Anatomy and Physiology I

Lumen Learning

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CONTENTS

MODULE 1: BODY PLAN AND ORGANIZATION

AN INTRODUCTION TO THE HUMAN BODY

Learning Objectives

- Distinguish between anatomy and physiology, and identify several branches of each
- Describe the structure of the body, from simplest to most complex, in terms of the six levels of organization
- Identify the functional characteristics of human life
- Identify the four requirements for human survival
- Define homeostasis and explain its importance to normal human functioning
- Use appropriate anatomical terminology to identify key body structures, body regions, and directions in the body
- Compare and contrast at least four medical imagining techniques in terms of their function and use in medicine

Though you may approach a course in anatomy and physiology strictly as a requirement for your field of study, the knowledge you gain in this course will serve you well in many aspects of your life. An understanding of anatomy and physiology is not only fundamental to any career in the health professions, but it can also benefit your own health. Familiarity with the human body can help you make healthful choices and prompt you to take appropriate action when signs of illness arise. Your knowledge in this field will help you understand news about nutrition, medications, medical devices, and procedures and help you understand genetic or infectious diseases. At some point, everyone will have a problem with some aspect of his or her body and your knowledge can help you to be a better parent, spouse, partner, friend, colleague, or caregiver.

Figure 1. Blood Pressure. *A proficiency in anatomy and physiology is fundamental to any career in the health professions. (Credit: Bryan Mason/flickr)*

This chapter begins with an overview of anatomy and physiology and a preview of the body regions and functions. It then covers the characteristics of life and how the body works to maintain stable conditions. It introduces a set of standard terms for body structures and for planes and positions in the body that will serve as a foundation for more comprehensive information covered later in the text. It ends with examples of medical imaging used to see inside the living body.

OVERVIEW OF ANATOMY AND PHYSIOLOGY

Learning Objectives

- Compare and contrast anatomy and physiology, including their specializations and methods of study
- Discuss the fundamental relationship between anatomy and physiology

Human **anatomy** is the scientific study of the body's structures. Some of these structures are very small and can only be observed and analyzed with the assistance of a microscope. Other larger structures can readily be seen, manipulated, measured, and weighed. The word "anatomy" comes from a Greek root that means "to cut apart." Human anatomy was first studied by observing the exterior of the body and observing the wounds of soldiers and other injuries. Later, physicians were allowed to dissect bodies of the dead to augment their knowledge. When a body is dissected, its structures are cut apart in order to observe their physical attributes and their relationships to one another. Dissection is still used in medical schools, anatomy courses, and in pathology labs. In order to observe structures in living people, however, a number of imaging techniques have been developed. These techniques allow clinicians to visualize structures inside the living body such as a cancerous tumor or a fractured bone.

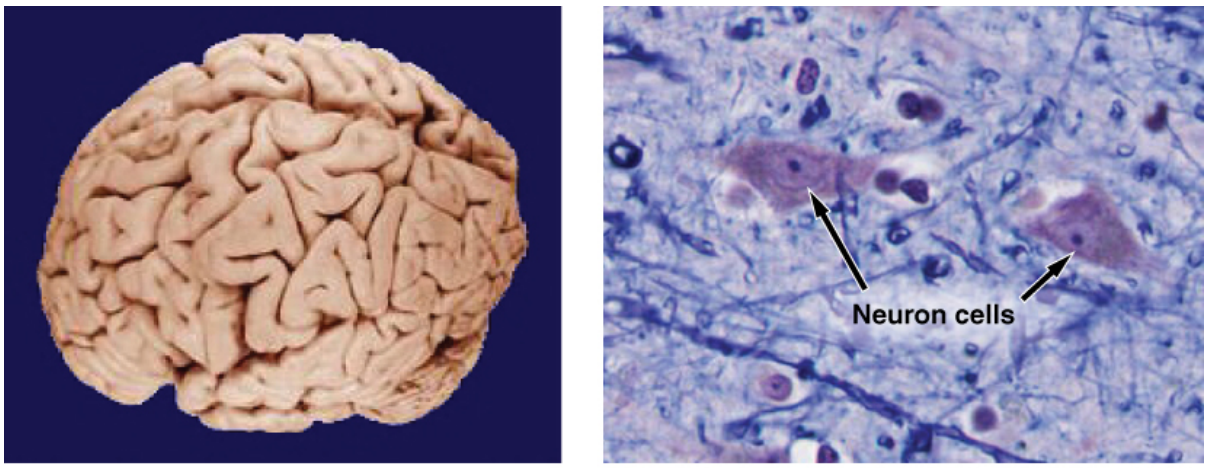


Figure 1. Gross and Microscopic Anatomy. *(a) Gross anatomy considers large structures such as the brain. (b) Microscopic anatomy can deal with the same structures, though at a different scale. This is a micrograph of nerve cells from the brain. LM × 1600. (credit a: "WriterHound"/Wikimedia Commons; credit b: Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

Like most scientific disciplines, anatomy has areas of specialization. ***Gross anatomy*** is the study of the larger structures of the body, those visible without the aid of magnification (Figure 1**a**). *Macro–* means "large," thus, gross anatomy is also referred to as macroscopic anatomy. In contrast, *micro–* means "small," and **microscopic anatomy** is the study of structures that can be observed only with the use of a microscope or other magnification devices (Figure 1**b**). Microscopic anatomy includes cytology, the study of cells and histology, the study of tissues. As the technology of microscopes has advanced, anatomists have been able to observe smaller and smaller structures of the body, from slices of large structures like the heart, to the three-dimensional structures of large molecules in the body.

Anatomists take two general approaches to the study of the body's structures: regional and systemic. **Regional anatomy** is the study of the interrelationships of all of the structures in a specific body region, such as the abdomen. Studying regional anatomy helps us appreciate the interrelationships of body structures, such as how

muscles, nerves, blood vessels, and other structures work together to serve a particular body region. In contrast, **systemic anatomy** is the study of the structures that make up a discrete body system—that is, a group of structures that work together to perform a unique body function. For example, a systemic anatomical study of the muscular system would consider all of the skeletal muscles of the body.

Whereas anatomy is about structure, physiology is about function. Human **physiology** is the scientific study of the chemistry and physics of the structures of the body and the ways in which they work together to support the functions of life. Much of the study of physiology centers on the body's tendency toward homeostasis. **Homeostasis** is the state of steady internal conditions maintained by living things. The study of physiology certainly includes observation, both with the naked eye and with microscopes, as well as manipulations and measurements. However, current advances in physiology usually depend on carefully designed laboratory experiments that reveal the functions of the many structures and chemical compounds that make up the human body.

Like anatomists, physiologists typically specialize in a particular branch of physiology. For example, neurophysiology is the study of the brain, spinal cord, and nerves and how these work together to perform functions as complex and diverse as vision, movement, and thinking. Physiologists may work from the organ level (exploring, for example, what different parts of the brain do) to the molecular level (such as exploring how an electrochemical signal travels along nerves).

Form is closely related to function in all living things. For example, the thin flap of your eyelid can snap down to clear away dust particles and almost instantaneously slide back up to allow you to see again. At the microscopic level, the arrangement and function of the nerves and muscles that serve the eyelid allow for its quick action and retreat. At a smaller level of analysis, the function of these nerves and muscles likewise relies on the interactions of specific molecules and ions. Even the three-dimensional structure of certain molecules is essential to their function.

Your study of anatomy and physiology will make more sense if you continually relate the form of the structures you are studying to their function. In fact, it can be somewhat frustrating to attempt to study anatomy without an understanding of the physiology that a body structure supports. Imagine, for example, trying to appreciate the unique arrangement of the bones of the human hand if you had no conception of the function of the hand. Fortunately, your understanding of how the human hand manipulates tools—from pens to cell phones—helps you appreciate the unique alignment of the thumb in opposition to the four fingers, making your hand a structure that allows you to pinch and grasp objects and type text messages.

STRUCTURAL ORGANIZATION OF THE HUMAN BODY

Learning Objectives

- Describe the structure of the human body in terms of six levels of organization
- List the eleven organ systems of the human body and identify at least one organ and one major function of each

Before you begin to study the different structures and functions of the human body, it is helpful to consider its basic architecture; that is, how its smallest parts are assembled into larger structures. It is convenient to consider the structures of the body in terms of fundamental levels of organization that increase in complexity: subatomic

particles, atoms, molecules, organelles, cells, tissues, organs, organ systems, organisms and biosphere (Figure 1).

The Levels of Organization

To study the chemical level of organization, scientists consider the simplest building blocks of matter: subatomic particles, atoms and molecules. All matter in the universe is composed of one or more unique pure substances called elements, familiar examples of which are hydrogen, oxygen, carbon, nitrogen, calcium, and iron. The smallest unit of any of these pure substances (elements) is an atom. Atoms are made up of subatomic particles such as the proton, electron and neutron. Two or more atoms combine to form a molecule, such as the water molecules, proteins, and sugars found in living things. Molecules are the chemical building blocks of all body structures.

A **cell** is the smallest independently functioning unit of a living organism. Even bacteria, which are extremely small, independently-living organisms, have a cellular structure. Each bacterium is a single cell. All living structures of human anatomy contain cells, and almost all functions of human physiology are performed in cells or are initiated by cells.

A human cell typically consists of flexible membranes that enclose cytoplasm, a water-based cellular fluid together with a variety of tiny functioning units called **organelles**. In humans, as in all organisms, cells perform all functions of life. A **tissue** is a group of many similar cells (though sometimes composed of a few related types) that work together to perform a specific function. An **organ** is an anatomically distinct structure of the body composed of two or more tissue types. Each organ performs one or more specific physiological functions. **An organ system** is a group of organs that work together to perform major functions or meet physiological needs of the body.

This book covers eleven distinct organ systems in the human body (Figure 2 and Figure 3). Assigning organs to organ systems can be imprecise since organs that “belong” to one system can also have functions integral to another system. In fact, most organs contribute to more than one system.

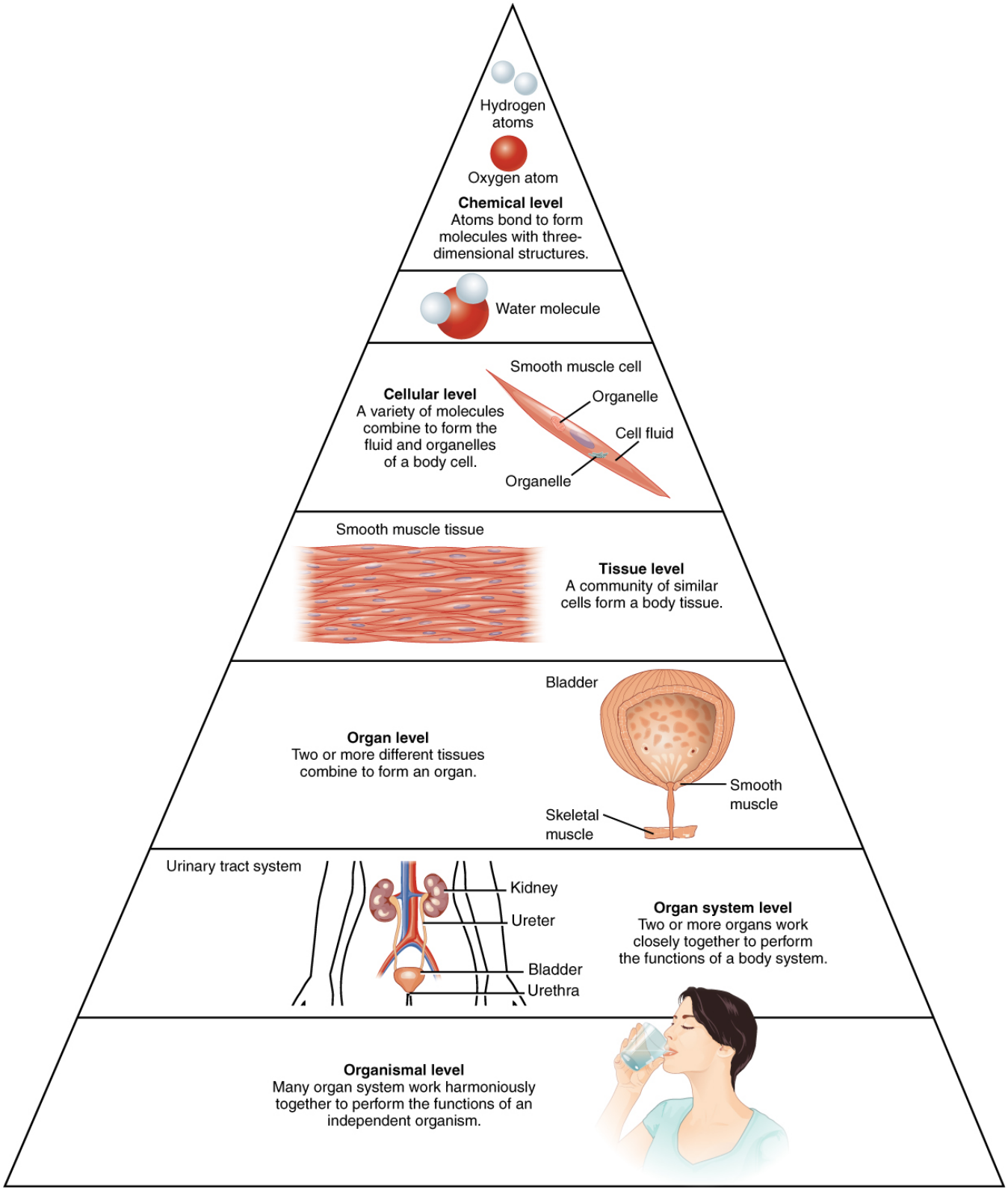


Figure 1. Levels of Structural Organization of the Human Body. *The organization of the body often is discussed in terms of six distinct levels of increasing complexity, from the smallest chemical building blocks to a unique human organism.*

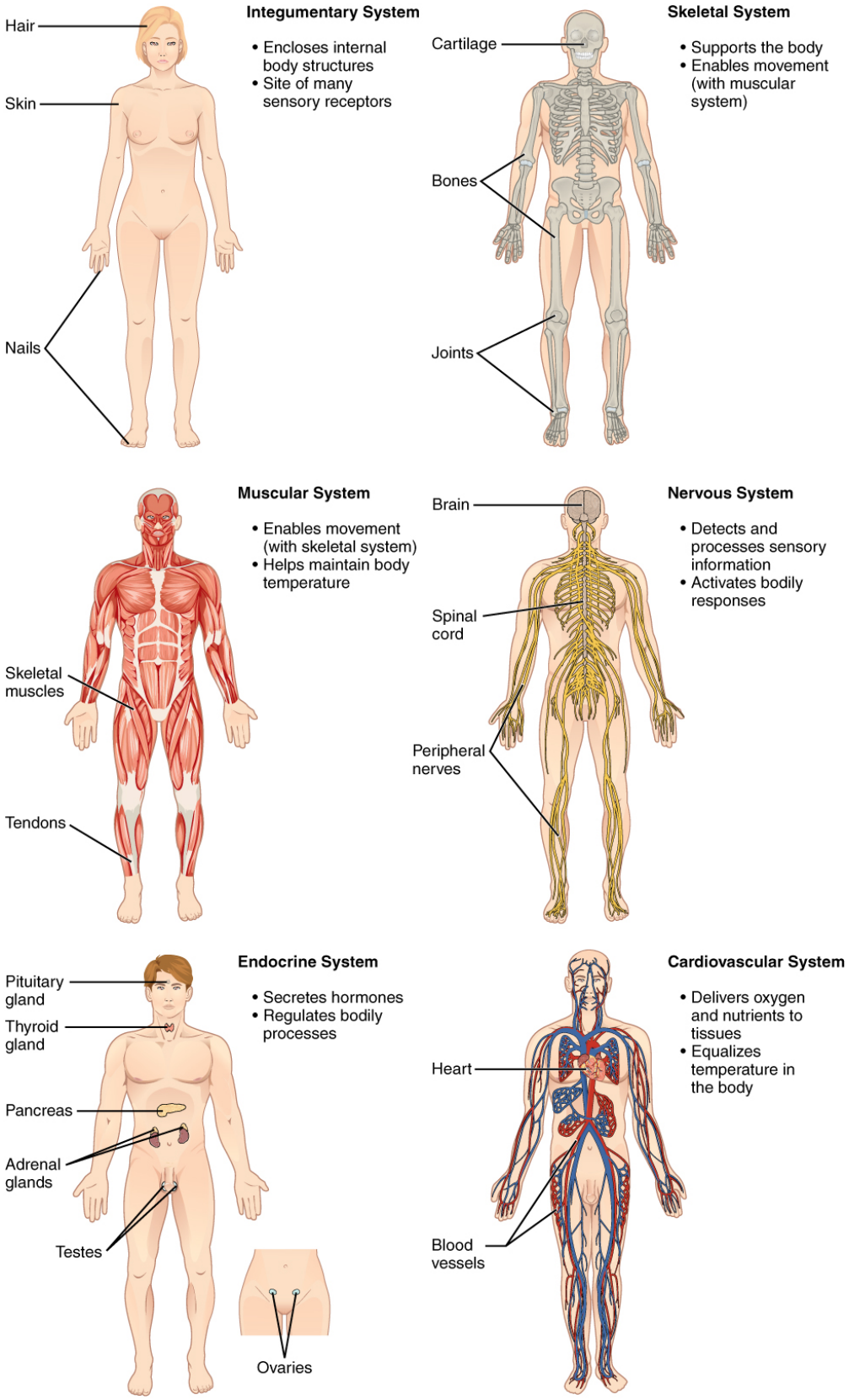


Figure 2. Organ Systems of the Human Body. *Organs that work together are grouped into organ systems.*

