cornea*. The cornea not only protects the eye but also is the structure that focuses most of the light coming into the eye. The cornea has a fixed curvature, like a camera that has no option to adjust the focus. However, this curvature can be changed somewhat through vision-improving techniques that change the shape of the cornea. For example, ophthalmologists can use both *photoreactive keratectomy (PRK)* and *laser-assisted in situ keratomileusis (LASIK)* procedures to remove small portions of the cornea, changing its curvature, and thus the focus in the eye.

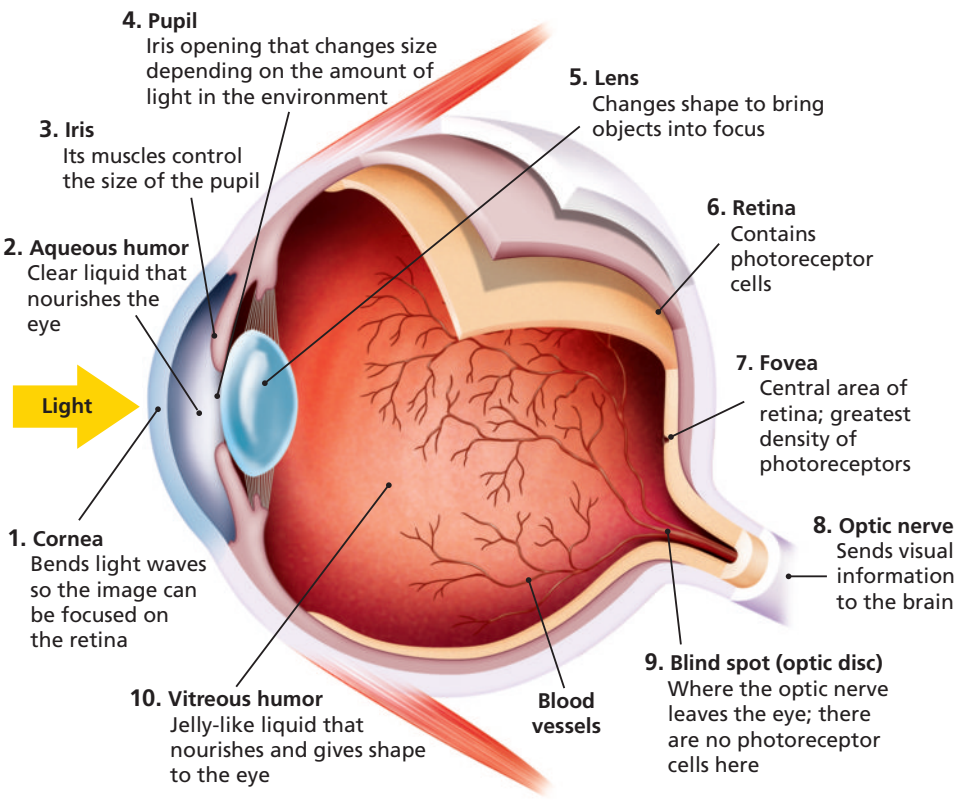

Figure 3.2 Structure of the Eye
Light enters the eye through the cornea and pupil. The iris controls the size of the pupil. From the pupil, light passes through the lens to the retina, where it is transformed into nerve impulses. The nerve impulses travel to the brain along the optic nerve.

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The next visual layer is a clear, watery fluid called the *aqueous humor*. This fluid is continually replenished and supplies nourishment to the eye. The light from the visual image then enters the interior of the eye through a hole, called the *pupil*, in a round muscle called the *iris* (the colored part of the eye). The iris can change the size of the pupil, letting more or less light into the eye. That also helps focus the image; people try to do the same thing by squinting.

Behind the iris, suspended by muscles, is another clear structure called the *lens*. The flexible lens finishes the focusing process begun by the cornea. In a process called **visual accommodation**, the lens changes its shape from thick to thin, enabling it to focus on objects that are close or far away. The variation in thickness allows the lens to project a sharp image on the retina. People lose this ability as the lens hardens through aging (a disorder called *presbyopia*). Although people try to compensate* for their inability to focus on things that are close to them, eventually they usually need bifocals because their arms just aren't long enough anymore.

Once past the lens, light passes through a large, open space filled with a clear, jelly-like fluid called the *vitreous humor*. This fluid, like the aqueous humor, also nourishes the eye and gives it shape.

RETINA, RODS, AND CONES The final stop for light within the eye is the *retina*, a light-sensitive area at the back of the eye containing three layers: ganglion cells, bipolar cells, and the **rods** and **cones**, special cells (*photoreceptors*) that respond to the various light waves. (See Figures 3.3a and b.) The rods and the cones are the business end of the retina—the part that actually receives the photons of light and turns them into neural signals to the brain, sending them first to the *bipolar cells* (a type of interneuron; called bipolar or "two-ended" because they have a single dendrite at one end and a single axon on the other; LINK to Chapter Two: The Biological Perspective, p. 57) and then to the retinal *ganglion cells* whose axons form the optic nerve. (See Figure 3.3a.)

visual accommodation the change in the thickness of the lens as the eye focuses on objects that are far away or close.

rods visual sensory receptors found at the back of the retina, responsible for non-color sensitivity to low levels of light.

cones visual sensory receptors found at the back of the retina, responsible for color vision and sharpness of vision.

This photo illustrates an optical illusion caused by the refraction of light. The straw is not really broken although it appears that way.

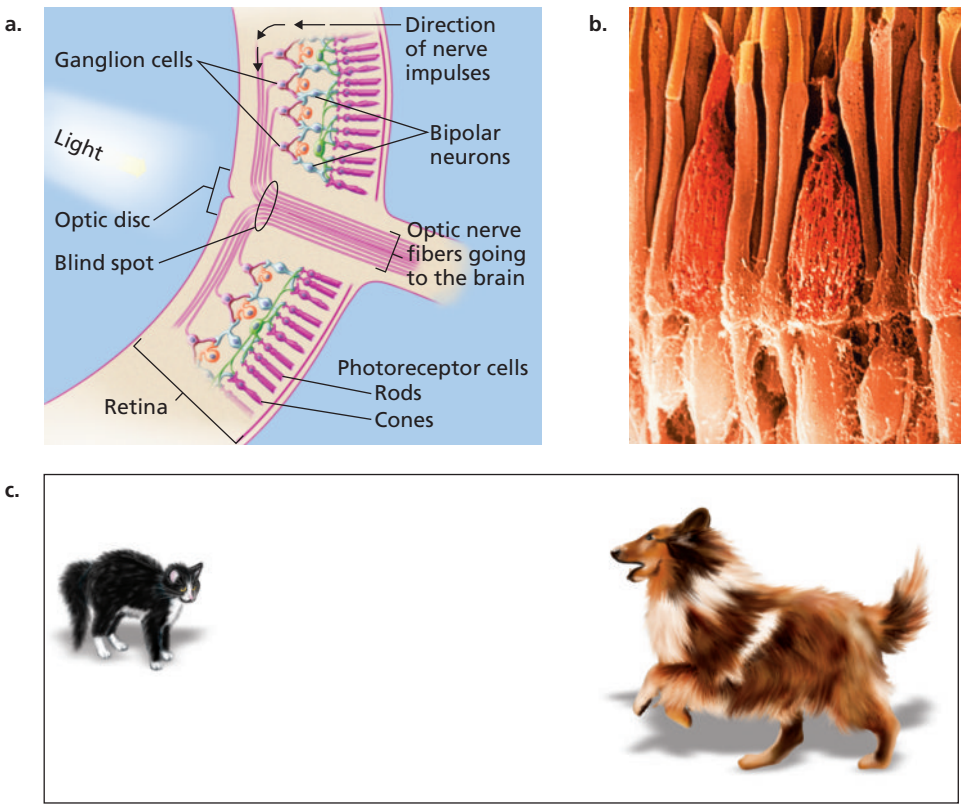

Figure 3.3 The Parts of the Retina
(a) Light passes through ganglion and bipolar cells until it reaches and stimulates the rods and cones. Nerve impulses from the rods and cones travel along a nerve pathway to the brain. (b) On the right of the figure is a photomicrograph of the long, thin rods and the shorter, thicker cones; the rods outnumber the cones by a ratio of about 20 to 1. (c) The blind spot demonstration. Hold the book in front of you. Close your right eye and stare at the picture of the dog with your left eye. Slowly bring the book closer to your face. The picture of the cat will disappear at some point because the light from the picture of the cat is falling on your blind spot.

*compensate: to correct for an error or defect.

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blind spot area in the retina where the axons of the three layers of retinal cells exit the eye to form the optic nerve, insensitive to light.

dark adaptation the recovery of the eye's sensitivity to visual stimuli in darkness after exposure to bright lights.

THE BLIND SPOT The eyes don't adapt to constant stimuli under normal circumstances because of saccadic movements. But if people stare with one eye at one spot long enough, objects that slowly cross their visual field may at one point disappear briefly because there is a "hole" in the retina—the place where all the axons of those ganglion cells leave the retina to become the optic nerve. There are no rods or cones here, so this is referred to as the **blind spot**. You can demonstrate the blind spot for yourself by following the directions in Figure 3.3c.