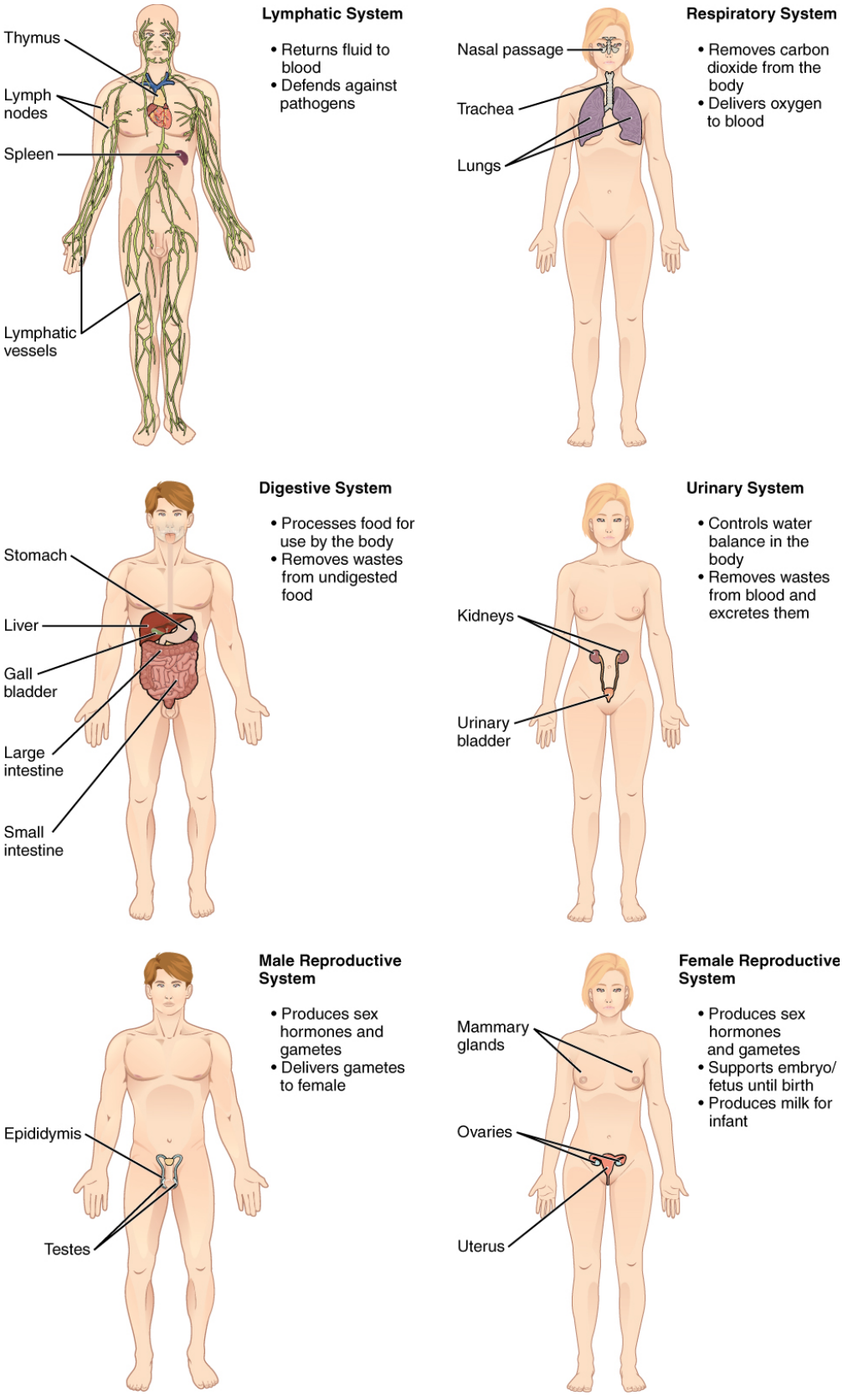


Figure 3. Organ Systems of the Human Body (continued). *Organs that work together are grouped into organ systems. The organism level is the highest level of organization. An* ***organism*** *is a living being that has a cellular structure and that can independently perform all physiologic functions necessary for life. In multicellular organisms, including humans, all cells, tissues, organs, and organ systems of the body work together to maintain the life and health of the organism.*

FUNCTIONS OF HUMAN LIFE

Learning Objectives

- Explain the importance of organization to the function of the human organism
- Distinguish between metabolism, anabolism, and catabolism
- Provide at least two examples of human responsiveness and human movement
- Compare and contrast growth, differentiation, and reproduction

The different organ systems each have different functions and therefore unique roles to perform in physiology. These many functions can be summarized in terms of a few that we might consider definitive of human life: organization, metabolism, responsiveness, movement, development, and reproduction.

Organization

A human body consists of trillions of cells organized in a way that maintains distinct internal compartments. These compartments keep body cells separated from external environmental threats and keep the cells moist and nourished. They also separate internal body fluids from the countless microorganisms that grow on body surfaces, including the lining of certain tracts, or passageways. The intestinal tract, for example, is home to even more bacteria cells than the total of all human cells in the body, yet these bacteria are outside the body and cannot be allowed to circulate freely inside the body.

Cells, for example, have a cell membrane (also referred to as the plasma membrane) that keeps the intracellular environment—the fluids and organelles—separate from the extracellular environment. Blood vessels keep blood inside a closed circulatory system, and nerves and muscles are wrapped in connective tissue sheaths that separate them from surrounding structures. In the chest and abdomen, a variety of internal membranes keep major organs such as the lungs, heart, and kidneys separate from others.

The body's largest organ system is the integumentary system, which includes the skin and its associated structures, such as hair and nails. The surface tissue of skin is a barrier that protects internal structures and fluids from potentially harmful microorganisms and other toxins.

Metabolism

The first law of thermodynamics holds that energy can neither be created nor destroyed—it can only change form. Your basic function as an organism is to consume (ingest) energy and molecules in the foods you eat, convert some of it into fuel for movement, sustain your body functions, and build and maintain your body structures. There are two types of reactions that accomplish this: **anabolism** and **catabolism**.

- **Anabolism** is the process whereby smaller, simpler molecules are combined into larger, more complex substances. Your body can assemble, by utilizing energy, the complex chemicals it needs by combining small molecules derived from the foods you eat
- **Catabolism** is the process by which larger more complex substances are broken down into smaller simpler molecules. Catabolism releases energy. The complex molecules found in foods are broken down so the body can use their parts to assemble the structures and substances needed for life.

Taken together, these two processes are called metabolism. **Metabolism** is the sum of all anabolic and catabolic reactions that take place in the body (Figure 1). Both anabolism and catabolism occur simultaneously and continuously to keep you alive.

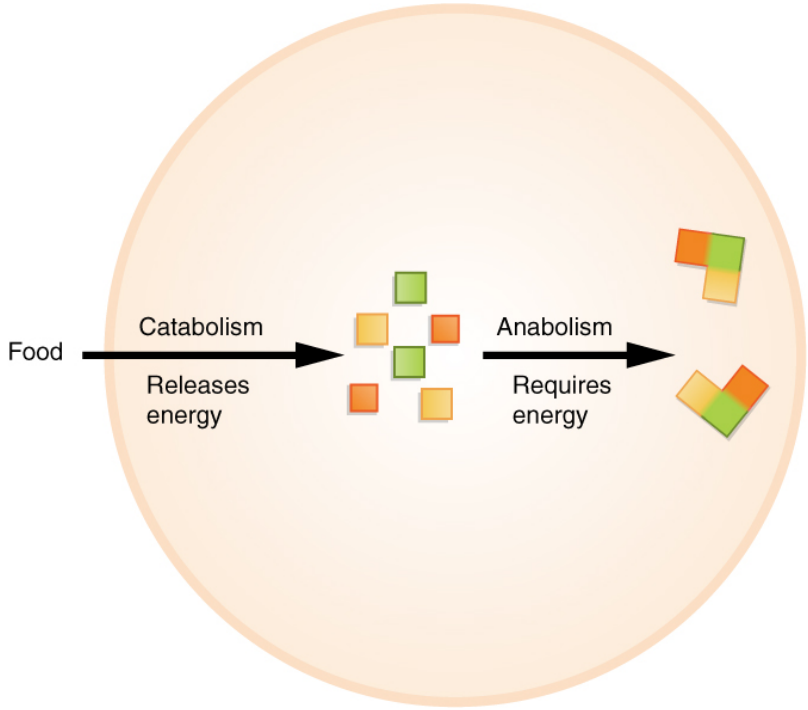


Figure 1. Metabolism. *Anabolic reactions are building reactions, and they consume energy. Catabolic reactions break materials down and release energy. Metabolism includes both anabolic and catabolic reactions. Every cell in your body makes use of a chemical compound, adenosine triphosphate (ATP), to store and release energy. The cell stores energy in the synthesis (anabolism) of ATP, then moves the ATP molecules to the location where energy is needed to fuel cellular activities. Then the ATP is broken down (catabolism) and a controlled amount of energy is released, which is used by the cell to perform a particular job.*

View this animation to learn more about metabolic processes. What kind of catabolism occurs in the heart?

Responsiveness

Responsiveness is the ability of an organism to adjust to changes in its internal and external environments. An example of responsiveness to external stimuli could include moving toward sources of food and water and away from perceived dangers. Changes in an organism's internal environment, such as increased body temperature, can cause the responses of sweating and the dilation of blood vessels in the skin in order to decrease body temperature, as shown by the runners in Figure 2.

Figure 2. Marathon Runners. *Runners demonstrate two characteristics of living humans—responsiveness and movement. Anatomic structures and physiological processes allow runners to coordinate the action of muscle groups and sweat in response to rising internal body temperature. (credit: Phil Roeder/flickr)*

Movement

Human movement includes not only actions at the joints of the body, but also the motion of individual organs and even individual cells. As you read these words, red and white blood cells are moving throughout your body, muscle cells are contracting and relaxing to maintain your posture and to focus your vision, and glands are secreting chemicals

to regulate body functions. Your body is coordinating the action of entire muscle groups to enable you to move air into and out of your lungs, to push blood throughout your body, and to propel the food you have eaten through your digestive tract. Consciously, of course, you contract your skeletal muscles to move the bones of your skeleton to get from one place to another (as the runners are doing in Figure 2), and to carry out all of the activities of your daily life.

Development, growth and reproduction

Development is all of the changes the body goes through in life. Development includes the processes of differentiation, growth, and renewal.

Growth is the increase in body size. Humans, like all multicellular organisms, grow by increasing the number of existing cells, increasing the amount of non-cellular material around cells (such as mineral deposits in bone), and, within very narrow limits, increasing the size of existing cells.

Reproduction is the formation of a new organism from parent organisms. In humans, reproduction is carried out by the male and female reproductive systems. Because death will come to all complex organisms, without reproduction, the line of organisms would end.

REQUIREMENTS FOR HUMAN LIFE

Learning Objectives

- Discuss the role of oxygen and nutrients in maintaining human survival
- Explain why extreme heat and extreme cold threaten human survival
- Explain how the pressure exerted by gases and fluids influences human survival
- Discuss the role of homeostasis in healthy functioning
- Contrast negative and positive feedback, giving one physiologic example of each mechanism

Humans have been adapting to life on Earth for at least the past 200,000 years. Earth and its atmosphere have provided us with air to breathe, water to drink, and food to eat, but these are not the only requirements for survival. Although you may rarely think about it, you also cannot live outside of a certain range of temperature and pressure that the surface of our planet and its atmosphere provides. The next sections explore these four requirements of life.

Oxygen

Atmospheric air is only about 20 percent oxygen, but that oxygen is a key component of the chemical reactions that keep the body alive, including the reactions that produce ATP. Brain cells are especially sensitive to lack of oxygen because of their requirement for a high-and-steady production of ATP. Brain damage is likely within five minutes without oxygen, and death is likely within ten minutes.

Nutrients

A **nutrient** is a substance in foods and beverages that is essential to human survival. The three basic classes of nutrients are water, the energy-yielding and body-building nutrients, and the micronutrients (vitamins and minerals).

The most critical nutrient is water. Depending on the environmental temperature and our state of health, we may be able to survive for only a few days without water. The body's functional chemicals are dissolved and transported in water, and the chemical reactions of life take place in water. Moreover, water is the largest component of cells, blood, and the fluid between cells, and water makes up about 70 percent of an adult's body mass. Water also helps regulate our internal temperature and cushions, protects, and lubricates joints and many other body structures.

The energy-yielding nutrients are primarily carbohydrates and lipids, while proteins mainly supply the amino acids that are the building blocks of the body itself. You ingest these in plant and animal foods and beverages, and the digestive system breaks them down into molecules small enough to be absorbed. The breakdown products of carbohydrates and lipids can then be used in the metabolic processes that convert them to ATP. Although you might feel as if you are starving after missing a single meal, you can survive without consuming the energy-yielding nutrients for at least several weeks.

Water and the energy-yielding nutrients are also referred to as macronutrients because the body needs them in large amounts. In contrast, micronutrients are vitamins and minerals. These elements and compounds participate in many essential chemical reactions and processes, such nerve impulses, and some, such as calcium, also contribute to the body's structure. Your body can store some of the micronutrients in its tissues, and draw on those reserves if you fail to consume them in your diet for a few days or weeks. Some others micronutrients, such as vitamin C and most of the B vitamins, are water-soluble and cannot be stored, so you need to consume them every day or two.

Narrow Range of Temperature

You have probably seen news stories about athletes who died of heat stroke, or hikers who died of exposure to cold. Such deaths occur because the chemical reactions upon which the body depends can only take place within a narrow range of body temperature, from just below to just above 37°C (98.6°F). When body temperature rises well above or drops well below normal, certain proteins (enzymes) that facilitate chemical reactions lose their normal structure and their ability to function and the chemical reactions of metabolism cannot proceed.

That said, the body can respond effectively to short-term exposure to heat (Figure 1) or cold. One of the body's responses to heat is, of course, sweating. As sweat evaporates from skin, it removes some thermal energy from the body, cooling it. Adequate water (from the extracellular fluid in the body) is necessary to produce sweat, so adequate fluid intake is essential to balance that loss during the sweat response. Not surprisingly, the sweat response is much less effective in a humid environment because the air is already saturated with water. Thus, the sweat on the skin's surface is not able to evaporate, and internal body temperature can get dangerously high.

Figure 1. Extreme Heat. *Humans adapt to some degree to repeated exposure to high temperatures. (credit: McKay Savage/flickr)*

The body can also respond effectively to short-term exposure to cold. One response to cold is shivering, which is random muscle movement that generates heat. Another response is increased breakdown of stored energy to generate heat. When that energy reserve is depleted, however, and the core temperature begins to drop significantly, red blood cells will lose their ability to give up oxygen, denying the brain of this critical component of ATP production. This lack of oxygen can cause confusion, lethargy, and eventually loss of consciousness and death. The body responds to cold by reducing blood circulation to the extremities, the hands and feet, in order to prevent blood from cooling there and so that the body's core can stay warm. Even when core body temperature

remains stable, however, tissues exposed to severe cold, especially the fingers and toes, can develop frostbite when blood flow to the extremities has been much reduced. This form of tissue damage can be permanent and lead to gangrene, requiring amputation of the affected region.

Everyday Connection: Controlled Hypothermia

As you have learned, the body continuously engages in coordinated physiological processes to maintain a stable temperature. In some cases, however, overriding this system can be useful, or even life-saving. Hypothermia is the clinical term for an abnormally low body temperature (*hypo–* = "below" or "under"). Controlled hypothermia is clinically induced hypothermia performed in order to reduce the metabolic rate of an organ or of a person's entire body.

Controlled hypothermia often is used, for example, during open-heart surgery because it decreases the metabolic needs of the brain, heart, and other organs, reducing the risk of damage to them. When controlled hypothermia is used clinically, the patient is given medication to prevent shivering. The body is then cooled to 25–32°C (79–89°F). The heart is stopped and an external heart-lung pump maintains circulation to the patient's body. The heart is cooled further and is maintained at a temperature below 15°C (60°F) for the duration of the surgery. This very cold temperature helps the heart muscle to tolerate its lack of blood supply during the surgery.

Some emergency department physicians use controlled hypothermia to reduce damage to the heart in patients who have suffered a cardiac arrest. In the emergency department, the physician induces coma and lowers the patient's body temperature to approximately 91 degrees. This condition, which is maintained for 24 hours, slows the patient's metabolic rate. Because the patient's organs require less blood to function, the heart's workload is reduced.

Narrow Range of Atmospheric Pressure

Pressure is a force exerted by a substance that is in contact with another substance. Atmospheric pressure is pressure exerted by the mixture of gases (primarily nitrogen and oxygen) in the Earth's atmosphere. Although you may not perceive it, atmospheric pressure is constantly pressing down on your body. This pressure keeps gases within your body, such as the gaseous nitrogen in body fluids, dissolved. If you were suddenly ejected from a space ship above Earth's atmosphere, you would go from a situation of normal pressure to one of very low pressure. The pressure of the nitrogen gas in your blood would be much higher than the pressure of nitrogen in the space surrounding your body. As a result, the nitrogen gas in your blood would expand, forming bubbles that could block blood vessels and even cause cells to break apart.

Figure 2. Harsh Conditions. *Climbers on Mount Everest must accommodate extreme cold, low oxygen levels, and low barometric pressure in an environment hostile to human life. (credit: Melanie Ko/flickr)*

Atmospheric pressure does more than just keep blood gases dissolved. Your ability to breathe—that is, to take in oxygen and release carbon dioxide—also depends upon a precise atmospheric pressure. Altitude sickness occurs in part because the atmosphere at high altitudes exerts less pressure, reducing the exchange of these gases, and causing shortness of breath, confusion, headache, lethargy, and nausea. Mountain climbers carry oxygen to reduce the effects of both low oxygen levels and low barometric pressure at higher altitudes (Figure 2).

Homeostatic Imbalances: Decompression Sickness

Decompression sickness (DCS) is a condition in which gases dissolved in the blood or in other body tissues are no longer dissolved following a reduction in pressure on the body. This condition affects underwater divers who surface from a deep dive too quickly, and it can affect pilots flying at high altitudes in planes with unpressurized cabins. Divers often call this condition “the bends,” a reference to joint pain that is a symptom of DCS.

In all cases, DCS is brought about by a reduction in barometric pressure. At high altitude, barometric pressure is much less than on Earth’s surface because pressure is produced by the weight of the column of air above the body pressing down on the body. The very great pressures on divers in deep water are likewise from the weight of a column of water pressing down on the body. For divers, DCS occurs at normal barometric pressure (at sea level), but it is brought on by the relatively rapid decrease of pressure as divers rise from the high pressure conditions of deep water to the now low, by comparison, pressure at sea level. Not surprisingly, diving in deep mountain lakes, where barometric pressure at the surface of the lake is less than that at sea level is more likely to result in DCS than diving in water at sea level.

In DCS, gases dissolved in the blood (primarily nitrogen) come rapidly out of solution, forming bubbles in the blood and in other body tissues. This occurs because when pressure of a gas over a liquid is decreased, the amount of gas that can remain dissolved in the liquid also is decreased. It is air pressure that keeps your normal blood gases dissolved in the blood. When pressure is reduced, less gas remains dissolved. You have seen this in effect when you open a carbonated drink. Removing the seal of the bottle reduces the pressure of the gas over the liquid. This in turn causes bubbles as dissolved gases (in this case, carbon dioxide) come out of solution in the liquid.

The most common symptoms of DCS are pain in the joints, with headache and disturbances of vision occurring in 10 percent to 15 percent of cases. Left untreated, very severe DCS can result in death. Immediate treatment is with pure oxygen. The affected person is then moved into a hyperbaric chamber. A hyperbaric chamber is a reinforced, closed chamber that is pressurized to greater than atmospheric pressure. It treats DCS by repressurizing the body so that pressure can then be removed much more gradually. Because the hyperbaric chamber introduces oxygen to the body at high pressure, it increases the concentration of oxygen in the blood. This has the effect of replacing some of the nitrogen in the blood with oxygen, which is easier to tolerate out of solution.

The dynamic pressure of body fluids is also important to human survival. For example, blood pressure, which is the pressure exerted by blood as it flows within blood vessels, must be great enough to enable blood to reach all body tissues, and yet low enough to ensure that the delicate blood vessels can withstand the friction and force of the pulsating flow of pressurized blood.

A second example of positive feedback centers on reversing extreme damage to the body. Following a penetrating wound, the most immediate threat is excessive blood loss. Less blood circulating means reduced blood pressure and reduced perfusion (penetration of blood) to the brain and other vital organs. If perfusion is severely reduced, vital organs will shut down and the person will die. The body responds to this potential catastrophe by releasing substances in the injured blood vessel wall that begin the process of blood clotting. As each step of clotting occurs, it stimulates the release of more clotting substances. This accelerates the processes of clotting and sealing off the damaged area. Clotting is contained in a local area based on the tightly controlled availability of clotting proteins. This is an adaptive, life-saving cascade of events.

ANATOMICAL TERMINOLOGY

Learning Objectives

- Demonstrate the anatomical position
- Describe the human body using directional and regional terms
- Identify three planes most commonly used in the study of anatomy
- Distinguish between the posterior (dorsal) and the anterior (ventral) body cavities, identifying their subdivisions and representative organs found in each
- Describe serous membrane and explain its function

Anatomists and health care providers use terminology that can be bewildering to the uninitiated. However, the purpose of this language is not to confuse, but rather to increase precision and reduce medical errors. For example, is a scar "above the wrist" located on the forearm two or three inches away from the hand? Or is it at the base of the hand? Is it on the palm-side or back-side? By using precise anatomical terminology, we eliminate ambiguity. Anatomical terms derive from ancient Greek and Latin words. Because these languages are no longer used in everyday conversation, the meaning of their words does not change.

Anatomical terms are made up of roots, prefixes, and suffixes. The root of a term often refers to an organ, tissue, or condition, whereas the prefix or suffix often describes the root. For example, in the disorder hypertension, the prefix "hyper-" means "high" or "over," and the root word "tension" refers to pressure, so the word "hypertension" refers to abnormally high blood pressure.

Anatomical Position

To further increase precision, anatomists standardize the way in which they view the body. Just as maps are normally oriented with north at the top, the standard body "map," or *anatomical position*, is that of the body standing upright, with the feet at shoulder width and parallel, toes forward. The upper limbs are held out to each side, and the palms of the hands face forward as illustrated in Figure 1. Using this standard position reduces confusion. It does not matter how the body being described is oriented, the terms are used as if it is in anatomical position. For example, a scar in the "anterior (front) carpal (wrist) region" would be present on the palm side of the wrist. The term "anterior" would be used even if the hand were palm down on a table.

A body that is lying down is described as either prone or supine. *Prone* describes a face-down orientation, and *supine* describes a face up orientation. These terms are sometimes used in describing the position of the body during specific physical examinations or surgical procedures.

Regional Terms

The human body's numerous regions have specific terms to help increase precision (see Figure 2). Notice that the term "brachium" or "arm" is reserved for the "upper arm" and "antebrachium" or "forearm" is used rather than "lower arm." Similarly, "femur" or "thigh" is correct, and "leg" or "crus" is reserved for the portion of the lower limb between the knee and the ankle. You will be able to describe the body's regions using the terms from the figure.

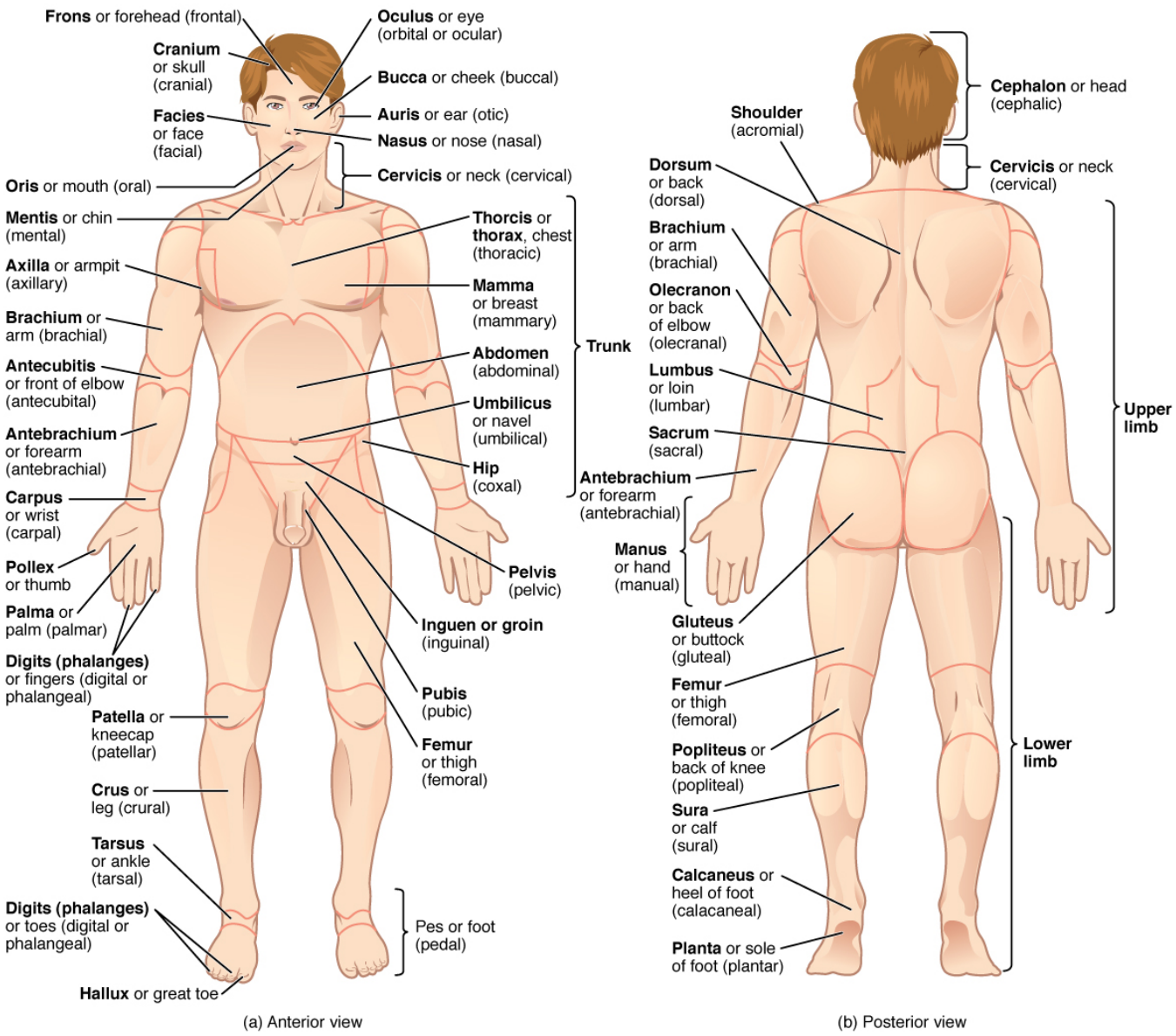


Figure 1. Regions of the Human Body. *The human body is shown in anatomical position in an (a) anterior view and a (b) posterior view. The regions of the body are labeled in boldface.*

Directional Terms

Certain directional anatomical terms appear throughout this and any other anatomy textbook (Figure 2). These terms are essential for describing the relative locations of different body structures. For instance, an anatomist might describe one band of tissue as “inferior to” another or a physician might describe a tumor as “superficial to” a deeper body structure. Commit these terms to memory to avoid confusion when you are studying or describing the locations of particular body parts.

- Anterior (or *ventral*) Describes the front or direction toward the front of the body. The toes are anterior to the foot.
- Posterior (or *dorsal*) Describes the back or direction toward the back of the body. The popliteus is posterior to the patella.
- Superior (or *cranial*) describes a position above or higher than another part of the body proper. The orbits are superior to the oris.

- **Inferior** (or *caudal*) describes a position below or lower than another part of the body proper; near or toward the tail (in humans, the coccyx, or lowest part of the spinal column). The pelvis is inferior to the abdomen.
- **Lateral** describes the side or direction toward the side of the body. The thumb (pollex) is lateral to the digits.
- **Medial** describes the middle or direction toward the middle of the body. The hallux is the medial toe.
- **Proximal** describes a position in a limb that is nearer to the point of attachment or the trunk of the body. The brachium is proximal to the antebrachium.
- **Distal** describes a position in a limb that is farther from the point of attachment or the trunk of the body. The crus is distal to the femur.
- **Superficial** describes a position closer to the surface of the body. The skin is superficial to the bones.
- **Deep** describes a position farther from the surface of the body. The brain is deep to the skull.