HOW THE EYE WORKS

3.3 How do the eyes see, and how do the eyes see different colors?

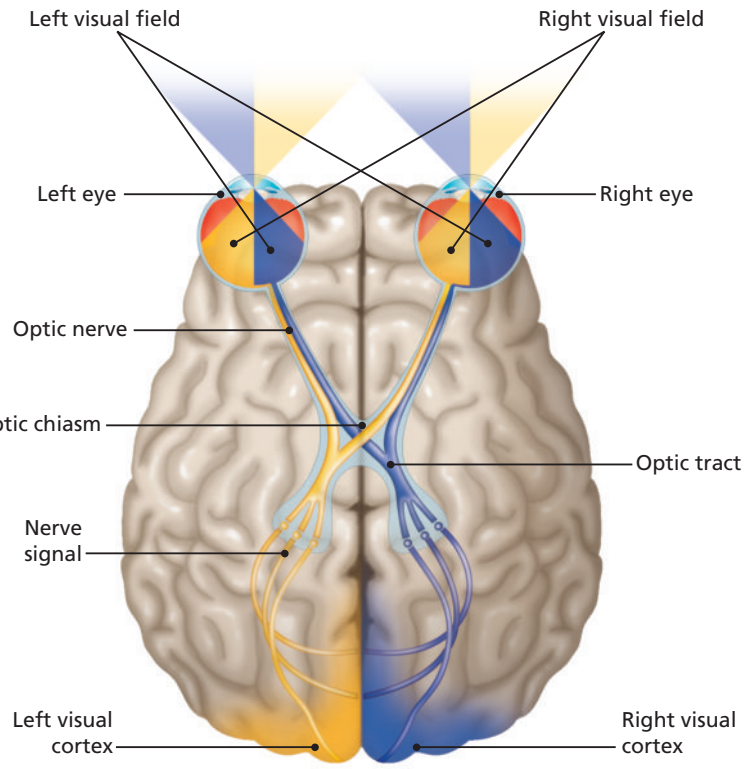

Figure 3.4 Crossing of the Optic Nerve

Light falling on the left side of each eye's retina (from the right visual field, shown in yellow) will stimulate a neural message that will travel along the optic nerve to the visual cortex in the occipital lobe of the left hemisphere. Notice that the message from the temporal half of the left retina goes directly to the left occipital lobe, while the message from the nasal half of the right retina crosses over to the left hemisphere (the optic chiasm is the point of crossover). The optic nerve tissue from both eyes joins together to form the left optic tract before going on to the left occipital lobe. For the left visual field (shown in blue), the messages from both right sides of the retinas will travel along the right optic tract to the right visual cortex in the same manner.

THROUGH THE EYES TO THE BRAIN You may want to first look at Figure 3.4 for a moment before reading this section. Light entering the eyes can be separated into the left and right visual fields. Light from the right visual field falls on the left side of each eye's retina; light from the left visual field falls on the right side of each retina. Light travels in a straight line through the cornea and lens; resulting in the image projected on the retina actually being upside down and reversed from left to right as compared to the visual fields. Thank goodness our brains can compensate for this!

The areas of the retina can be divided into halves, with the halves toward the temples of the head referred to as the temporal retinas and the halves toward the center, or nose, called the nasal retinas. Look at Figure 3.4 again. Notice that the information from the left visual field (falling on the right side of each retina) goes directly to the right visual cortex, while the information from the right visual field (falling on the left side of each retina) goes directly to the left visual cortex. This is because the axons from the temporal halves of each retina project to the visual cortex on the same side of the brain while the axons from the nasal halves cross over to the visual cortex on the opposite side of the brain. The optic chiasm is the point of crossover.

Let's go back now to the photoreceptors in the retina, the rods and cones responsible for different aspects of vision. The rods (about 120 million of them in each eye) are found all over the retina except in the very center, which contains only cones. Rods are sensitive to changes in brightness but not to changes in wavelength, so they see only in black and white and shades of gray. They can be very sensitive because many rods are connected to a single bipolar cell, so that if even only one rod is stimulated by a photon of light, the brain perceives the whole area of those rods as stimulated (because the brain is receiving the message from the single bipolar cell). But because the brain doesn't know exactly what part of the area (which rod) is actually sending the message, the visual acuity (sharpness) is quite low. That's why things seen in low levels of light, such as twilight or a dimly lit room, are fuzzy and grayish. Because rods are located on the periphery of the retina, they are also responsible for peripheral vision.

Because rods work well in low levels of light, they are also the cells that allow the eyes to adapt to low light. **Dark adaptation** occurs as the eye recovers its ability to see when going from a brightly lit state to a dark state. (The light-sensitive pigments that

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allow us to see are able to regenerate or "recharge" in the dark.) The brighter the light was, the longer it takes the rods to adapt to the new lower levels of light (Bartlett, 1965). This is why the bright headlights of an oncoming car can leave a person less able to see for a while after that car has passed. Fortunately, this is usually a temporary condition because the bright light was on so briefly and the rods readapt to the dark night relatively quickly. Full dark adaptation, which occurs when going from more constant light to darkness such as turning out one's bedroom lights, takes about 30 minutes. As people get older this process takes longer, causing many older persons to be less able to see at night and in darkened rooms (Klaver et al., 1998). This age-related change can cause *night blindness*, in which a person has difficulty seeing well enough to drive at night or get around in a darkened room or house. Some research indicates that taking supplements such as vitamin A can reverse or relieve this symptom in some cases (Jacobsen et al., 1995).

When going from a darkened room to one that is brightly lit, the opposite process occurs. The cones have to adapt to the increased level of light, and they accomplish this **light adaptation** much more quickly than the rods adapt to darkness—it takes a few seconds at most (Hood, 1998). There are 6 million cones in each eye; of these, 50,000 have a private line to the optic nerve (one bipolar cell for each cone). This means that the cones are the receptors for visual acuity. Cones are located all over the retina but are more concentrated at its very center where there are no rods (the area called the *fovea*). Cones also need a lot more light to function than the rods do, so cones work best in bright light, which is also when people see things most clearly. Cones are also sensitive to different wavelengths of light, so they are responsible for color vision.

While this deer may see quite well when using its rods at night, the bright headlights of a car will activate the cones. The cones will adapt rather quickly, but it takes time for the deer's pupil to contract, leaving the deer blinded by the light until then.

PERCEPTION OF COLOR

Earlier you said the cones are used in color vision. There are so many colors in the world—are there cones that detect each color? Or do all cones detect all colors?

Earlier you said the cones are used in color vision. There are so many colors in the world—are there cones that detect each color? Or do all cones detect all colors?

Although experts in the visual system have been studying color and its nature for many years, at this point in time there is an ongoing theoretical discussion about the role the cones play in the sensation of color.

THEORIES OF COLOR VISION Two theories about how people see colors were originally proposed in the 1800s. The first is called the **trichromatic** ("three colors") **theory**. First proposed by Thomas Young in 1802 and later modified by Hermann von Helmholtz in 1852, this theory proposed three types of cones: red cones, blue cones, and green cones, one for each of the three primary colors of light.

Most people probably think that the primary colors are red, yellow, and blue, but these are the primary colors when talking about *painting*—not when talking about *light*. Paints *reflect* light, and the way reflected light mixes is different from the way direct light mixes. For example, if an artist were to blend red, yellow, and blue paints together, the result would be a mess—a black mess. The mixing of paint (reflected light) is subtractive, removing more light as you mix in more colors. As all of the colors are mixed, the more light waves are absorbed and we see black. But if the artist were to blend a red, green, and blue light together by focusing lights of those three colors on one common spot, the result would be white, not black. The mixing of direct light is additive, resulting in lighter colors, more light, and when mixing red, blue, and green, we see white, the reflection of the entire visual spectrum.

In the trichromatic theory, different shades of colors correspond to different amounts of light received by each of these three types of cones. These cones then fire their message to the brain's vision centers. It is the combination of cones and the rate at which they are firing that determine the color that will be seen. For example, if the red and green cones are firing in response to a stimulus at fast enough rates, the color the person sees is yellow. If the red and blue cones are firing fast enough, the result is magenta. If the blue and green cones are firing fast enough, a kind of cyan color (blue-green) appears.

In trichromatic theory, the three types of cones combine to form different colors much as these three colored lights combine.

light adaptation the recovery of the eye's sensitivity to visual stimuli in light after exposure to darkness.

trichromatic theory theory of color vision that proposes three types of cones: red, blue, and green.

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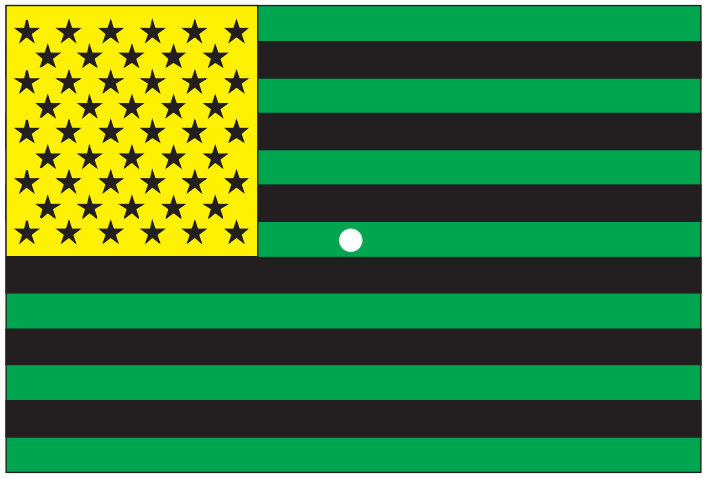

Figure 3.5 Color Afterimage

Stare at the white dot in the center of this oddly colored flag for about 30 seconds. Now look at a white piece of paper or a white wall. Notice that the colors are now the normal, expected colors of the American flag. They are also the primary colors that are opposites of the colors in the picture and provide evidence for the opponent-process theory of color vision.