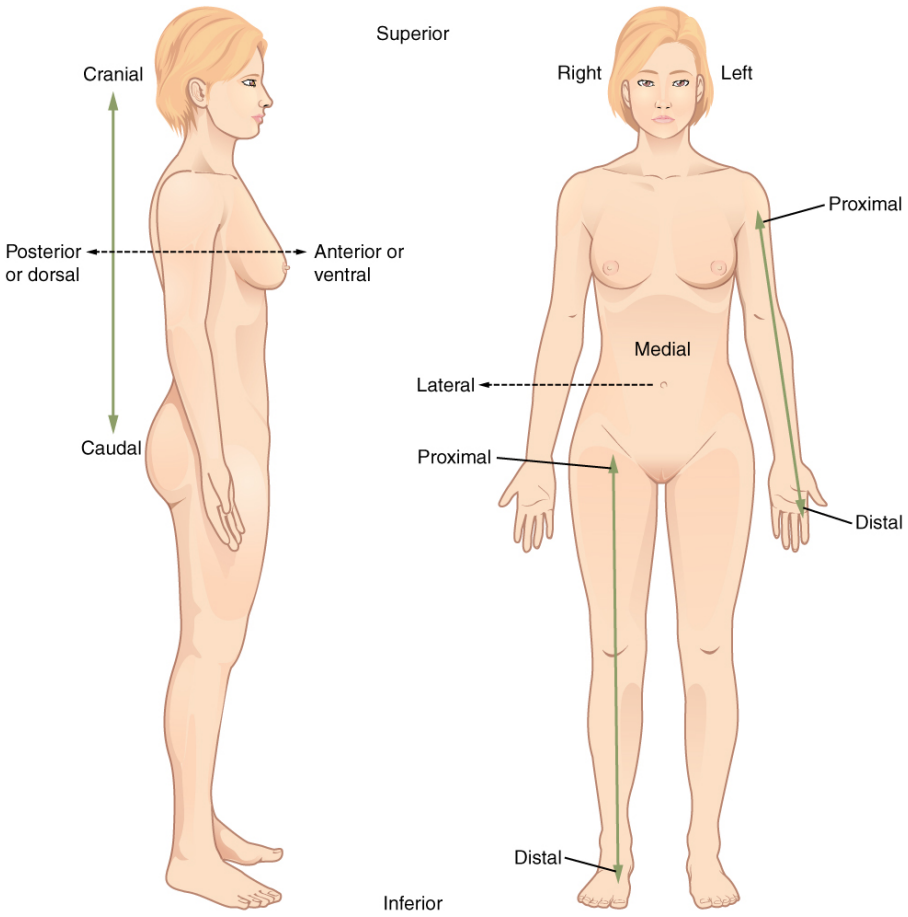


Figure 2. Directional Terms Applied to the Human Body. *Paired directional terms are shown as applied to the human body.*

Body Planes

A **section** is a two-dimensional surface of a three-dimensional structure that has been cut. Modern medical imaging devices enable clinicians to obtain “virtual sections” of living bodies. We call these scans. Body sections and scans can be correctly interpreted, however, only if the viewer understands the plane along which the section was made. A **plane** is an imaginary two-dimensional surface that passes through the body. There are three planes commonly referred to in anatomy and medicine, as illustrated in Figure 3.

- The **sagittal plane** is the plane that divides the body or an organ vertically into right and left sides. If this vertical plane runs directly down the middle of the body, it is called the midsagittal or median plane. If it divides the body into unequal right and left sides, it is called a parasagittal plane or less commonly a longitudinal section.

- The **frontal plane** is the plane that divides the body or an organ into an anterior (front) portion and a posterior (rear) portion. The frontal plane is often referred to as a coronal plane. (“Corona” is Latin for “crown.”)
- The **transverse plane** is the plane that divides the body or organ horizontally into upper and lower portions. Transverse planes produce images referred to as cross sections.

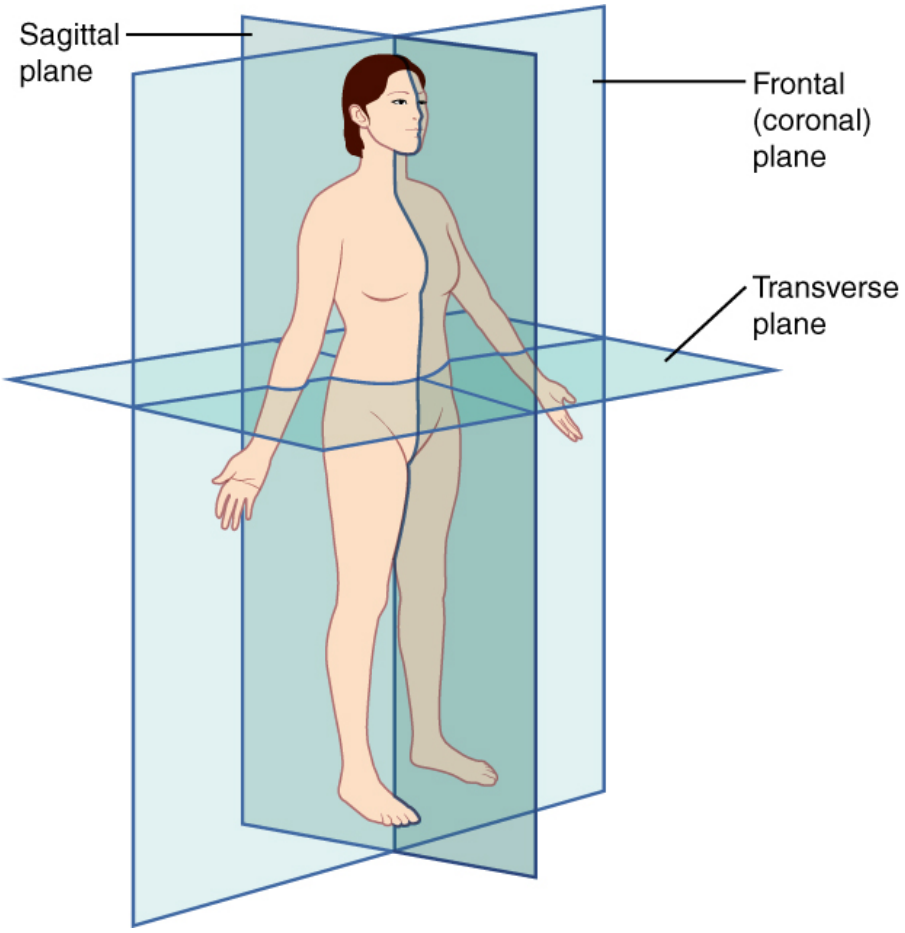


Figure 3. Planes of the Body. *The three planes most commonly used in anatomical and medical imaging are the sagittal, frontal (or coronal), and transverse plane.*

Body Cavities and Serous Membranes

The body maintains its internal organization by means of membranes, sheaths, and other structures that separate compartments. The *dorsal (posterior) cavity* and the *ventral (anterior) cavity* are the largest body compartments (Figure 4). These cavities contain and protect delicate internal organs, and the ventral cavity allows for significant changes in the size and shape of the organs as they perform their functions. The lungs, heart, stomach, and intestines, for example, can expand and contract without distorting other tissues or disrupting the activity of nearby organs.

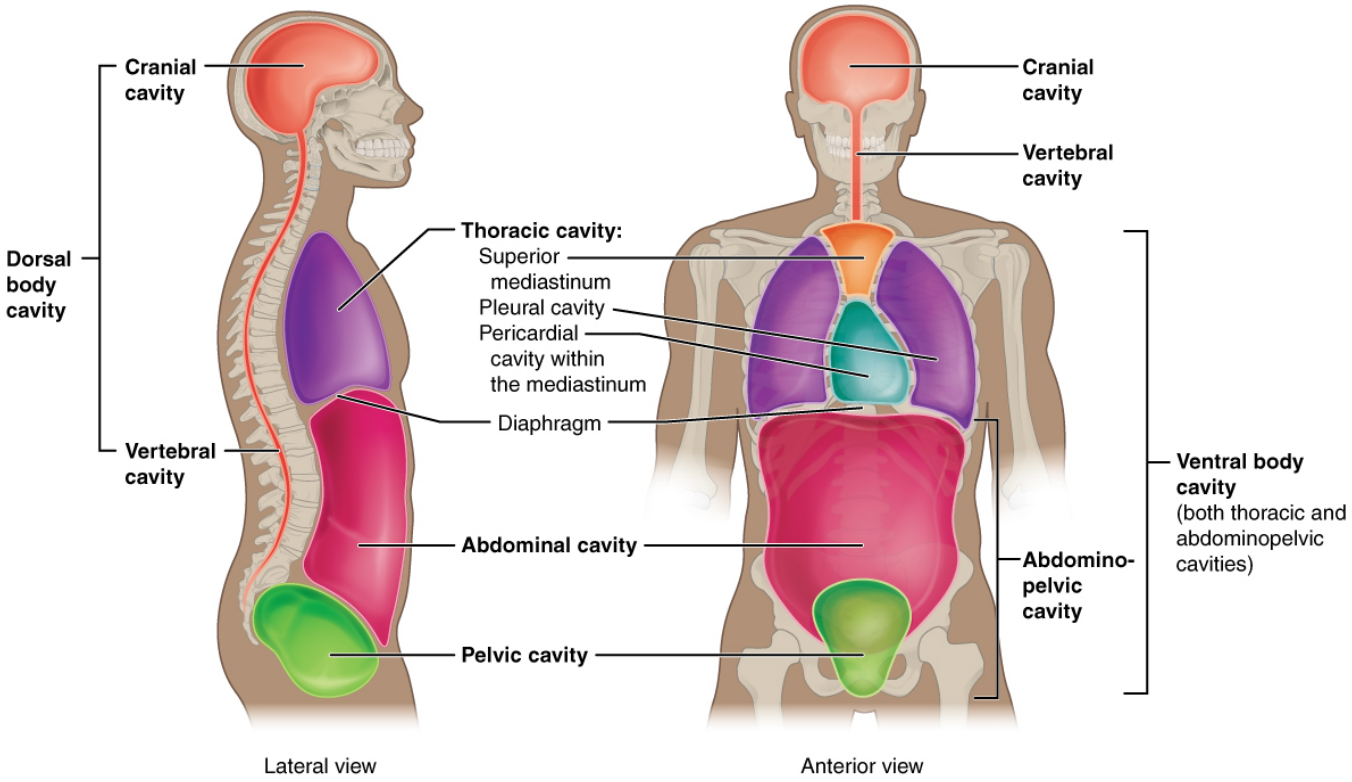


Figure 4. Dorsal and Ventral Body Cavities. *The ventral cavity includes the thoracic and abdominopelvic cavities and their subdivisions. The dorsal cavity includes the cranial and spinal cavities.*

Subdivisions of the Posterior (Dorsal) and Anterior (Ventral) Cavities

The posterior (dorsal) and anterior (ventral) cavities are each subdivided into smaller cavities. In the posterior (dorsal) cavity, the **cranial cavity** houses the brain, and the **spinal cavity** (or vertebral cavity) encloses the spinal cord. Just as the brain and spinal cord make up a continuous, uninterrupted structure, the cranial and spinal cavities that house them are also continuous. The brain and spinal cord are protected by the bones of the skull and vertebral column and by cerebrospinal fluid, a colorless fluid produced by the brain, which cushions the brain and spinal cord within the posterior (dorsal) cavity.

The anterior (ventral) cavity has two main subdivisions: the thoracic cavity and the abdominopelvic cavity (see Figure 4). The **thoracic cavity** is the more superior subdivision of the anterior cavity, and it is enclosed by the rib cage. The thoracic cavity contains the lungs and the heart, which is located in the mediastinum. The diaphragm forms the floor of the thoracic cavity and separates it from the more inferior abdominopelvic cavity. The **abdominopelvic cavity** is the largest cavity in the body. Although no membrane physically divides the abdominopelvic cavity, it can be useful to distinguish between the abdominal cavity, the division that houses the digestive organs, and the pelvic cavity, the division that houses the organs of reproduction.

Abdominal Regions and Quadrants

To promote clear communication, for instance about the location of a patient's abdominal pain or a suspicious mass, health care providers typically divide up the cavity into either nine regions or four quadrants (Figure 5).

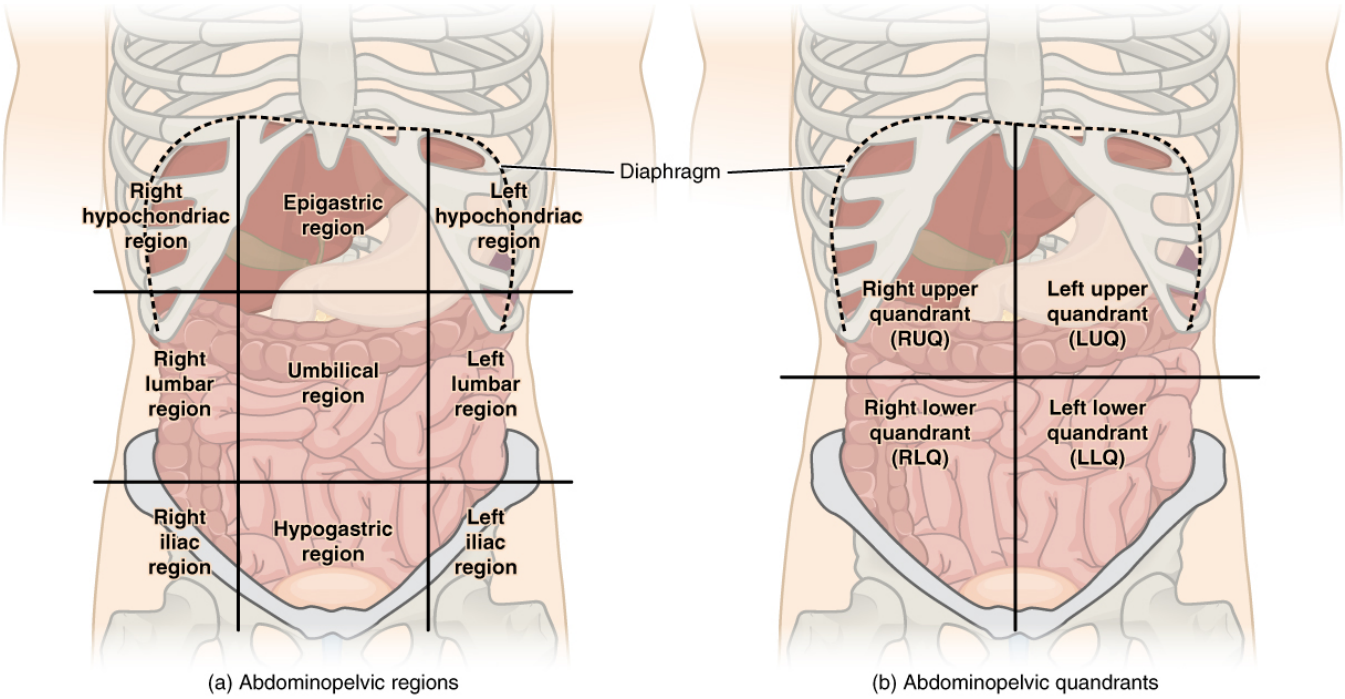


Figure 5. Regions and Quadrants of the Peritoneal Cavity. *There are (a) nine abdominal regions and (b) four abdominal quadrants in the peritoneal cavity.*

The more detailed regional approach subdivides the cavity with one horizontal line immediately inferior to the ribs and one immediately superior to the pelvis, and two vertical lines drawn as if dropped from the midpoint of each clavicle (collarbone). There are nine resulting regions. The simpler quadrants approach, which is more commonly used in medicine, subdivides the cavity with one horizontal and one vertical line that intersect at the patient's umbilicus (navel).

Membranes of the Anterior (Ventral) Body Cavity

A serous membrane (also referred to a serosa) is one of the thin membranes that cover the walls and organs in the thoracic and abdominopelvic cavities. The parietal layers of the membranes line the walls of the body cavity (pariet- refers to a cavity wall). The visceral layer of the membrane covers the organs (the viscera). Between the parietal and visceral layers is a very thin, fluid-filled serous space, or cavity (Figure 6).