Brown and Wald (1964) identified three types of cones in the retina, each sensitive to a range of wavelengths, measured in nanometers (nm), and a peak sensitivity that roughly corresponds to three different colors (although hues/colors can vary depending on brightness and saturation). The peak wavelength of light the cones seem to be most sensitive to turns out to be just a little different from Young and von Helmholtz's original three corresponding colors: Short wavelength cones detect what we see as blue-violet (about 420 nm), medium wavelength cones detect what we see as green (about 530 nm), and long wavelength cones detect what we see as green-yellow (about 560 nm). Interestingly, none of the cones identified by Brown and Wald have a peak sensitivity to light where most of us see red (around 630 nm). Keep in mind though, each cone responds to light across a range of wavelengths, not just its wavelength of peak sensitivity. Depending on the intensity of the light, both the medium and long wavelength cones respond to light that appears red.

THE AFTERIMAGE The trichromatic theory would, at first glance, seem to be more than adequate to explain how people perceive color. But there's an interesting phenomenon that this theory cannot explain. If a person stares at a picture of the American flag for a little while—say, a minute—and then looks away to a blank white wall or sheet of paper, that person will see an afterimage of the flag. **Afterimages** occur when a visual sensation persists for a brief time even after the original stimulus is removed. The person would also notice rather quickly that the colors of the flag in the afterimage are all wrong—green for red, black for white, and yellow for blue. If you follow the directions for Figure 3.5, in which the flag is yellow, green, and black, you should see a flag with the usual red, white, and blue.

Hey, now the afterimage of the flag has normal colors! Why does this happen?

Hey, now the afterimage of the flag has normal colors! Why does this happen?

The phenomenon of the color afterimage is explained by the second theory of color perception, called the **opponent-process theory** (De Valois & De Valois, 1993; Hurvich & Jameson, 1957), based on an idea first suggested by Edwald Hering in 1874 (Finger, 1994). In opponent-process theory, there are four primary colors: red, green, blue, and yellow. The colors are arranged in pairs, red with green and blue with yellow. If one member of a pair is strongly stimulated, the other member is inhibited and cannot be working—so there are no reddish-greens or bluish-yellows.

So how can this kind of pairing cause a color afterimage? From the level of the bipolar and ganglion cells in the retina, all the way through the thalamus, and on to the visual cortical areas in the brain, some neurons (or groups of neurons) are stimulated by light from one part of the visual spectrum and inhibited by light from a different part of the spectrum. For example, let's say we have a red-green ganglion cell in the retina whose baseline activity is rather weak when we expose it to white light. However, the cell's activity is increased by red light, so we experience the color red. If we stimulate the cell with red light for a long enough period of time, the cell becomes fatigued. If we then swap out the red light with white light, the now-tired cell responds even less than the original baseline. Now we experience the color green, because green is associated with a decrease in the responsiveness of this cell.

So which theory is the right one? Both theories play a part in color vision. Trichromatic theory can explain what is happening with the raw stimuli, the actual detection of various wavelengths of light. Opponent-process theory can explain afterimages and other aspects of visual perception that occur after the initial detection of light from our environment. In addition to the retinal bipolar and ganglion cells, opponent-process cells are contained inside the thalamus in an area called the lateral

afterimages images that occur when a visual sensation persists for a brief time even after the original stimulus is removed.

opponent-process theory theory of color vision that proposes visual neurons (or groups of neurons) are stimulated by light of one color and inhibited by light of another color.

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geniculate nucleus (LGN). The LGN is part of the pathway that visual information takes to the occipital lobe. It is when the cones in the retina send signals through the retinal bipolar and ganglion cells that we see the red versus green pairings and blue versus yellow pairings. Together with the retinal cells, the cells in the LGN appear to be the ones responsible for opponent-processing of color vision and the afterimage effect.

So which theory accounts for color blindness? I've heard that there are two kinds of color blindness, when you can't tell red from green and when you can't tell blue from yellow.

So which theory accounts for color blindness? I've heard that there are two kinds of color blindness, when you can't tell red from green and when you can't tell blue from yellow.

COLOR BLINDNESS From the mention of red-green and yellow-blue color blindness, one might think that the opponent-process theory explains this problem. But in reality "color blindness" is caused by defective cones in the retina of the eye and as a more general term, *color-deficient vision* is more accurate, as most people with "color blindness" have two type of cones working and can see many colors.

There are really three kinds of color-deficient vision. In a very rare type, *monochrome color blindness*, people either have no cones or have cones that are not working at all. Essentially, if they have cones, they only have one type and, therefore, everything looks the same to the brain—shades of gray. The other types of color-deficient vision, or *dichromatic vision*, are caused by the same kind of problem—having one cone that does not work properly. *Protanopia* (red-green color deficiency) is due to the lack of functioning red cones and *deuteranopia* (another type of red-green color deficiency) results from the lack of functioning green cones. In both of these, the individual confuses reds and greens, seeing the world primarily in blues, yellows, and shades of gray. A lack of functioning blue cones is much less common and called *tritanopia* (blue-yellow color deficiency). These individuals see the world primarily in reds, greens, and shades of gray. To get an idea of what a test for color-deficient vision is like, look at Figure 3.6.

Why are most of the people with color-deficient vision men?

Why are most of the people with color-deficient vision men?

Color-deficient vision involving one set of cones is inherited in a pattern known as *sex-linked inheritance*. The gene for color-deficient vision is *recessive*. To inherit a recessive trait, you normally need two of the genes, one from each parent. LINK to Chapter Eight: Development Across the Life Span, p. 301. But the gene for color-deficient vision is attached to a particular chromosome (a package of genes) that helps to determine the sex of a person. Men have one X chromosome and one smaller Y chromosome (named for their shapes), whereas women have two X chromosomes. The smaller Y has fewer genes than the larger X, and one of the genes missing is the one that would suppress the gene for color-deficient vision. For a woman to have color-deficient vision, she must inherit two recessive genes, one from each parent, but a man only needs to inherit *one* recessive gene—the one passed on to him on his mother's X chromosome. His odds are greater; therefore, more males than females have color-deficient vision. **Read** on **mypsychlab.com**

Read and learn more about color blindness on **mypsychlab.com**

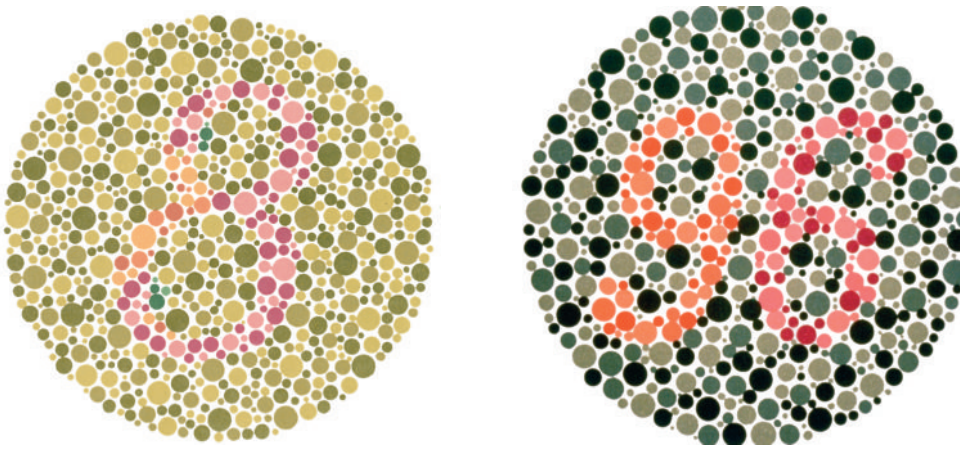

Figure 3.6 The Ishihara Color Test
In the circle on the left, the number 8 is visible only to those with normal color vision. In the circle on the right, people with normal vision will see the number 96, while those with red-green color blindness will see nothing but a circle of dots.

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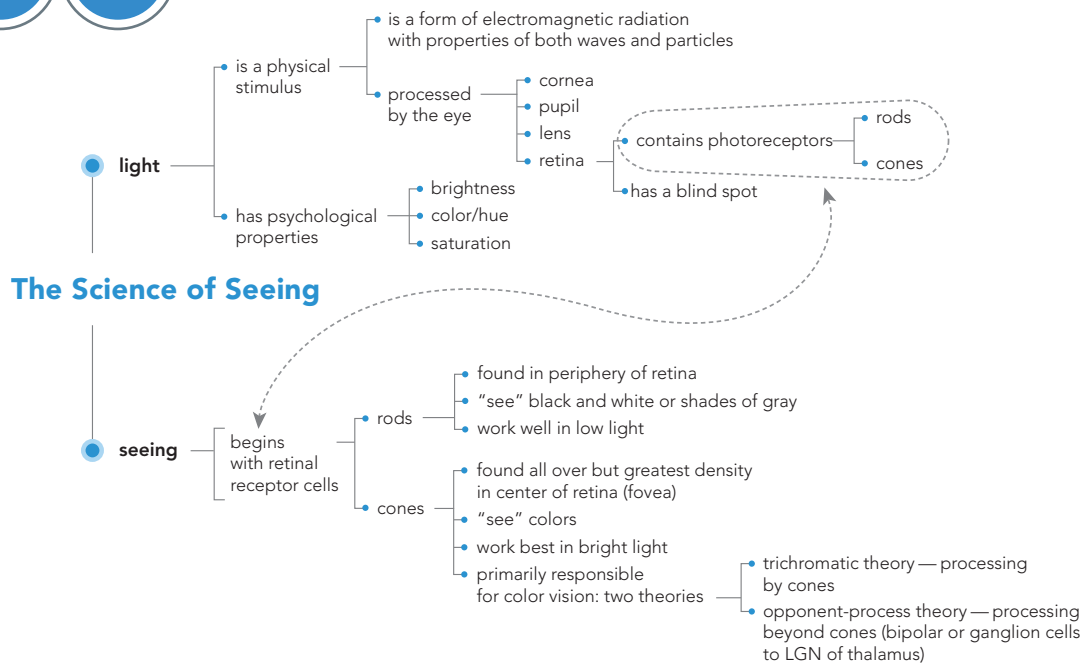
3.2 3.3

CONCEPT MAP



PRACTICE quiz How much do you remember? ANSWERS ON PAGE AK-1.