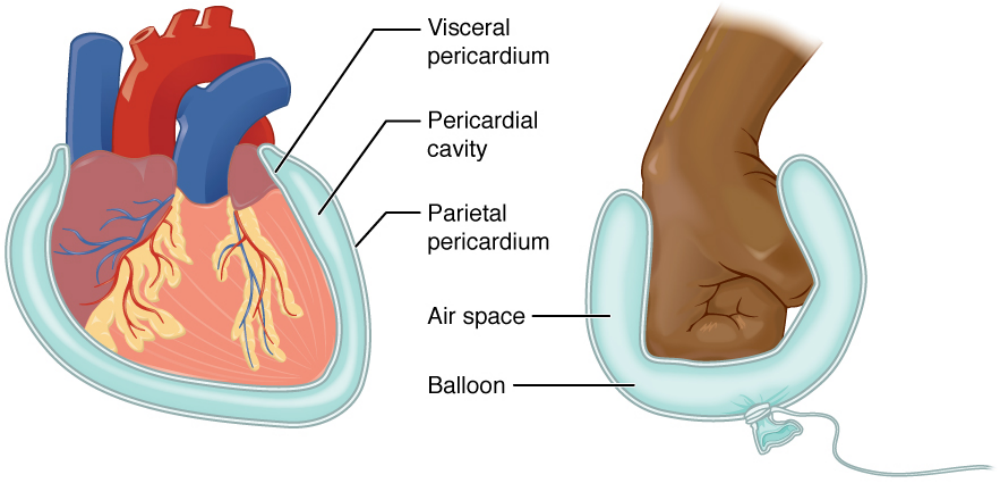


Figure 6. Serous Membrane. *Serous membrane lines the pericardial cavity and reflects back to cover the heart—much the same way that an underinflated balloon would form two layers surrounding a fist.*

There are three serous cavities and their associated membranes. The **pleura** is the serous membrane that surrounds the lungs in the pleural cavity; the **pericardium** is the serous membrane that surrounds the heart in the pericardial cavity; and the **peritoneum** is the serous membrane that surrounds several organs in the abdominopelvic cavity. The serous fluid produced by the serous membranes reduces friction between the walls of the cavities and the internal organs when they move, such as when the lungs inflate or the heart beats. Both the parietal and visceral serosa secrete the thin, slippery serous fluid that prevents friction when an organ slides past the walls of a cavity. In the pleural cavities, pleural fluid prevents friction between the lungs and the walls of the cavity. In the pericardial sac, pericardial fluid prevents friction between the heart and the walls of the pericardial sac. And in the peritoneal cavity, peritoneal fluid prevents friction between abdominal and pelvic organs and the wall of the cavity. The serous membranes therefore provide additional protection to the viscera they enclose by reducing friction that could lead to inflammation of the organs.

VIDEO: Anatomy Terminology

Watch this 3D Anatomical tutorial from AnatomyZone to learn about key terms used in anatomy:
Watch this video online: https://youtu.be/3KpQHae6LGI

Self-Check Questions

Visit your course online to take a quiz to check your understanding of Anatomical Terminology:

ANATOMICAL LOCATION

To better identify the locations of the organs that contribute to vital functions, you need some points of reference for description. To serve that function, we will now define different planes of the body. These imaginary flat surfaces run through the body in different directions. They are used by medical professionals to examine various internal body parts. Directional orientation is another anatomical tool used to describe how parts of the body are related to one another.

Each organ system spans large regions of the human body. It is helpful, therefore, to establish reference planes and directions that can help us describe specific locations of structures as we discuss them. To make sure everyone is talking about the same thing, anatomists and physiologists often refer to anatomical position and the body planes that penetrate it. Anatomical position describes a person standing upright, with the arms at the sides and the palms facing forward (as demonstrated in the image below). Body planes (a plane is a flat, two-dimensional surface) are imaginary surfaces that run through the body and divide it into different sections. We can talk about a specific location using the planes as reference points within the anatomical position.

There are an infinite number of planes running through the human body in all directions. However, we will focus on the three planes that are traditionally used when discussing human anatomy (see Figure 1). First is the transverse plane, (also called the horizontal plane), which divides the body into top and bottom. In anatomical position, transverse planes are parallel to the ground. The second is the coronal plane, which is a vertical plane that divides the body into the front and back sections. If you do a “belly flop” into the water, you sink into the water via the coronal planes. Finally, we will refer to the sagittal plane, which divides the body into left and right sections with a vertical plane that passes from the front to the rear.

You can use other terms to further pinpoint an anatomical location. These terms are used to describe a location in relation to other structures. Some of them may be terms you have heard in everyday conversation; a lateral pass in football, for example, is a pass toward the sideline.

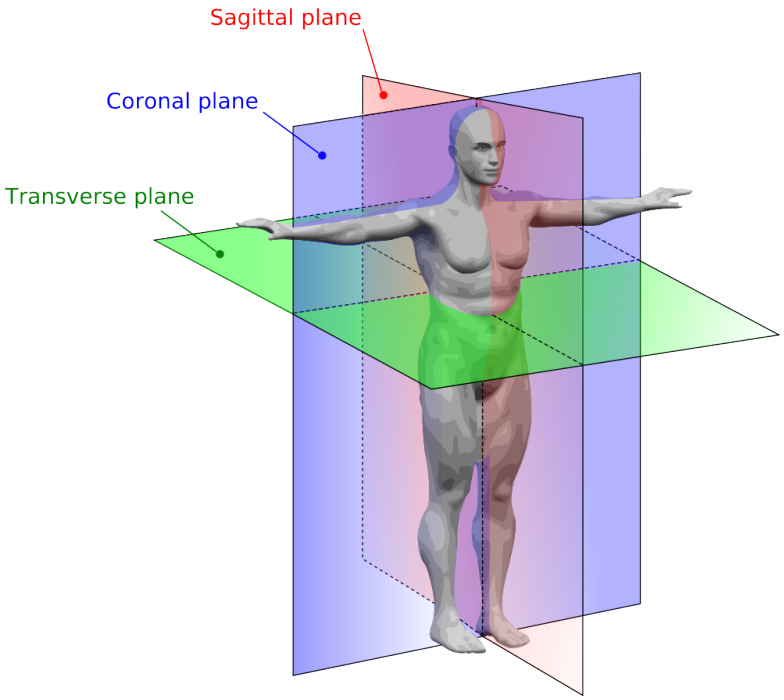


Figure 1. Sagittal, Coronal, and Transverse body planes and their intersections. *By YassineMrabet (Human Anatomy Planes)/Wikimedia Commons/CC-BY-SA.*

Superior, Inferior, Anterior and Posterior

The first set of directions that we will explore are superior, inferior, anterior, and posterior.

In humans, which stand upright on two feet, there are other terms that are synonymous with these four terms. Cephalic means toward the head and is the same as superior for a human in anatomical position. Caudal means toward the tail, or same as inferior for a human in anatomical position. Dorsal means toward the back and ventral means toward the belly; so dorsal and posterior are the same direction and ventral and anterior are the same direction for a human in anatomical position. This would not be true for a four-legged animal, such as a rat or cat you might dissect in lab.

Medial and Lateral

Next are the terms that relate structures to the midline. These are medial, lateral, and intermediate.

Watch this video online: https://youtu.be/olF39pDz9x0

Proximal, Distal, Superficial, Deep

These next terms are used when referring to either appendicular parts of the body (arms and legs) or position in body relative to the external surface. These are proximal, distal, superficial, and deep.

Watch this video online: https://youtu.be/rMojfWZsRz8

Directions and Orientation

Table 1 lists all of the human anatomical directions that we discussed.

Table 1. Anatomical Directions and Orientation	
Directional Term	**Meaning**
superior	above (or toward the head)
inferior	below (or toward the feet)
distal	farther from the trunk or origin
proximal	closer to the trunk or origin
deep (internal)	away from the surface
anterior (ventral)	toward the front (or toward the belly)
posterior (dorsal)	toward the rear (or toward the back)
medial	toward the midline
lateral	toward the side

LECTURE: Anatomical Toolbox

Watch these lectures from Wendy Riggs to learn more about Directional Terminology and Planes of Section.
Watch this video online: https://youtu.be/cKB1bOVEXaY
Watch this video online: https://youtu.be/ptAkN7Ir1pA

MEDICAL IMAGING

Learning Objectives

- Discuss the uses and drawbacks of X-ray imaging
- Identify four modern medical imaging techniques and how they are used

For thousands of years, fear of the dead and legal sanctions limited the ability of anatomists and physicians to study the internal structures of the human body. An inability to control bleeding, infection, and pain made

surgeries infrequent, and those that were performed—such as wound suturing, amputations, tooth and tumor removals, skull drilling, and cesarean births—did not greatly advance knowledge about internal anatomy. Theories about the function of the body and about disease were therefore largely based on external observations and imagination. During the fourteenth and fifteenth centuries, however, the detailed anatomical drawings of Italian artist and anatomist Leonardo da Vinci and Flemish anatomist Andreas Vesalius were published, and interest in human anatomy began to increase. Medical schools began to teach anatomy using human dissection; although some resorted to grave robbing to obtain corpses. Laws were eventually passed that enabled students to dissect the corpses of criminals and those who donated their bodies for research. Still, it was not until the late nineteenth century that medical researchers discovered non-surgical methods to look inside the living body.

X-Rays

German physicist Wilhelm Röntgen (1845–1923) was experimenting with electrical current when he discovered that a mysterious and invisible "ray" would pass through his flesh but leave an outline of his bones on a screen coated with a metal compound. In 1895, Röntgen made the first durable record of the internal parts of a living human: an "X-ray" image (as it came to be called) of his wife's hand. Scientists around the world quickly began their own experiments with X-rays, and by 1900, X-rays were widely used to detect a variety of injuries and diseases. In 1901, Röntgen was awarded the first Nobel Prize for physics for his work in this field.

The **X-ray** is a form of high energy electromagnetic radiation with a short wavelength capable of penetrating solids and ionizing gases. As they are used in medicine, X-rays are emitted from an X-ray machine and directed toward a specially treated metallic plate placed behind the patient's body. The beam of radiation results in darkening of the X-ray plate. X-rays are slightly impeded by soft tissues, which show up as gray on the X-ray plate, whereas hard tissues, such as bone, largely block the rays, producing a light-toned "shadow." Thus, X-rays are best used to visualize hard body structures such as teeth and bones (Figure 1). Like many forms of high energy radiation, however, X-rays are capable of damaging cells and initiating changes that can lead to cancer. This danger of excessive exposure to X-rays was not fully appreciated for many years after their widespread use.

Refinements and enhancements of X-ray techniques have continued throughout the twentieth and twenty-first centuries. Although often supplanted by more sophisticated imaging techniques, the X-ray remains a "workhorse" in medical imaging, especially for viewing fractures and for dentistry. The disadvantage of irradiation to the patient and the operator is now attenuated by proper shielding and by limiting exposure.

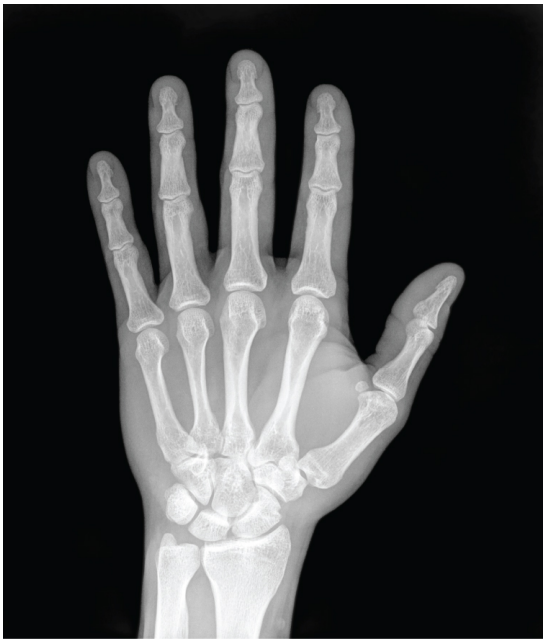


Figure 1. X-Ray of a Hand. *High energy electromagnetic radiation allows the internal structures of the body, such as bones, to be seen in X-rays like these. (credit: Trace Meek/flickr)*

Modern Medical Imaging

X-rays can depict a two-dimensional image of a body region, and only from a single angle. In contrast, more recent medical imaging technologies produce data that is integrated and analyzed by computers to produce three-dimensional images or images that reveal aspects of body functioning.

Computed Tomography

Tomography refers to imaging by sections. **Computed tomography (CT)** is a noninvasive imaging technique that uses computers to analyze several cross-sectional X-rays in order to reveal minute details about structures in the body (Figure 2). The technique was invented in the 1970s and is based on the principle that, as X-rays pass through the body, they are absorbed or reflected at different levels. In the technique, a patient lies on a motorized

platform while a computerized axial tomography (CAT) scanner rotates 360 degrees around the patient, taking X-ray images. A computer combines these images into a two-dimensional view of the scanned area, or “slice.”

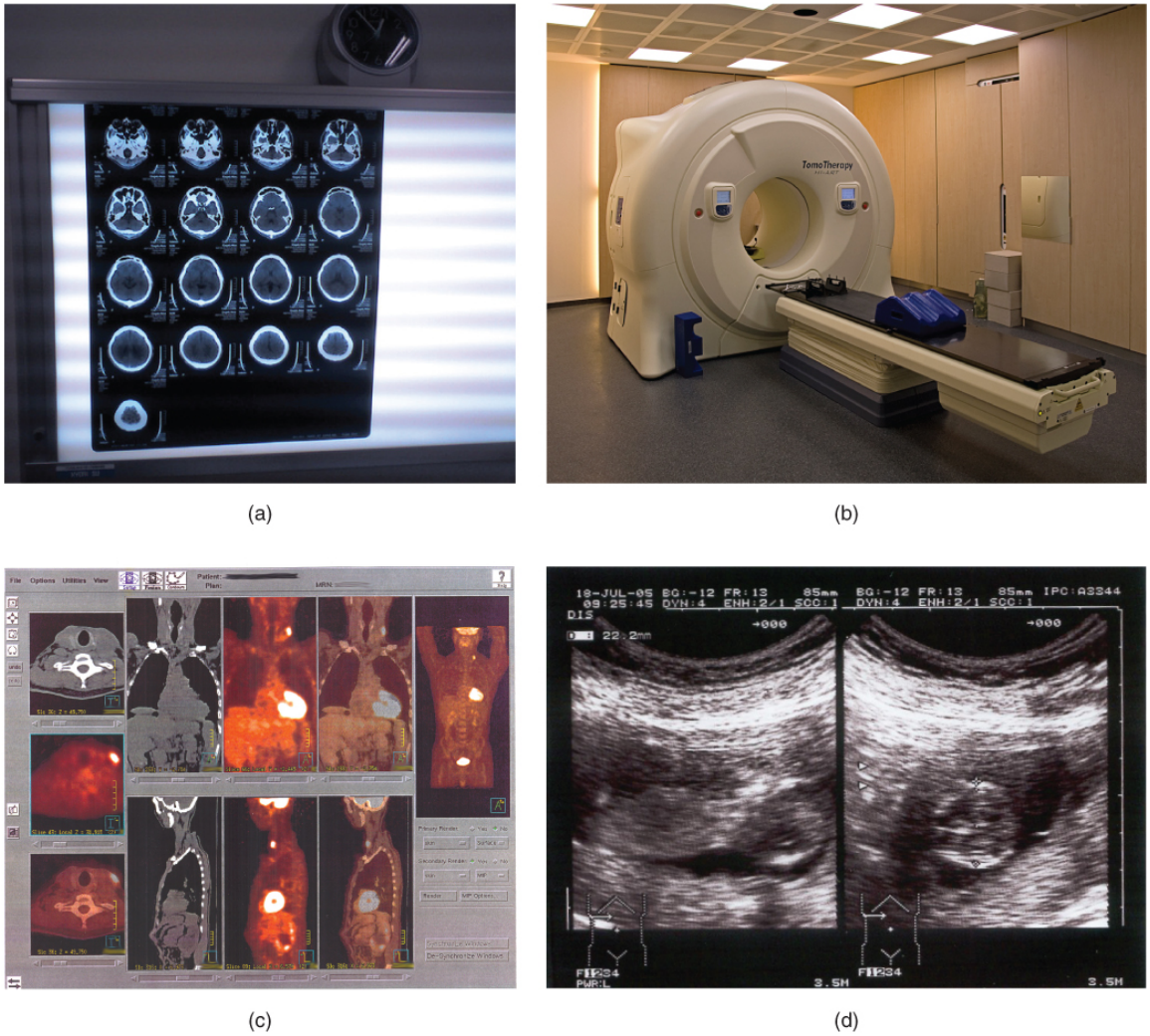


Figure 2. Medical Imaging Techniques. *(a) The results of a CT scan of the head are shown as successive transverse sections. (b) An MRI machine generates a magnetic field around a patient. (c) PET scans use radiopharmaceuticals to create images of active blood flow and physiologic activity of the organ or organs being targeted. (d) Ultrasound technology is used to monitor pregnancies because it is the least invasive of imaging techniques and uses no electromagnetic radiation. (credit a: Akira Ohgaki/flickr; credit b: “Digital Cate”/flickr; credit c: “Raziel”/Wikimedia Commons; credit d: “Isis”/Wikimedia Commons)*

Since 1970, the development of more powerful computers and more sophisticated software has made CT scanning routine for many types of diagnostic evaluations. It is especially useful for soft tissue scanning, such as of the brain and the thoracic and abdominal viscera. Its level of detail is so precise that it can allow physicians to measure the size of a mass down to a millimeter. The main disadvantage of CT scanning is that it exposes patients to a dose of radiation many times higher than that of X-rays. In fact, children who undergo CT scans are at increased risk of developing cancer, as are adults who have multiple CT scans.

A CT or CAT scan relies on a circling scanner that revolves around the patient’s body. Watch this video to learn more about CT and CAT scans. What type of radiation does a CT scanner use?

Watch this video online: https://youtu.be/M-4o0DxBgZk

Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) is a noninvasive medical imaging technique based on a phenomenon of nuclear physics discovered in the 1930s, in which matter exposed to magnetic fields and radio waves was found to emit radio signals. In 1970, a physician and researcher named Raymond Damadian noticed that malignant (cancerous) tissue gave off different signals than normal body tissue. He applied for a patent for the first MRI scanning device, which was in use clinically by the early 1980s. The early MRI scanners were crude, but advances in digital computing and electronics led to their advancement over any other technique for precise imaging, especially to discover tumors. MRI also has the major advantage of not exposing patients to radiation.

Drawbacks of MRI scans include their much higher cost, and patient discomfort with the procedure. The MRI scanner subjects the patient to such powerful electromagnets that the scan room must be shielded. The patient must be enclosed in a metal tube-like device for the duration of the scan (see Figure 2b), sometimes as long as thirty minutes, which can be uncomfortable and impractical for ill patients. The device is also so noisy that, even with earplugs, patients can become anxious or even fearful. These problems have been overcome somewhat with the development of "open" MRI scanning, which does not require the patient to be entirely enclosed in the metal tube. Patients with iron-containing metallic implants (internal sutures, some prosthetic devices, and so on) cannot undergo MRI scanning because it can dislodge these implants.

Functional MRIs (fMRIs), which detect the concentration of blood flow in certain parts of the body, are increasingly being used to study the activity in parts of the brain during various body activities. This has helped scientists learn more about the locations of different brain functions and more about brain abnormalities and diseases.

A patient undergoing an MRI is surrounded by a tube-shaped scanner. Watch this video to learn more about MRIs. What is the function of magnets in an MRI?

Watch this video online: https://youtu.be/fKzN7AcCatI

Positron Emission Tomography

Positron emission tomography (PET) is a medical imaging technique involving the use of so-called radiopharmaceuticals, substances that emit radiation that is short-lived and therefore relatively safe to administer to the body. Although the first PET scanner was introduced in 1961, it took 15 more years before radiopharmaceuticals were combined with the technique and revolutionized its potential. The main advantage is that PET (see Figure 2c) can illustrate physiologic activity—including nutrient metabolism and blood flow—of the organ or organs being targeted, whereas CT and MRI scans can only show static images. PET is widely used to diagnose a multitude of conditions, such as heart disease, the spread of cancer, certain forms of infection, brain abnormalities, bone disease, and thyroid disease.

PET relies on radioactive substances administered several minutes before the scan. Watch this video to learn more about PET. How is PET used in chemotherapy?

Watch this video online: https://youtu.be/ijmwQzfjNQo

Ultrasonography

Ultrasonography is an imaging technique that uses the transmission of high-frequency sound waves into the body to generate an echo signal that is converted by a computer into a real-time image of anatomy and physiology (see Figure 2d). Ultrasonography is the least invasive of all imaging techniques, and it is therefore used more freely in sensitive situations such as pregnancy. The technology was first developed in the 1940s and 1950s.

Ultrasonography is used to study heart function, blood flow in the neck or extremities, certain conditions such as gallbladder disease, and fetal growth and development. The main disadvantages of ultrasonography are that the image quality is heavily operator-dependent and that it is unable to penetrate bone and gas.

ANATOMY PRONUNCIATION GUIDE

In this course, you will encounter new terms and vocabulary. Most of these words aren't a part of common vocabulary, and will likely be unfamiliar to you. This Anatomy & Physiology Pronunciation Guide, from OpenStax, will help you learn the correct pronunciation of terms as you learn what they mean.

GLOSSARY: INTRODUCTION

abdominopelvic cavity: division of the anterior (ventral) cavity that houses the abdominal and pelvic viscera

anabolism: assembly of more complex molecules from simpler molecules

anatomical position: standard reference position used for describing locations and directions on the human body

anatomy: science that studies the form and composition of the body's structures

anterior cavity: larger body cavity located anterior to the posterior (dorsal) body cavity; includes the serous membrane-lined pleural cavities for the lungs, pericardial cavity for the heart, and peritoneal cavity for the abdominal and pelvic organs; also referred to as ventral cavity

anterior: describes the front or direction toward the front of the body; also referred to as ventral

catabolism: breaking down of more complex molecules into simpler molecules

caudal: describes a position below or lower than another part of the body proper; near or toward the tail (in humans, the coccyx, or lowest part of the spinal column); also referred to as inferior

cell: smallest independently functioning unit of all organisms; in animals, a cell contains cytoplasm, composed of fluid and organelles

computed tomography (CT): medical imaging technique in which a computer-enhanced cross-sectional X-ray image is obtained

control center: compares values to their normal range; deviations cause the activation of an effector

cranial cavity: division of the posterior (dorsal) cavity that houses the brain

cranial: describes a position above or higher than another part of the body proper; also referred to as superior

deep: describes a position farther from the surface of the body

development: changes an organism goes through during its life

differentiation: process by which unspecialized cells become specialized in structure and function

distal: describes a position farther from the point of attachment or the trunk of the body

dorsal cavity: posterior body cavity that houses the brain and spinal cord; also referred to the posterior body cavity

dorsal: describes the back or direction toward the back of the body; also referred to as posterior

effector: organ that can cause a change in a value

frontal plane: two-dimensional, vertical plane that divides the body or organ into anterior and posterior portions

gross anatomy: study of the larger structures of the body, typically with the unaided eye; also referred to macroscopic anatomy

growth: process of increasing in size

homeostasis: steady state of body systems that living organisms maintain

inferior: describes a position below or lower than another part of the body proper; near or toward the tail (in humans, the coccyx, or lowest part of the spinal column); also referred to as caudal

lateral: describes the side or direction toward the side of the body

magnetic resonance imaging (MRI): medical imaging technique in which a device generates a magnetic field to obtain detailed sectional images of the internal structures of the body

medial: describes the middle or direction toward the middle of the body

metabolism: sum of all of the body's chemical reactions

microscopic anatomy: study of very small structures of the body using magnification

negative feedback: homeostatic mechanism that tends to stabilize an upset in the body's physiological condition by preventing an excessive response to a stimulus, typically as the stimulus is removed

normal range: range of values around the set point that do not cause a reaction by the control center

nutrient: chemical obtained from foods and beverages that is critical to human survival

organ system: group of organs that work together to carry out a particular function

organism: living being that has a cellular structure and that can independently perform all physiologic functions necessary for life

organ: functionally distinct structure composed of two or more types of tissues

pericardium: sac that encloses the heart

peritoneum: serous membrane that lines the abdominopelvic cavity and covers the organs found there

physiology: science that studies the chemistry, biochemistry, and physics of the body's functions

plane: imaginary two-dimensional surface that passes through the body

pleura: serous membrane that lines the pleural cavity and covers the lungs

positive feedback: mechanism that intensifies a change in the body's physiological condition in response to a stimulus

positron emission tomography (PET): medical imaging technique in which radiopharmaceuticals are traced to reveal metabolic and physiological functions in tissues

posterior cavity: posterior body cavity that houses the brain and spinal cord; also referred to as dorsal cavity

posterior: describes the back or direction toward the back of the body; also referred to as dorsal

pressure: force exerted by a substance in contact with another substance

prone: face down

proximal: describes a position nearer to the point of attachment or the trunk of the body

regional anatomy: study of the structures that contribute to specific body regions

renewal: process by which worn-out cells are replaced

reproduction: process by which new organisms are generated

responsiveness: ability of an organisms or a system to adjust to changes in conditions

sagittal plane: two-dimensional, vertical plane that divides the body or organ into right and left sides

section: in anatomy, a single flat surface of a three-dimensional structure that has been cut through

sensor: (also, receptor) reports a monitored physiological value to the control center

serosa: membrane that covers organs and reduces friction; also referred to as serous membrane

serous membrane: membrane that covers organs and reduces friction; also referred to as serosa

set point: ideal value for a physiological parameter; the level or small range within which a physiological parameter such as blood pressure is stable and optimally healthful, that is, within its parameters of homeostasis

spinal cavity: division of the dorsal cavity that houses the spinal cord; also referred to as vertebral cavity

superficial: describes a position nearer to the surface of the body

superior: describes a position above or higher than another part of the body proper; also referred to as cranial

supine: face up

systemic anatomy: study of the structures that contribute to specific body systems

thoracic cavity: division of the anterior (ventral) cavity that houses the heart, lungs, esophagus, and trachea

tissue: group of similar or closely related cells that act together to perform a specific function

transverse plane: two-dimensional, horizontal plane that divides the body or organ into superior and inferior portions

ultrasonography: application of ultrasonic waves to visualize subcutaneous body structures such as tendons and organs

ventral cavity: larger body cavity located anterior to the posterior (dorsal) body cavity; includes the serous membrane-lined pleural cavities for the lungs, pericardial cavity for the heart, and peritoneal cavity for the abdominal and pelvic organs; also referred to as anterior body cavity

ventral: describes the front or direction toward the front of the body; also referred to as anterior

X-ray: form of high energy electromagnetic radiation with a short wavelength capable of penetrating solids and ionizing gases; used in medicine as a diagnostic aid to visualize body structures such as bones

PRACTICE TEST: BODY PLAN AND ORGANIZATION

Review the material from Body Plan and Organization by completing the practice test below:

MODULE 2: HOMEOSTASIS

HOMEOSTASIS

Maintaining homeostasis requires that the body continuously monitor its internal conditions. From body temperature to blood pressure to levels of certain nutrients, each physiological condition has a particular set point. A **set point** is the physiological value around which the normal range fluctuates. A **normal range** is the restricted set of values that is optimally healthful and stable. For example, the set point for normal human body temperature is approximately 37°C (98.6°F) Physiological parameters, such as body temperature and blood pressure, tend to fluctuate within a normal range a few degrees above and below that point. Control centers in the brain play roles in regulating physiological parameters and keeping them within the normal range. As the body works to maintain homeostasis, any significant deviation from the normal range will be resisted and homeostasis restored through a process called negative feedback. **Negative feedback** is a mechanism that prevents a physiological response from going beyond the normal range by reversing the action once the normal range is exceeded. The maintenance of homeostasis by negative feedback goes on throughout the body at all times, and an understanding of negative feedback is thus fundamental to an understanding of human physiology.

Negative Feedback

A negative feedback system has three basic components (Figure 1a). A **sensor**, also referred to a receptor, is a component of a feedback system that monitors a physiological value. This value is reported to the control center. The **control center** is the component in a feedback system that compares the value to the normal range. If the value deviates too much from the set point, then the control center activates an effector. An **effector** is the component in a feedback system that causes a change to reverse the situation and return the value to the normal range.

In order to set the system in motion, a stimulus must drive a physiological parameter beyond its normal range (that is, beyond homeostasis). This stimulus is “heard” by a specific sensor. For example, in the control of blood glucose, specific endocrine cells in the pancreas detect excess glucose (the stimulus) in the bloodstream. These pancreatic beta cells respond to the increased level of blood glucose by releasing the hormone insulin into the bloodstream. The insulin signals skeletal muscle fibers, fat cells (adipocytes), and liver cells to take up the excess glucose, removing it from the bloodstream. As glucose concentration in the bloodstream drops, the decrease in concentration—the actual negative feedback—is detected by pancreatic alpha cells, and insulin release stops. This prevents blood sugar levels from continuing to drop below the normal range.

Humans have a similar temperature regulation feedback system that works by promoting either heat loss or heat gain (Figure 1b). When the brain’s temperature regulation center receives data from the sensors indicating that the body’s temperature exceeds its normal range, it stimulates a cluster of brain cells referred to as the “heat-loss center.” This stimulation has three major effects:

- Blood vessels in the skin begin to dilate allowing more blood from the body core to flow to the surface of the skin allowing the heat to radiate into the environment.
- As blood flow to the skin increases, sweat glands are activated to increase their output. As the sweat evaporates from the skin surface into the surrounding air, it takes heat with it.
- The depth of respiration increases, and a person may breathe through an open mouth instead of through the nasal passageways. This further increases heat loss from the lungs.