Pick the best answer.

1. Which of the following terms refers to the perceived effect of the amplitude of light waves?
   a. color **c.** saturation
   b. brightness **d.** hue
2. Which of the following represents the correct path of light through the eye?
   a. iris, cornea, lens, retina
   b. cornea, vitreous humor, iris, lens, aqueous humor, retina
   c. cornea, pupil, lens, vitreous humor, retina
   d. cornea, lens, pupil, iris, retina
3. If you wanted to locate a dimly lit star better at night, what should you do?
   a. Look directly at it because the cones will focus better at night.
   b. Look off to the side, using the cones in the periphery of the retina.
   c. Look directly at it because the rods can see sharply at night.
   d. Look off to the side, using the rods in the periphery of the retina.
4. Which theory of color vision best accounts for afterimages?
   a. trichromatic theory **c.** both a and b
   b. opponent-process theory **d.** neither a nor b
5. Which statement about color-deficient vision is TRUE?
   a. There are more men with color-deficient vision than women.
   b. All people with color-deficient vision see only in black and white.
   c. Some people with color-deficient vision see only in blue.
   d. Some people with color-deficient vision see only in blue and red.

If light works like waves, then do sound waves have similar properties?

The Hearing Sense: Can You Hear Me Now?

If light works like waves, then do sound waves have similar properties?

The properties of sound are indeed similar to those of light, as both senses rely on waves. But the similarity ends there, as the physical properties of sound are different from those of light.

PERCEPTION OF SOUND: GOOD VIBRATIONS

3.4 What is sound, and how does it travel through the various parts of the ear?

Sound waves do not come in little packets the way light comes in photons. Sound waves are simply the vibrations of the molecules of air that surround us. Sound waves do have the same properties of light waves though—wavelength, amplitude, and

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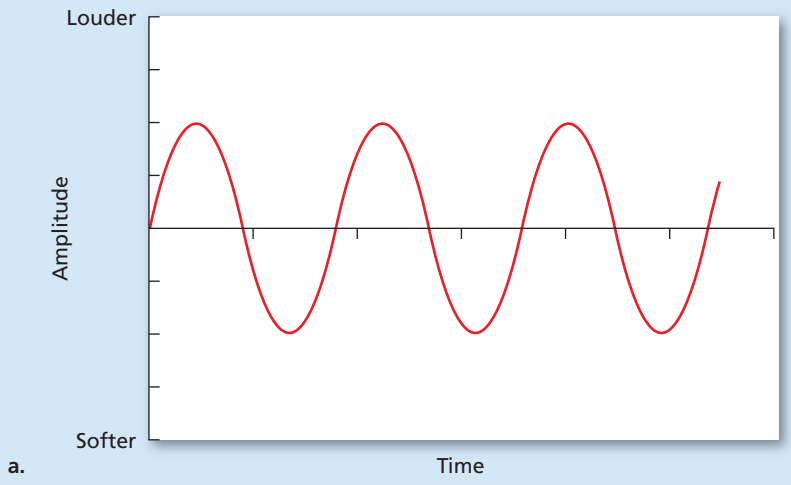

Figure 3.7 Sound Waves and Decibels
(a) A typical sound wave. The higher the wave, the louder the sound; the lower the wave, the softer the sound. If the waves are close together in time (high frequency), the pitch will be perceived as a high pitch. Waves that are farther apart (low frequency) will be perceived as having a lower pitch. (b) Decibels of various stimuli. A *decibel* is a unit of measure for loudness. Psychologists study the effects that noise has on stress, learning, performance, aggression, and psychological and physical well-being.

purity. Wavelengths are interpreted by the brain as the frequency or *pitch* (high, medium, or low). Amplitude is interpreted as *volume*, how soft or loud a sound is. (See Figure 3.7.) Finally, what would correspond to saturation or purity in light is called *timbre* in sound, a richness in the tone of the sound. And just as people rarely see pure colors in the world around us, they also seldom hear pure sounds. The everyday noises that surround people do not allow them to hear many pure tones.

Just as a person's vision is limited by the visible spectrum of light, a person is also limited in the range of frequencies he or she can hear. Frequency is measured in cycles (waves) per second, or **hertz (Hz)**. Human limits are between 20 and 20,000 Hz, with the most sensitivity from about 2000 to 4000 Hz, very important for conversational speech. (In comparison, dogs can hear between 50 and 60,000 Hz, and dolphins can hear up to 200,000 Hz.) To hear the higher and lower frequencies of a piece of music on a CD, for example, a person would need to increase the amplitude or volume—which explains why some people like to "crank it up."

"And only you can hear this whistle?"

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hertz (Hz) cycles or waves per second, a measurement of frequency.

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pinna the visible part of the ear.

auditory canal short tunnel that runs from the pinna to the eardrum.

cochlea snail-shaped structure of the inner ear that is filled with fluid.

auditory nerve bundle of axons from the hair cells in the inner ear.

Explore the structures of the ear on **mypsychlab.com**

THE STRUCTURE OF THE EAR: FOLLOW THE VIBES

The ear is a series of structures, each of which plays a part in the sense of hearing, as shown in Figure 3.8.

THE OUTER EAR The **pinna** is the visible, external part of the ear that serves as a kind of concentrator, funneling* the sound waves from the outside into the structure of the ear. The pinna is also the entrance to the **auditory canal** (or ear canal), the short tunnel that runs down to the *tympanic membrane*, or eardrum. When sound waves hit the eardrum, they cause three tiny bones in the middle ear to vibrate. **Explore** on **mypsychlab.com**

THE MIDDLE EAR: HAMMER, ANVIL, AND STIRRUP The three tiny bones in the middle ear are known as the hammer (*malleus*), anvil (*incus*), and stirrup (*stapes*), each name stemming from the shape of the respective bone. The vibration of these three bones amplifies the vibrations from the eardrum. The stirrup, the last bone in the chain, causes a membrane covering the opening of the inner ear to vibrate.

THE INNER EAR This membrane is called the *oval window*, and its vibrations set off another chain reaction within the inner ear.

Cochlea The inner ear is a snail-shaped structure called the **cochlea**, which is filled with fluid. When the oval window vibrates, it causes the fluid in the cochlea to vibrate. This fluid surrounds a membrane running through the middle of the cochlea called the *basilar membrane*.

Basilar Membrane and the Organ of Corti The *basilar membrane* is the resting place of the *organ of Corti*, which contains the receptor cells for the sense of hearing. When the basilar membrane vibrates, it vibrates the organ of Corti, causing it to brush against a membrane above it. On the organ of Corti are special cells called *hair cells*, which are the receptors for sound. When these auditory receptors or hair cells are bent up against the other membrane, it causes them to send a neural message through the **auditory nerve** (which contains

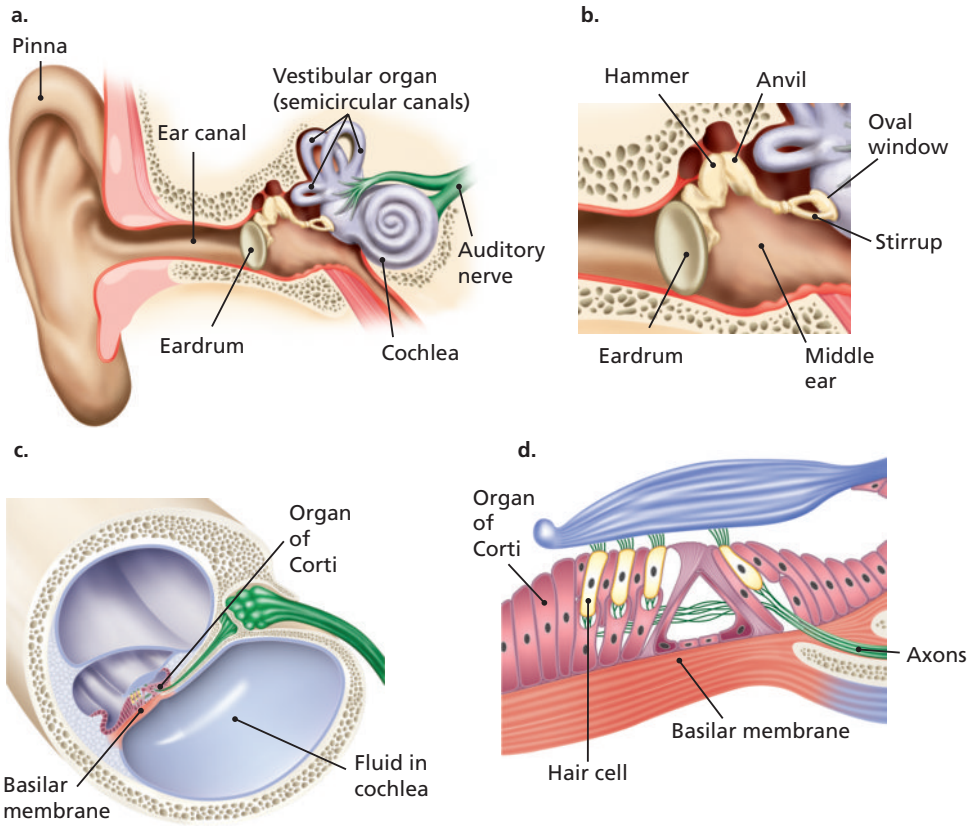

Figure 3.8 The Structure of the Ear

(a) This drawing shows the entire ear, beginning with the outer ear (pinna, ear canal, and eardrum). The vestibular organ includes the semicircular canals and the otolith organs (inside the round structures just above the cochlea). (b) The middle ear. Sound waves entering through the ear canal cause the eardrum to vibrate, which causes each of the three bones of the middle ear to vibrate, amplifying the sound. The stirrup rests on the oval window, which transmits its vibration to the fluid in the inner ear. (c) The inner ear. Large spaces are filled with fluid (shown in purple) that vibrates as the oval window vibrates. A thin membrane suspended in this fluid is called the basilar membrane, which contains the organ of Corti, the structure composed of the hairlike cells that send signals to the auditory cortex of the brain by way of the auditory nerve. (d) A close-up view of the basilar membrane (in dark pink) with the hair cells of the organ of Corti (in lighter pink). Notice the axons (small green lines) leaving the hair cells to form the auditory nerve.