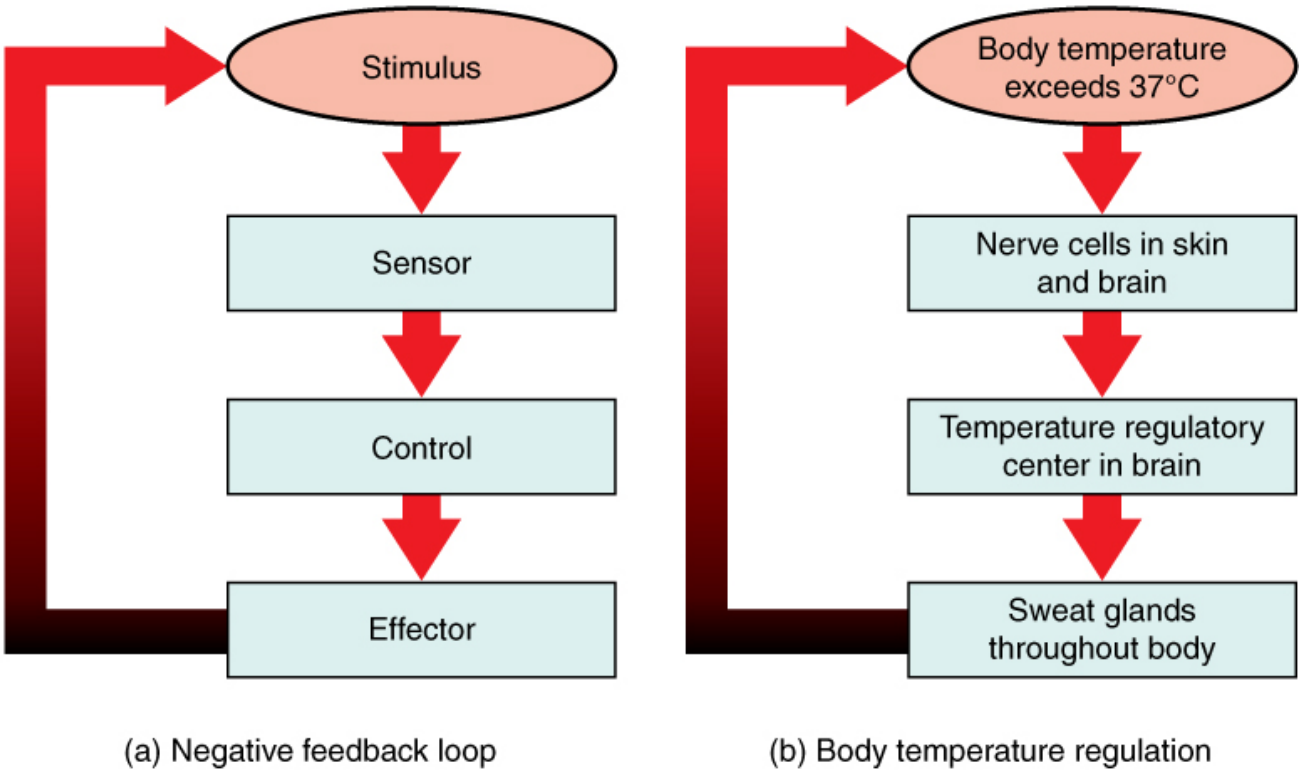


Figure 1. Negative Feedback Loop. *In a negative feedback loop, a stimulus—a deviation from a set point—is resisted through a physiological process that returns the body to homeostasis. (a) A negative feedback loop has four basic parts. (b) Body temperature is regulated by negative feedback.*

In contrast, activation of the brain's heat-gain center by exposure to cold reduces blood flow to the skin, and blood returning from the limbs is diverted into a network of deep veins. This arrangement traps heat closer to the body core and restricts heat loss. If heat loss is severe, the brain triggers an increase in random signals to skeletal muscles, causing them to contract and producing shivering. The muscle contractions of shivering release heat while using up ATP. The brain triggers the thyroid gland in the endocrine system to release thyroid hormone, which increases metabolic activity and heat production in cells throughout the body. The brain also signals the adrenal glands to release epinephrine (adrenaline), a hormone that causes the breakdown of glycogen into glucose, which can be used as an energy source. The breakdown of glycogen into glucose also results in increased metabolism and heat production.

Think about It

Water concentration in the body is critical for proper functioning. A person's body retains very tight control on water levels without conscious control by the person. Watch this video to learn more about water concentration in the body.

Watch this video online: https://youtu.be/vB7tSHqR1eY

Which organ has primary control over the amount of water in the body?

Answer

Kidneys have primary control over the amount of water in the body.

Positive Feedback

Positive feedback intensifies a change in the body's physiological condition rather than reversing it. A deviation from the normal range results in more change, and the system moves farther away from the normal range. Positive feedback in the body is normal only when there is a definite end point. Childbirth and the body's response to blood loss are two examples of positive feedback loops that are normal but are activated only when needed.

Childbirth at full term is an example of a situation in which the maintenance of the existing body state is not desired. Enormous changes in the mother's body are required to expel the baby at the end of pregnancy. And the events of childbirth, once begun, must progress rapidly to a conclusion or the life of the mother and the baby are at risk. The extreme muscular work of labor and delivery are the result of a positive feedback system (Figure 2).

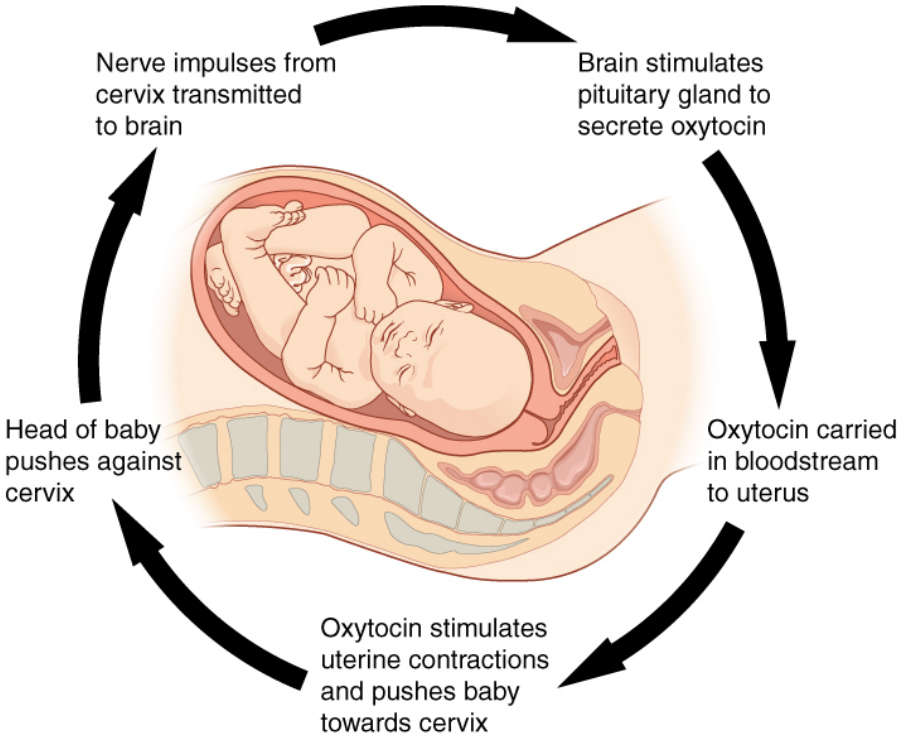


Figure 2. Positive Feedback Loop. *Normal childbirth is driven by a positive feedback loop. A positive feedback loop results in a change in the body's status, rather than a return to homeostasis.*

The first contractions of labor (the stimulus) push the baby toward the cervix (the lowest part of the uterus). The cervix contains stretch-sensitive nerve cells that monitor the degree of stretching (the sensors). These nerve cells send messages to the brain, which in turn causes the pituitary gland at the base of the brain to release the hormone oxytocin into the bloodstream. Oxytocin causes stronger contractions of the smooth muscles in of the uterus (the effectors), pushing the baby further down the birth canal. This causes even greater stretching of the cervix. The cycle of stretching, oxytocin release, and increasingly more forceful contractions stops only when the baby is born. At this point, the stretching of the cervix halts, stopping the release of oxytocin.

A second example of positive feedback centers on reversing extreme damage to the body. Following a penetrating wound, the most immediate threat is excessive blood loss. Less blood circulating means reduced blood pressure and reduced perfusion (penetration of blood) to the brain and other vital organs. If perfusion is severely reduced, vital organs will shut down and the person will die. The body responds to this potential catastrophe by releasing substances in the injured blood vessel wall that begin the process of blood clotting. As each step of clotting occurs, it stimulates the release of more clotting substances. This accelerates the processes of clotting and sealing off the damaged area. Clotting is contained in a local area based on the tightly controlled availability of clotting proteins. This is an adaptive, life-saving cascade of events.

Self-Check Questions

Visit your course online to take a quiz to check your understanding of Homeostasis:

HOMEOSTASIS AND FEEDBACK LOOPS

Homeostasis relates to dynamic physiological processes that help us maintain an internal environment suitable for normal function. Homeostasis is *not* the same as chemical or physical equilibrium. Such equilibrium occurs when no net change is occurring: add milk to the coffee and eventually, when equilibrium is achieved, there will be no net diffusion of milk in the coffee mug. Homeostasis, however, is the process by which internal variables, such as body temperature, blood pressure, etc., are kept within a range of values appropriate to the system. When a stimulus changes one of these internal variables, it creates a detected signal that the body will respond to as part of its ability to carry out homeostasis.

Homeostasis

Homeostasis is the tendency of biological systems to maintain relatively constant conditions in the internal environment while continuously interacting with and adjusting to changes originating within or outside the system.

Consider that when the outside temperature drops, the body does not just “equilibrate” with (become the same as) the environment. Multiple systems work together to help maintain the body’s temperature: we shiver, develop “goose bumps”, and blood flow to the skin, which causes heat loss to the environment, decreases.

Many medical conditions and diseases result from altered homeostasis. This section will review the terminology and explain the physiological mechanisms that are associated with homeostasis. We will discuss homeostasis in every subsequent system. Many aspects of the body are in a constant state of change—the volume and location of blood flow, the rate at which substances are exchanged between cells and the environment, and the rate at which cells are growing and dividing, are all examples. But these changes actually contribute to keeping many of the body’s variables, and thus the body’s overall internal conditions, within relatively narrow ranges. For example, blood flow will increase to a tissue when that tissue becomes more active. This ensures that the tissue will have enough oxygen to support its higher level of metabolism.

Maintaining internal conditions in the body is called homeostasis(from homeo-, meaning similar, and stasis, meaning standing still). The root “stasis” of the term “homeostasis” may seem to imply that nothing is happening. But if you think about anatomy and physiology, even maintaining the body at rest requires a lot of internal activity. Your brain is constantly receiving information about the internal and external environment, and incorporating that information into responses that you may not even be aware of, such as slight changes in heart rate, breathing pattern, activity of certain muscle groups, eye movement, etc. Any of these actions that help maintain the internal environment contribute to homeostasis.

We can consider the maintenance of homeostasis on a number of different levels. For example, consider what happens when you exercise, which can represent challenges to various body systems. Yet instead of these challenges damaging your body, our systems adapt to the situation. At the whole-body level, you notice some specific changes: your breathing and heart rate increase, your skin may flush, and you may sweat. If you continue to exercise, you may feel thirsty. These effects are all the result of your body trying to maintain conditions suitable for normal function:

- Your muscle cells use oxygen to convert the energy stored in glucose into the energy stored in ATP (adenosine triphosphate), which they then use to drive muscle contractions. When you exercise, your muscles need more oxygen. Therefore, to maintain an adequate oxygen level in all of the tissues in your body, you breathe more deeply and at a higher rate when you exercise. This allows you to take in more oxygen. Your heart also pumps faster and harder, which allows it to deliver more oxygen-rich blood to your muscles and other organs that will need more oxygen and ATP.
- As your muscles carry out cellular respiration to release the energy from glucose, they produce carbon dioxide and water as waste products. These wastes must be eliminated to help your body maintain its fluid and pH balance. Your increased breathing and heart rates also help eliminate a great deal of carbon dioxide and some of the excess water.

- Your muscles use the energy stored in ATP molecules to generate the force they need to contract. A byproduct of releasing that energy is heat, so exercising increases your body temperature. To maintain an appropriate body temperature, your body compensates for the extra heat by causing blood vessels near your skin to dilate and by causing sweat glands in your skin to release sweat. These actions allow heat to more easily dissipate into the air and through evaporation of the water in sweat.
- As you exercise for longer periods of time, you lose more and more water and salts to sweat (and, to a smaller extent, from breathing more). If you exercise too long, your body may lose enough water and salt that its other functions begin to be affected. Low concentrations of water in the blood prompt the release of hormones that make you feel thirsty. Your kidneys also produce more concentrated urine with less water if your fluid levels are low. These actions help you maintain fluid balance.

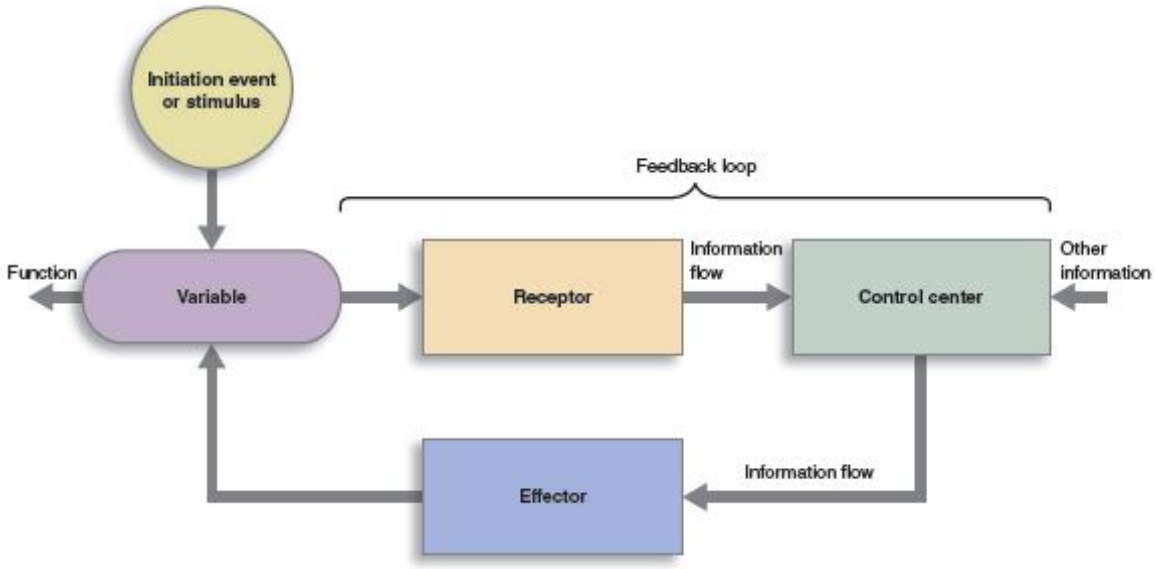
Homeostasis Terminology

The maintenance of homeostasis in the body typically occurs through the use of feedback loops that control the body's internal conditions.

Feedback loop is defined as a system used to control the level of a variable in which there is an identifiable receptor (sensor), control center (integrator or comparator), effectors, and methods of communication.

We use the following terminology to describe feedback loops:

- Variables are parameters that are monitored and controlled or affected by the feedback system.
- Receptors (sensors) detect changes in the variable.
- Control centers (integrators) compare the variable in relation to a set point and signal the effectors to generate a response. Control centers sometimes consider infomration other than just the level of the variable in their decision-making, such as time of day, age, external conditions, etc.
- Effectors execute the necessary changes to adjust the variable.
- Methods of communication among the commponents of a feedback loop are necessary in order for it to function. This often occurs through nerves or hormones, but in some cases receptors and control centers are the same structures, so that there is no need for these signaling modes in that part of the loop.



Terminology in this area is often inconsistent. For example, there are cases where components of a feedback loop are not easily identifiable, but variables are maintained in a range. Such situations are still examples of homeostasis and are sometimes described as a feedback cycle instead of a feedback loop.

Feedback Cycle is defined as any situation in which a variable is regulated and the level of the variable impacts the direction in which the variable changes (i.e. increases or decreases), even if there is not clearly identified loop components.

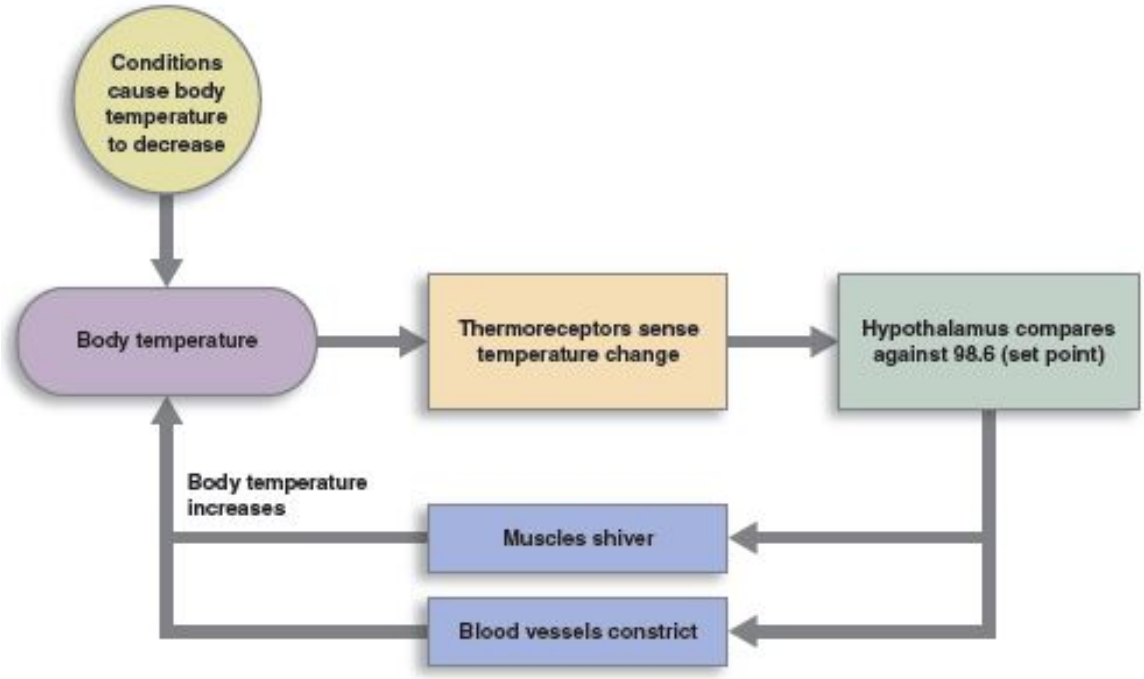
With this terminology in mind, homeostasis then can be described as the totality of the feedback loops and feedback cycles that the body incorporates to maintain a suitable functioning status.