*funneling: moving to a focal point.

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the axons of all the receptor neurons) and into the brain, where the auditory cortex will interpret the sounds (the transformation of the vibrations of sound into neural messages is transduction). The louder the sound in the outside world, the stronger the vibrations that stimulate more of those hair cells—which the brain interprets as loudness.

I think I have it straight—but all of that just explains how soft and loud sounds get to the brain from the outside. How do we hear different kinds of sounds, like high pitches and low pitches?

I think I have it straight—but all of that just explains how soft and loud sounds get to the brain from the outside. How do we hear different kinds of sounds, like high pitches and low pitches?

PERCEIVING PITCH

Pitch refers to how high or low a sound is. For example, the bass tones in the music pounding through the wall of your apartment from the neighbors next door is a low pitch, whereas the scream of a 2-year-old child is a very high pitch. *Very* high. There are three primary theories about how the brain receives information about pitch.

The oldest of the three theories, **place theory**, is based on an idea proposed in 1863 by Hermann von Helmholtz and elaborated on and modified by Georg von Békésy, beginning with experiments first published in 1928 (Békésy, 1960). In this theory, the pitch a person hears depends on where the hair cells that are stimulated are located on the organ of Corti. For example, if the person is hearing a high-pitched sound, all of the hair cells near the oval window will be stimulated, but if the sound is low pitched, all of the hair cells that are stimulated will be located farther away on the organ of Corti.

Frequency theory, developed by Ernest Rutherford in 1886, states that pitch is related to how fast the basilar membrane vibrates. The faster this membrane vibrates, the higher the pitch; the slower it vibrates, the lower the pitch. (In this theory, all of the auditory neurons would be firing at the same time.)

So which of these first two theories is right? It turns out that both are right—up to a point. For place-theory research to be accurate, the basilar membrane has to vibrate unevenly—which it does when the frequency of the sound is *above* 1000 Hz. For the frequency theory to be correct, the neurons associated with the hair cells would have to fire as fast as the basilar membrane vibrates. This only works up to 1000 Hz, because neurons don't appear to fire at exactly the same time and rate when frequencies are faster than 1000 times per second.

The frequency theory works for low pitches, and place theory works for moderate to high pitches. Is there another explanation? Yes, and it is a third theory, developed by Ernest Wever and Charles Bray, called the **volley principle** (Wever, 1949; Wever & Bray, 1930), which appears to account for pitches from about 400 Hz up to about 4000. In this explanation, groups of auditory neurons take turns firing in a process called *volleying*. If a person hears a tone of about 3000 Hz, it means that three groups of neurons have taken turns sending the message to the brain—the first group for the first 1000 Hz, the second group for the next 1000 Hz, and so on.

pitch psychological experience of sound that corresponds to the frequency of the sound waves; higher frequencies are perceived as higher pitches.

place theory theory of pitch that states that different pitches are experienced by the stimulation of hair cells in different locations on the organ of Corti.

frequency theory theory of pitch that states that pitch is related to the speed of vibrations in the basilar membrane.

volley principle theory of pitch that states that frequencies from about 400 Hz to 4000 Hz cause the hair cells (auditory neurons) to fire in a volley pattern, or take turns in firing.

TYPES OF HEARING IMPAIRMENTS

Hearing impairment is the term used to refer to difficulties in hearing. A person can be partially hearing impaired or totally hearing impaired, and the treatment for hearing loss will vary according to the reason for the impairment.

3.5 Why are some people unable to hear, and how can their hearing be improved?

CONDUCTION HEARING IMPAIRMENT *Conduction hearing impairment* means that sound vibrations cannot be passed from the eardrum to the cochlea. The cause might be a damaged eardrum or damage to the bones of the middle ear (usually from an infection). In this kind of impairment, hearing aids may be of some use in restoring hearing.

NERVE HEARING IMPAIRMENT In *nerve hearing impairment*, the problem lies either in the inner ear or in the auditory pathways and cortical areas of the brain. Normal aging causes

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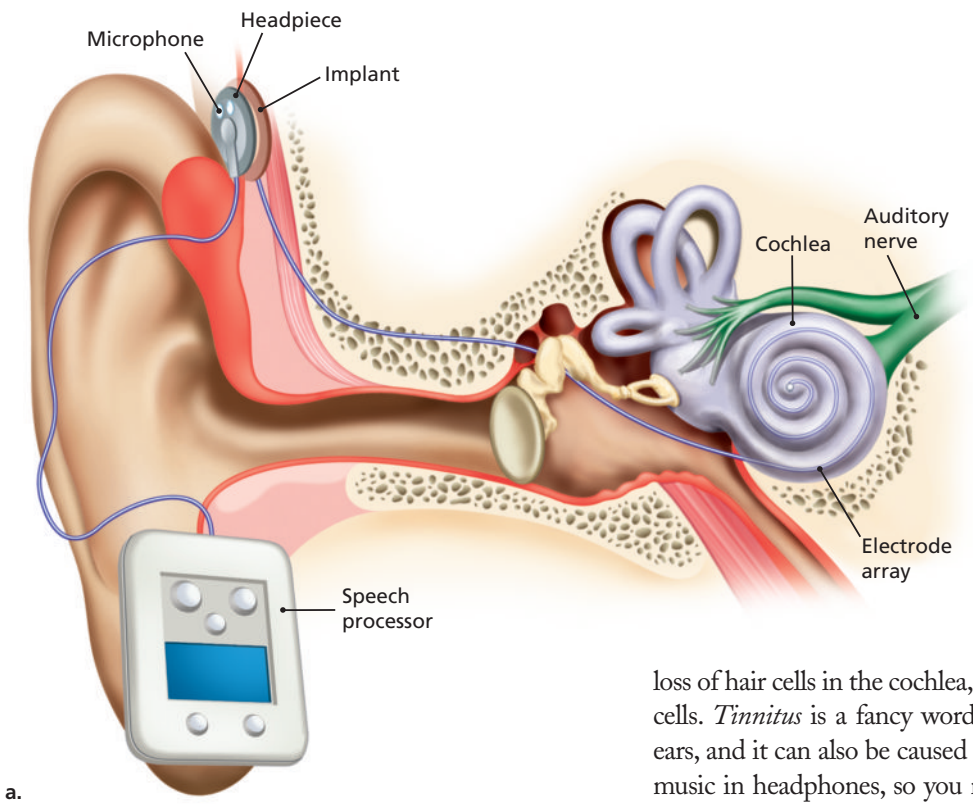

a.

b.

Figure 3.9 Cochlear Implant

(a) In a cochlear implant, a microphone implanted just behind the ear picks up sound from the surrounding environment. A speech processor, attached to the implant and worn outside the body, selects and arranges the sound picked up by the microphone. The implant itself is a transmitter and receiver, converting the signals from the speech processor into electrical impulses that are collected by the electrode array in the cochlea and then sent to the brain. (b) This child is able to hear with the help of a cochlear implant. Hearing spoken language during the early years of a child's life helps in the development of the child's own speech.

Listen to the Psychology in the News podcast on cochlear implants on **mypsychlab.com**

loss of hair cells in the cochlea, and exposure to loud noises can damage hair cells. *Tinnitus* is a fancy word for an extremely annoying ringing in one's ears, and it can also be caused by infections or loud noises—including loud music in headphones, so you might want to turn down that music player!

Because the damage is to the nerves or the brain, nerve hearing impairment cannot be helped with ordinary hearing aids, which are basically sound amplifiers. A technique for restoring some hearing to those with nerve hearing impairment makes use of an electronic device called a *cochlear implant*. This device sends signals from a microphone worn behind the ear to a sound processor worn on the belt or in a pocket, which then translates those signals into electrical stimuli that are sent to a series of electrodes implanted directly into the cochlea, allowing transduction to take place and stimulating the auditory nerve. (See Figure 3.9.) The brain then processes the electrode information as sound. **Listen** on **mypsychlab.com**

3.4 3.5

CONCEPT MAP

The Hearing Sense

- **sound**
  - is a physical stimulus
    - composed of sound waves
      - have wavelengths and wavelike properties that can be measured
      - result of vibrations of air molecules
    - processed by the ear
      - **outer ear**
      - **middle ear**
      - **inner ear**
    - processing can be impaired
  - has psychological properties
    - **frequency** or **pitch**
      - shorter wavelengths = more waves per second = higher frequencies
        - theories of pitch perception
          - place theory
          - frequency theory
          - volley theory
    - **volume**
      - larger wave amplitudes associated with louder volume
    - **timbre**
      - increase in number of sounds results in greater richness

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PRACTICE quiz How much do you remember? ANSWERS ON PAGE AK-1.

Pick the best answer.

1. Which of the following properties of sound would be the most similar to the color or hue of light?
   a. pitch **c.** purity
   b. loudness **d.** timbre
2. The eardrum is also called the _____.
   a. pinna. **c.** tympanic membrane.
   b. oval window. **d.** cochlea.
3. The _____ theory best explains how we hear sounds above 4000 Hz.
   a. place **c.** volley
   b. frequency **d.** adaptive
4. If the bones of the middle ear begin to deteriorate, you will develop _____ hearing impairment.
   a. nerve **c.** brain pathway
   b. stimulation **d.** conduction

Chemical Senses: It Tastes Good and Smells Even Better

3.6 How do the senses of taste and smell work, and how are they alike?

The sense of taste (taste in food, not taste in clothing or friends) and the sense of smell are very closely related. Have you ever noticed that when your nose is all stopped up, your sense of taste is affected, too? That's because the sense of taste is really a combination of taste and smell. Without the input from the nose, there are actually only four, and possibly five, kinds of taste sensors in the mouth.

GUSTATION: HOW WE TASTE THE WORLD

TASTE BUDS *Taste buds* are the common name for the taste receptor cells, special kinds of neurons found in the mouth that are responsible for the sense of taste, or **gustation**. Most taste buds are located on the tongue, but there are a few on the roof of the mouth, the cheeks, and under the tongue as well. How sensitive people are to various tastes depends on how many taste buds they have; some people have only around 500, whereas others have 20 times that number. The latter are called "supertasters" and need far less seasoning in their food than those with fewer taste buds (Bartoshuk, 1993).

So taste buds are those little bumps I can see when I look closely at my tongue?

No, those "bumps" are called *papillae*, and the taste buds line the walls of these papillae. (See Figure 3.10.)

So taste buds are those little bumps I can see when I look closely at my tongue?

Each taste bud has about 20 receptors that are very similar to the receptor sites on receiving neurons at the synapse. LINK to Chapter Two: The Biological Perspective, p. 52. In fact, the receptors on taste buds work exactly like receptor sites on neurons—they receive molecules of various substances that fit into the receptor like a key into a lock. Taste is often called a chemical sense because it works with the molecules of foods people eat in the same way the neural receptors work with neurotransmitters. When the molecules (dissolved in saliva) fit into the receptors, a signal is fired to the brain, which then interprets the taste sensation.

What happens to the taste buds when I burn my tongue? Do they repair themselves? I know when I have burned my tongue, I can't taste much for a while, but the taste comes back.

What happens to the taste buds when I burn my tongue? Do they repair themselves? I know when I have burned my tongue, I can't taste much for a while, but the taste comes back.

In general, the taste receptors get such a workout that they have to be replaced every 10 to 14 days (McLaughlin & Margolskee, 1994). And when the tongue is burned, the damaged cells no longer work. As time goes on, those cells get replaced and the taste sense comes back.

THE FIVE BASIC TASTES In 1916 a German psychologist named Hans Henning proposed that there are four primary tastes: sweet, sour, salty, and bitter. Lindemann (1996) supported the idea that there is a fifth kind of taste receptor that

gustation the sensation of a taste.

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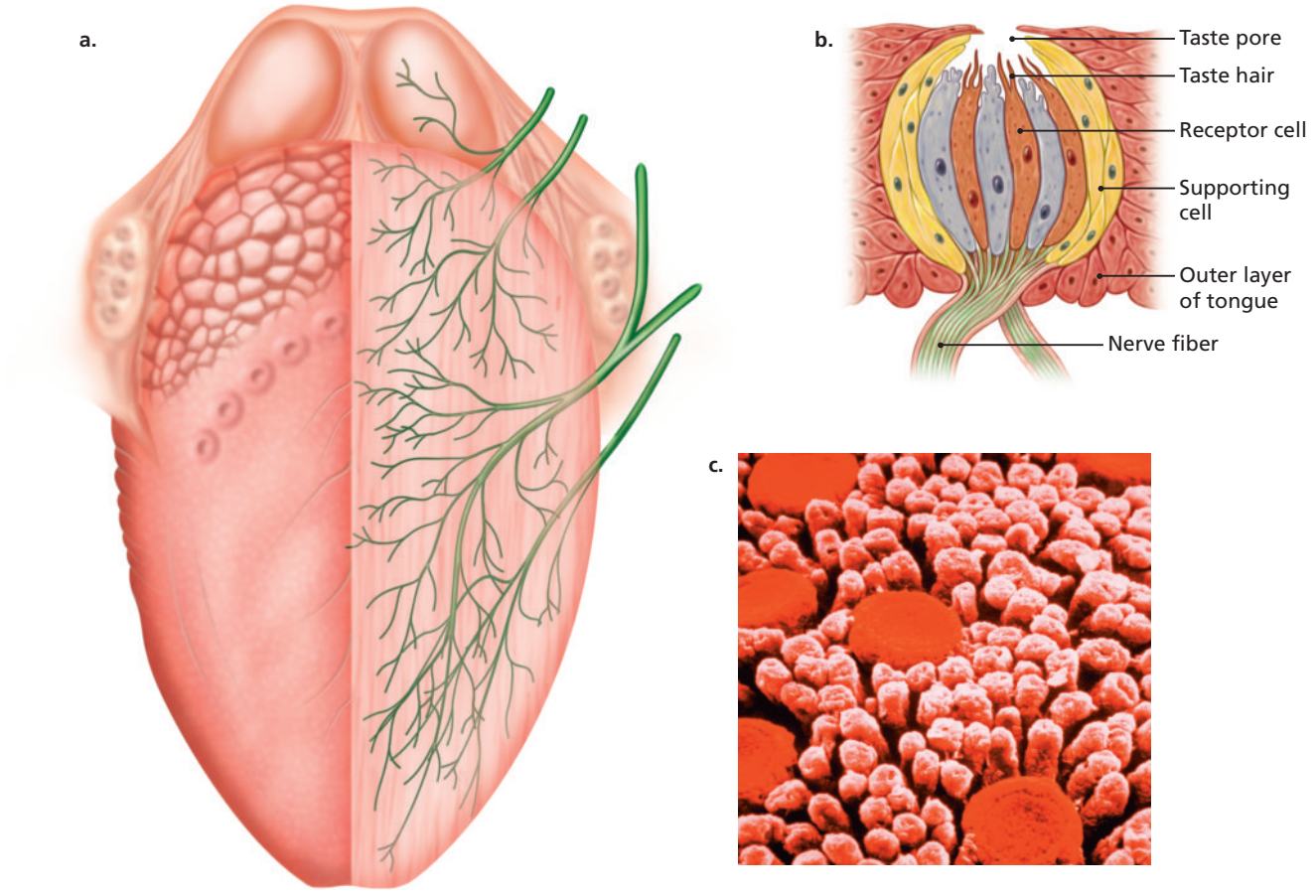

Figure 3.10 The Tongue and Taste Buds—A Crosscut View of the Tongue

(a) The right side of this drawing shows the nerves in the tongue's deep tissue. (b) The taste bud is located inside the papillae and is composed of small cells that send signals to the brain when stimulated by molecules of food. (c) Microphotograph of the surface of the tongue, showing two different sizes of papillae. The taste buds are located under the surface of the larger red papillae, whereas the smaller and more numerous papillae form a touch-sensitive rough surface that helps in chewing and moving food around the mouth.

detects a pleasant "brothy" taste associated with foods like chicken soup, tuna, kelp, cheese, and soy products, among others. Lindemann proposed that this fifth taste be called *umami*, a Japanese word first coined in 1908 by Dr. Kikunae Ikeda of Tokyo Imperial University to describe the taste. Dr. Ikeda had succeeded in isolating the substance in kelp that generated the sensation of umami—glutamate (Beyreuther et al., 2007). LINK to Chapter Two: The Biological Perspective, p. 53. Glutamate exists not only in the foods listed earlier, but is also present in human breast milk and is the reason that the seasoning MSG—monosodium *glutamate*—adds a pleasant flavor to foods.

The five taste sensations work together, along with the sense of smell and the texture, temperature, and "heat" of foods, to produce thousands of taste sensations. Although researchers used to believe that certain tastes were located on certain places on the tongue, it is now known that all of the taste sensations are processed all over the tongue (Bartoshuk, 1993).

Just as individuals and groups can vary on their food preferences, they can also vary on level of perceived sweetness. For example, obese individuals have been found to experience less sweetness than individuals who are not obese; foods that are both sweet and high in fat tend to be especially attractive to individuals who are obese (Bartoshuk et al., 2006). Such differences (as well as genetic variations like the supertasters) complicate direct comparison of food preferences. One possible solution is to have individuals rate taste in terms of an unrelated "standard" sensory experience of known intensity, such as the brightness of a light or loudness of a sound or preference in terms of all pleasurable experiences, and not just taste (Bartoshuk et al., 2005; Snyder & Bartoshuk, 2009).

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Turning our attention back to how things taste for us as individuals, have you ever noticed that when you have a cold, food tastes very bland? Everything becomes bland or muted because you can taste only sweet, salty, bitter, sour, and umami—and because your nose is stuffed up with a cold, you don't get all the enhanced variations of those tastes that come from the sense of smell.

olfaction (olfactory sense) the sensation of smell.

THE SENSE OF SCENTS: OLFACTION

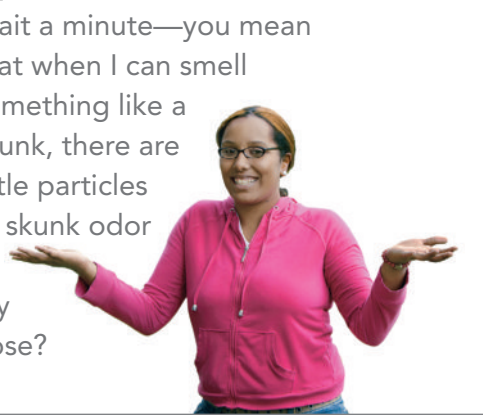
Like the sense of taste, the sense of smell is a chemical sense. The ability to smell odors is called **olfaction,** or the **olfactory sense**.

The outer part of the nose serves the same purpose for odors that the pinna and ear canal serve for sounds: Both are merely ways to collect the sensory information and get it to the part of the body that will translate it into neural signals.

The part of the olfactory system that transduces odors—turns odors into signals the brain can understand—is located at the top of the nasal passages. This area of olfactory receptor cells is only about an inch square in each cavity yet contains about 10 million olfactory receptors. (See Figure 3.11.)

OLFACTORY RECEPTOR CELLS The *olfactory receptor cells* each have about a half dozen to a dozen little "hairs," called *cilia*, that project into the cavity. Like taste buds, there are receptor sites on these hair cells that send signals to the brain when stimulated by the molecules of substances that are in the air moving past them.

Wait a minute—you mean that when I can smell something like a skunk, there are little particles of skunk odor IN my nose?



Yes. When a person is sniffing something, the sniffing serves to move molecules of whatever the person is trying to smell into the nose and into the nasal cavities. That's okay when it's the smell of baking bread, apple pie, flowers, and the like, but when it's skunk, rotten eggs, dead animals—well, try not to think about it too much.

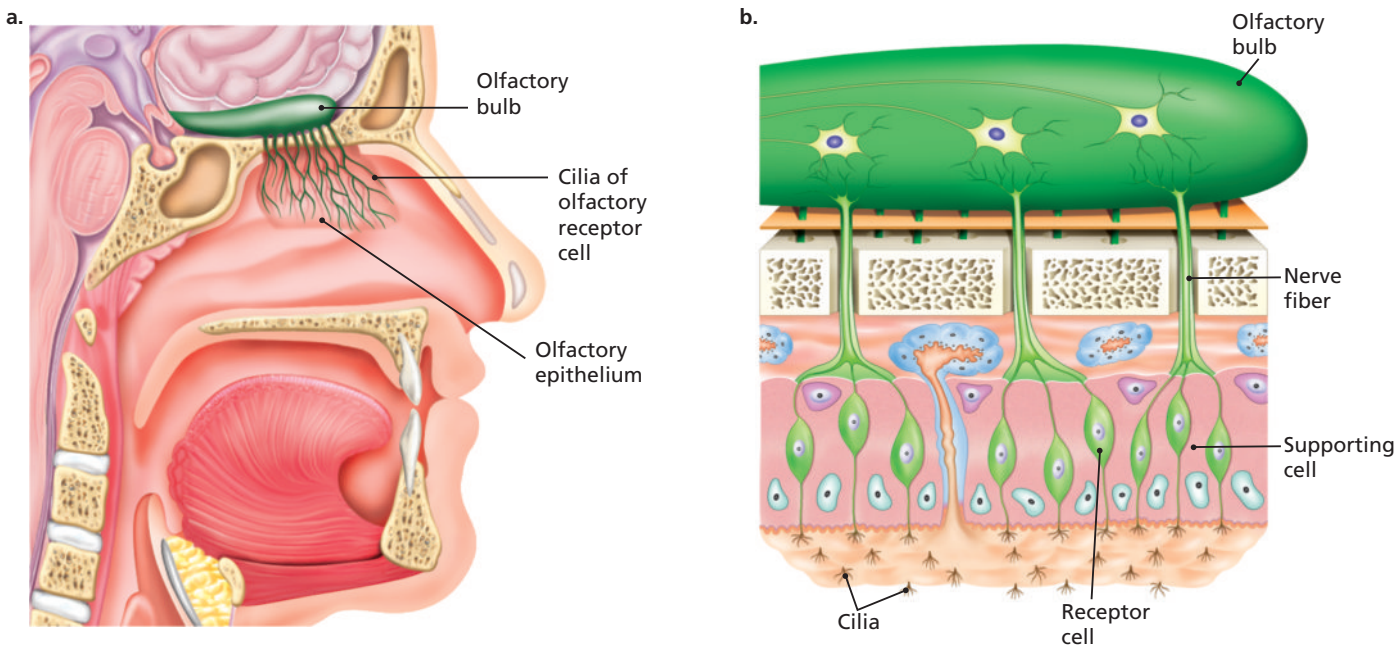


Figure 3.11 The Olfactory Receptors

(a) A cross section of the nose and mouth. This drawing shows the nerve fibers inside the nasal cavity that carry information about smell directly to the olfactory bulb just under the frontal lobe of the brain (shown in green). (b) A diagram of the cells in the nose that process smell. The olfactory bulb is on top. Notice the cilia, tiny hairlike cells that project into the nasal cavity. These are the receptors for the sense of smell.

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olfactory bulbs areas of the brain located just above the sinus cavity and just below the frontal lobes that receive information from the olfactory receptor cells.

somesthetic senses the body senses consisting of the skin senses, the kinesthetic sense, and the vestibular senses.

skin senses the sensations of touch, pressure, temperature, and pain.

kinesthetic sense sense of the location of body parts in relation to the ground and each other.

vestibular senses the sensations of movement, balance, and body position.

Olfactory receptors are like taste buds in another way, too. Olfactory receptors also have to be replaced as they naturally die off, about every 5 to 8 weeks. Unlike the taste buds, there are way more than five types of olfactory receptors—in fact, there are at least 1,000 of them.

You might remember from Chapter Two that signals from the olfactory receptors in the nasal cavity do not follow the same path as the signals from all the other senses. Vision, hearing, taste, and touch all pass through the thalamus and then on to the area of the cortex that processes that particular sensory information. But the sense of smell has its own special place in the brain—the olfactory bulbs, which are actually part of the brain.

THE OLFACTORY BULBS The **olfactory bulbs** are located right on top of the sinus cavity on each side of the brain directly beneath the frontal lobes. (Refer back to Figure 3.11.) The olfactory receptors send their neural signals directly up to these bulbs, bypassing the thalamus, the relay center for all other sensory information. The olfactory information is then sent from the olfactory bulbs to higher cortical areas, including the primary olfactory cortex (the *piriform cortex*), the orbitofrontal cortex, and the amygdala (remember from Chapter Two that the orbitofrontal cortex and amygdala play important roles in emotion). LINK to Chapter Two: The Biological Perspective, pp. 72 and 76.

Somesthetic Senses: What the Body Knows

So far, this chapter has covered vision, hearing, taste, and smell. That leaves touch. What is thought of as the sense of touch is really several sensations, originating in several different places in—and on—the body. It's really more accurate to refer to these as the body senses, or **somesthetic senses**. The first part of that word, *soma*, means "body," as mentioned in Chapter Two. The second part, *esthetic*, means "feeling," hence, the name. There are three somesthetic sense systems, the **skin senses** (having to do with touch, pressure, temperature, and pain), the **kinesthetic sense** (having to do with the location of body parts in relation to each other), and the **vestibular senses** (having to do with movement and body position).

Her sense of touch is allowing this blind girl to "read" a Braille book with her fingers. The fingertips are extremely sensitive to fine differences in texture, allowing her to distinguish between small dots representing the different letters of the alphabet.

PERCEPTION OF TOUCH, PRESSURE, AND TEMPERATURE

3.7 What allows people to experience the sense of touch, pain, motion, and balance?

Here's a good trivia question: What organ of the body is about 20 square feet in size? The answer is the skin. Skin is an organ. Its purposes include more than simply keeping bodily fluids in and germs out; skin also receives and transmits information from the outside world to the central nervous system (specifically, to the somatosensory cortex). LINK to Chapter Two: The Biological Perspective, p. 75. Information about light touch, deeper pressure, hot, cold, and even pain is collected by special receptors in the skin's layers.

TYPES OF SENSORY RECEPTORS IN THE SKIN There are about half a dozen different receptors in the layers of the skin. (See Figure 3.12.) Some of them will respond to only one kind of sensation. For example, the *Pacinian corpuscles* are just beneath the skin and respond to changes in pressure. There are nerve endings that wrap around the ends of the hair follicles, a fact people may be well aware of when they tweeze their eyebrows, or when someone pulls their hair. These nerve endings are sensitive to both pain and touch. There are *free nerve endings* just beneath the uppermost layer of the skin that respond to changes in temperature and to pressure—and to pain.

How exactly does pain work? Why is it that sometimes I feel pain deep inside? Are there pain receptors there, too?

How exactly does pain work? Why is it that sometimes I feel pain deep inside? Are there pain receptors there, too?

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Yes, there are pain nerve fibers in the internal organs as well as receptors for pressure. How else would people have a stomachache or intestinal* pain—or get that full feeling of pressure when they've eaten too much or their bladder is full?

There are actually different types of pain. There are receptors that detect pain (and pressure) in the organs, a type of pain called *visceral pain*. Pain sensations in the skin, muscles, tendons, and joints are carried on large nerve fibers and are called *somatic pain*. Somatic pain is the body's warning system that something is being, or is about to be, damaged and tends to be sharp and fast. Another type of somatic pain is carried on small nerve fibers and is slower and more of a general ache. This somatic pain acts as a kind of reminder system, keeping people from further injury by reminding them that the body has already been damaged. For example, if you hit your thumb with a hammer, the immediate pain sensation is of the first kind—sharp, fast, and bright. But later the bruised tissue simply aches, letting you know to take it easy on that thumb.

People may not like pain, but its function as a warning system is vitally important. There are people who are born without the ability to feel pain, rare conditions called *congenital analgesia* and *congenital insensitivity to pain with anhidrosis (CIPA)*. Children with these disorders cannot feel pain when they cut or scrape themselves, leading to an increased risk of infection when the cut goes untreated (Mogil, 1999). They fear nothing—which can be a horrifying trial for the parents and teachers of such a child. These disorders affect the neural pathways that carry pain, heat, and cold sensations. (Those with CIPA have an additional disruption in the body's heat–cold sensing perspiration system [anhidrosis], so that the person is unable to cool off the body by sweating.)

A condition called *phantom limb pain* occurs when a person who has had an arm or leg removed sometimes "feels" pain in the missing limb (Nikolajsen & Jensen, 2001; Woodhouse, 2005). As many as 50 to 80 percent of people who have had amputations experience various sensations: burning, shooting pains, or pins-and-needles sensations where the amputated limb used to be. Once believed to be a psychological problem, some now believe that it is caused by the traumatic injury to the nerves during amputation (Ephraim et al., 2005).

PAIN: GATE-CONTROL THEORY

The best current explanation for how the sensation of pain works is called *gate-control theory*, first proposed by Melzack and Wall (1965) and later refined and expanded (Melzack & Wall, 1996). In this theory, the pain signals must pass through a "gate" located in the spinal cord. The activity of the gate can be closed by nonpain signals coming into the spinal cord from the body and by signals coming from the brain. The gate is not a physical structure but instead represents the relative balance in neural activity of cells in the spinal cord that receive information from the body and then send information to the brain.

Stimulation of the pain receptor cells releases a chemical called *substance P* (for "pain," naturally). Substance P released into the spinal cord activates other neurons that send their messages through spinal gates (opened by the pain signal). From the

*intestinal: having to do with the tubes in the body that digest food and process waste material.

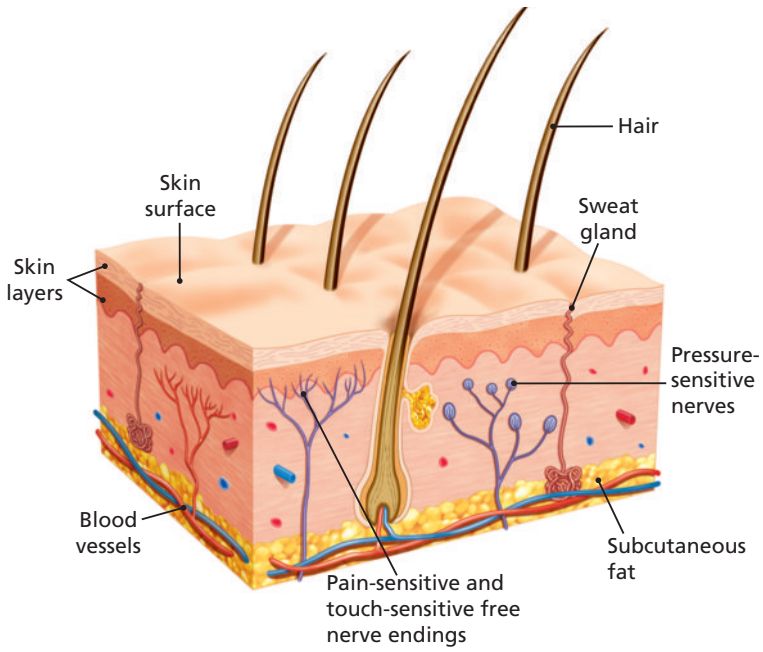

Figure 3.12 Cross Section of the Skin and Its Receptors

The skin is composed of several types of cells that process pain, pressure, and temperature. Some of these cells are wrapped around the ends of the hairs on the skin and are sensitive to touch on the hair itself, whereas others are located near the surface, and still others just under the top layer of tissue.

Congenital insensitivity to pain with anhidrosis (CIPA) is a rare genetic disorder that makes 5-year-old Ashlyn unable to feel pain. She must be examined carefully for scrapes and cuts after recess at school because she cannot feel when she hurts herself, putting her at risk for infection. What are some of the problems that Ashlyn and her parents may face as she grows older?

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spinal cord, the message goes to the brain, activating cells in the thalamus, somatosensory cortex, areas of the frontal lobes, and the limbic system. The brain then interprets the pain information and sends signals that either open the spinal gates farther, causing a greater experience of pain, or close them, dampening the pain. Of course, this decision by the brain is influenced by the psychological aspects of the pain-causing stimulus. Anxiety, fear, and helplessness intensify pain, whereas laughter, distraction, and a sense of control can diminish it. (This is why people might bruise themselves and not know it if they were concentrating on something else.) Pain can also be affected by competing signals from other skin senses, which is why rubbing a sore spot can reduce the feeling of pain.

Those same psychological aspects can also influence the release of the *endorphins*, the body's natural version of morphine. LINK to Chapter Two: The Biological Perspective, p. 54. Endorphins can inhibit the transmission of pain signals in the brain, and in the spinal cord they can inhibit the release of substance.

I've always heard that women are able to stand more pain than men. Is that true?

I've always heard that women are able to stand more pain than men. Is that true?

On the contrary, research has shown that women apparently feel pain more intensely than do men, and they also report pain more often than men do (Chesterton et al., 2003; Faucett et al., 1994; Norrbrink et al., 2003). Men have been shown to cope better with many kinds of pain, possibly because men are often found to have a stronger belief than women that they can (or should) control their pain by their own efforts (Jackson et al., 2002).

THE KINESTHETIC SENSE

Special receptors located in the muscles, tendons, and joints are part of the body's sense of movement and position in space—the movement and location of the arms, legs, and so forth in relation to one another. This sense is called *kinesthesia*, from the Greek words *kinein* ("to move") and *aesthesis* ("sensation"). When you close your eyes and raise your hand above your head, you know where your hand is because these special receptors, called proprioceptors, tell you about joint movement or the muscles stretching or contracting.

If you have ever gotten sick from traveling in a moving vehicle, you might be tempted to blame these proprioceptors. Actually, it's not the proprioceptors in the body that make people get sick. The culprits are special structures in the ear that tell us about the position of the body in relation to the ground and movement of the head that make up the *vestibular sense*—the sense of balance.

This tightrope-walking violinist is performing an amazing feat of coordination and muscular control. He must not only use his vestibular organs to help maintain his balance, but also his kinesthetic sense to be aware of exactly where each foot is in relation to the rope.

THE VESTIBULAR SENSE

The name of this particular sense comes from a Latin word that means "entrance" or "chamber." The structures for this sense are located in the innermost chamber of the ear. There are two kinds of vestibular organs, the otolith organs and the semicircular canals.

The *otolith organs* are tiny sacs found just above the cochlea. These sacs contain a gelatin-like fluid within which tiny crystals are suspended (much like pieces of fruit in a bowl of Jello®). The head moves and the crystals cause the fluid to vibrate, setting off some tiny hairlike receptors on the inner surface of the sac, telling the person that he or she is moving forward, backward, sideways, or up and down. (It's pretty much the way the cochlea works but with movement being the stimulus instead of sound vibrations.)

The *semicircular canals* are three somewhat circular tubes that are also filled with fluid that will stimulate hairlike receptors when rotated. Having three tubes allows one to be located in each of the three planes of motion. Remember learning in geometry class about the *x*-, *y*-, and *z*-axes? Those are the three planes through which the body can rotate, and when it does, it sets off the receptors in these canals. When you spin around and then stop, the fluid in the horizontal canal is still rotating and will make you feel dizzy

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because your body is telling you that you are still moving, but your eyes are telling you that you have stopped.

MOTION SICKNESS This disagreement between what the eyes say and what the body says is pretty much what causes *motion sickness*, the tendency to get nauseated when in a moving vehicle, especially one with an irregular movement. Normally, the vestibular sense coordinates with the other senses. But for some people, the information from the eyes may conflict a little too much with the vestibular organs, and dizziness, nausea, and disorientation are the result. This explanation of motion sickness is known as **sensory conflict theory** (Oman, 1990; Reason & Brand, 1975). The dizziness is the most likely cause of the nausea. Many poisons make a person dizzy, and the most evolutionarily adaptive thing to do is to expel the poison. Even without any poison in a case of motion sickness, the nausea occurs anyway (Treisman, 1977).

One way some people overcome motion sickness is to focus on a distant point or object. This provides visual information to the person about how he or she is moving, bringing the sensory input into agreement with the visual input. This is also how ballerinas and ice skaters manage not to get sick when turning rapidly and repeatedly—they focus their eyes at least once on some fixed object every so many turns.

Astronauts, who travel in low gravity conditions, can get a related condition called space motion sickness (SMS). This affects about 60 percent of those who travel in space, typically for about the first week of space travel. After that time of adjustment, the astronauts are able to adapt and the symptoms diminish. Repeated exposure to some environment that causes motion sickness—whether it is space, a car, a train, or some other vehicle—is actually one of the best ways to overcome the symptoms (Hu & Stern, 1999).

sensory conflict theory an explanation of motion sickness in which the information from the eyes conflicts with the information from the vestibular senses, resulting in dizziness, nausea, and other physical discomfort.

3.6 3.7

CONCEPT MAP

- **smell/olfaction**
  - called a chemical sense because substance molecules are suspended in the air, carried to the nasal cavity, and fit into receptor sites
  - nose serves as a collection device
  - unique in that signals do not first travel to the thalamus before going to the brain

Chemical Senses

- **taste/gustation**
  - made possible largely through the role of taste buds (taste receptor cells)
  - five basic tastes (receptor types)
    - **sweet**
    - **sour**
    - **salty**
    - **bitter**
    - **unami**
  - called a chemical sense because food molecules dissolve in saliva, which then fits into receptor sites

Somesthetic Senses

- **skin senses**
  - processed by the skin
    - is an organ—receives and transmits information from the outside world to the somatosensory cortex of the brain
    - sensitive to touch, pressure, temperature
      - **pain**
- **kinesthetic sense**
  - processed by proprioceptors in skin, joints, muscles, and tendons
- **vestibular sense**
  - processed by vestibular organs
    - convey information about movement and body position
    - found in the inner ear
      - **otolith organs**
      - **semicircular canals**
    - responsible for motion sickness

(*continued*)

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mark womble, youngstown state university
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