Air conditioning is a technological system that can be described in terms of a feedback loop. The thermostat senses the temperature, an electronic interface compares the temperature against a set point (the temperature that you want it to be). If the temperature matches or is cooler, then nothing happens. If the temperature is too hot, then the electronic interface triggers the air-conditioning unit to turn on. Once the temperature is lowered sufficiently to reach the set point, the electronic interface shuts the air-conditioning unit off. For this example, identify the steps of the feedback loop.

Cruise control is another technological feedback system. The idea of cruise control is to maintain a constant speed in your car. The car's speed is determined by the speedometer and an electronic interface measures the car's speed against a set point chosen by the driver. If the speed is too slow, the interface stimulates the engine; if the speed is too fast, the interface reduces the power to the tires.

Terms Applied to Temperature

Consider one of the feedback loops that controls body temperature.



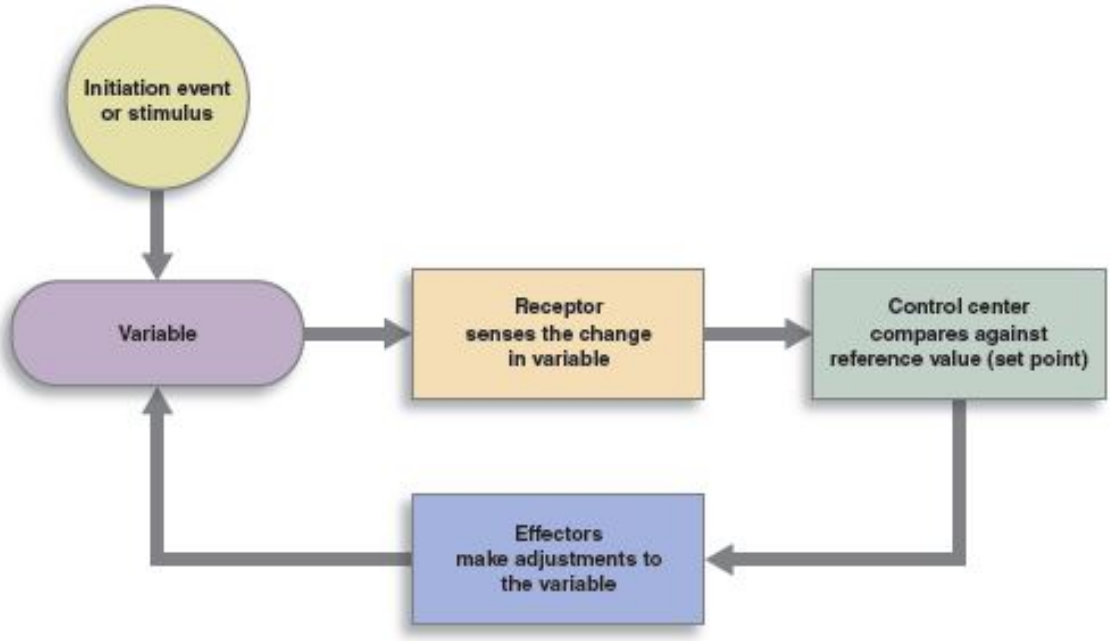
- Variable: In this instance, the variable is body temperature.
- Receptors: Thermoreceptors detect changes in body temperature. For example, thermoreceptors in your internal organs can detect a lowered body temperature and produce nerve impulses that travel to the control center, the hypothalamus.
- Control Center: The hypothalamus controls a variety of effectors that respond to a decrease in body temperature.
- Effectors: There are several effectors controlled by the hypothalamus.

- blood vessels near the skin constrict, reducing blood flow (and the resultant heat loss) to the environment.
- Skeletal muscles are also effectors in this feedback loop: they contract rapidly in response to a decrease in body temperature. This shivering helps to generate heat, which increases body temperature.

Feedback Loops

Remember that homeostasis is the maintenance of a relatively stable internal environment. When a stimulus, or change in the environment, is present, feedback loops respond to keep systems functioning near a set point, or ideal level.

Feedback is a situation when the output or response of a loop impacts or influences the input or stimulus.



Typically, we divide feedback loops into two main types:

1. positive feedback loops, in which a change in a given direction causes additional change in the same direction.For example, an increase in the concentration of a substance causes feedback that produces continued increases in concentration.
2. negative feedback loops, in which a change in a given direction causes change in the opposite direction.For example, an increase in the concentration of a substance causes feedback that ultimately causes the concentration of the substance to decrease.

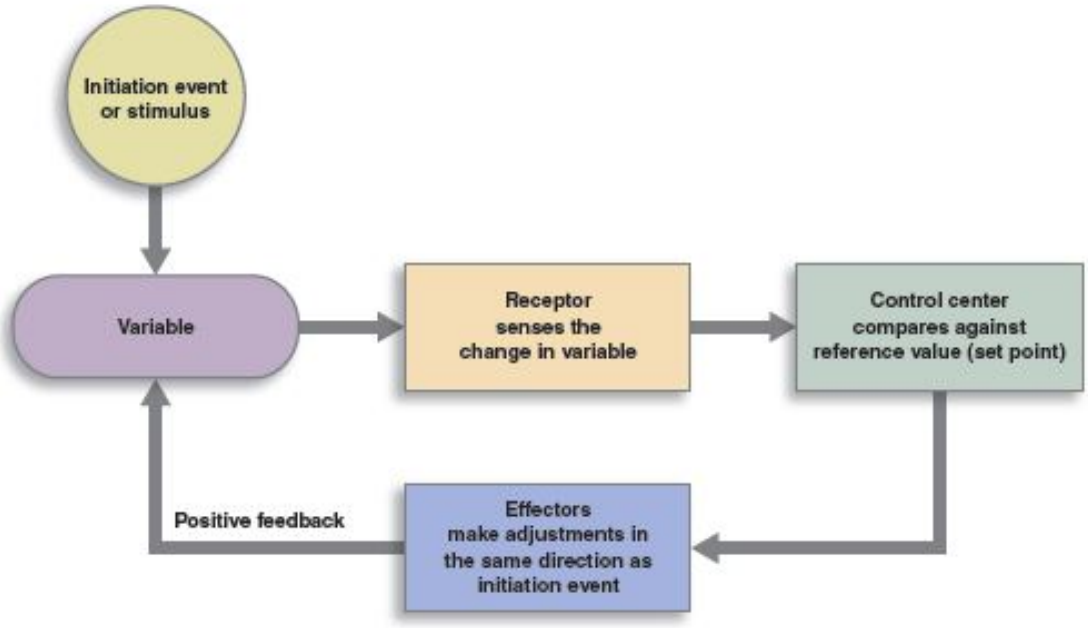
Positive feedback loops are inherently unstable systems. Because a change in an input causes responses that produce continued changes in the same direction, positive feedback loops can lead to runaway conditions. The term positive feedback is typically used as long as a variable has an ability to amplify itself, even if the components of a loop (receptor, control center and effector) are not easily identifiable. In most cases, positive feedback is harmful, but there are a few instances where positive feedback, when used in limited fashion, contributes to normal function. For example, during blood clotting, a cascade of enzymatic proteins activates each other, leading to the formation of a fibrin clot that prevents blood loss. One of the enzymes in the pathway, called thrombin, not only acts on the next protein in the pathway but also has an ability to activate a protein that

preceded it in the cascade. This latter step leads to a positive feedback cycle, where an increase in thrombin leads to further increases in thrombin. It should be noted that there are other aspects of blood clotting that keep the overall process in check, such that thrombin levels don't rise without limit. But if we just consider the effects of thrombin on itself, it is considered a positive feedback cycle. Although some may consider this a positive feedback loop, such terminology is not universally accepted.

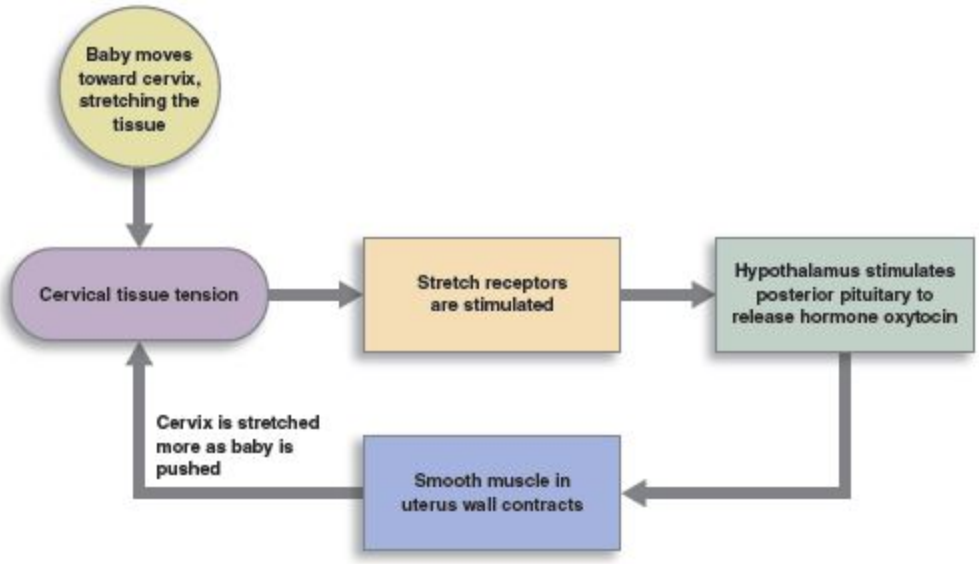
Negative feedback loops are inherently stable systems. Negative feedback loops, in conjunction with the various stimuli that can affect a variable, typically produce a condition in which the variable oscillates around the set point. For example, negative feedback loops involving insulin and glucagon help to keep blood glucose levels within a narrow concentration range. If glucose levels get too high, the body releases insulin into the bloodstream. Insulin causes the body's cells to take in and store glucose, lowering the blood glucose concentration. If blood glucose gets too low, the body releases glucagon, which causes the release of glucose from some of the body's cells.

Positive Feedback

In a positive feedback mechanism, the output of the system stimulates the system in such a way as to further increase the output. Common terms that could describe positive feedback loops or cycles include "snowballing" and "chain reaction". Without a counter-balancing or "shut-down" reaction or process, a positive feedback mechanism has the potential to produce a runaway process. As noted, there are some physiologic processes that are commonly considered to be positive feedback, although they may not all have identifiable components of a feedback loop. In these cases, the positive feedback loop always ends with counter-signaling that suppresses the original stimulus.



A good example of positive feedback involves the amplification of labor contractions. The contractions are initiated as the baby moves into position, stretching the cervix beyond its normal position. The feedback increases the strength and frequency of the contractions until the baby is born. After birth, the stretching stops and the loop is interrupted.



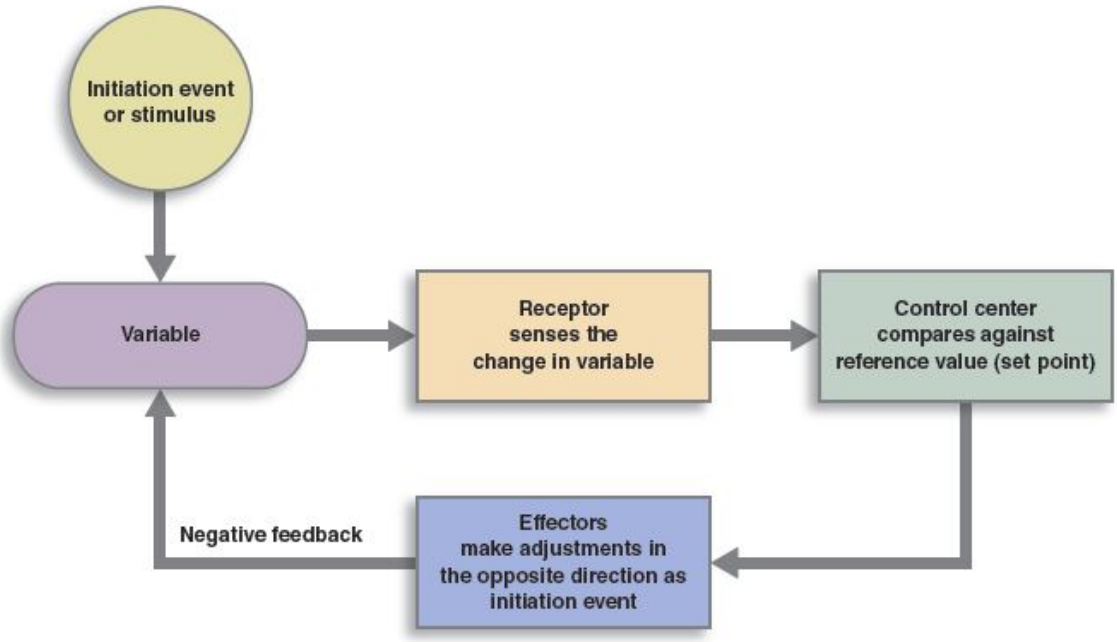
Another example of positive feedback occurs in lactation, during which a mother produces milk for her infant. During pregnancy, levels of the hormone prolactin increase. Prolactin normally stimulates milk production, but during pregnancy, progesterone inhibits milk production. At birth, when the placenta is released from the uterus, progesterone levels drop. As a result, milk production surges. As the baby feeds, its suckling stimulates the breast, promoting further release of prolactin, resulting in yet more milk production. This positive feedback ensures the baby has sufficient milk during feeding. When the baby is weaned and no longer nurses from the mother, stimulation ceases and prolactin in the mother's blood reverts to pre-breastfeeding levels.

The above provide examples of beneficial positive feedback mechanisms. However, in many instances, positive feedback can be potentially damaging to life processes. For example, blood pressure can fall significantly if a person loses a lot of blood due to trauma.

Blood pressure is a regulated variable that leads to the heart increasing its rate (i.e. heart rate increases) and contracting more strongly. These changes to the heart cause it to need more oxygen and nutrients, but if the blood volume in the body is too low, the heart tissue itself will not receive enough blood flow to meet these increased needs. The imbalance between oxygen demands of the heart and oxygen supply can lead to further heart damage, which actually lowers blood pressure, providing a larger change in the variable (blood pressure). The loop responds by trying to stimulate the heart even more strongly, leading to further heart damage…and the loop goes on until death ensues.

Negative Feedback

Most biological feedback systems are negative feedback systems. Negative feedback occurs when a system's output acts to reduce or dampen the processes that lead to the output of that system, resulting in less output. In general, negative feedback loops allow systems to self-stabilize. Negative feedback is a vital control mechanism for the body's homeostasis.

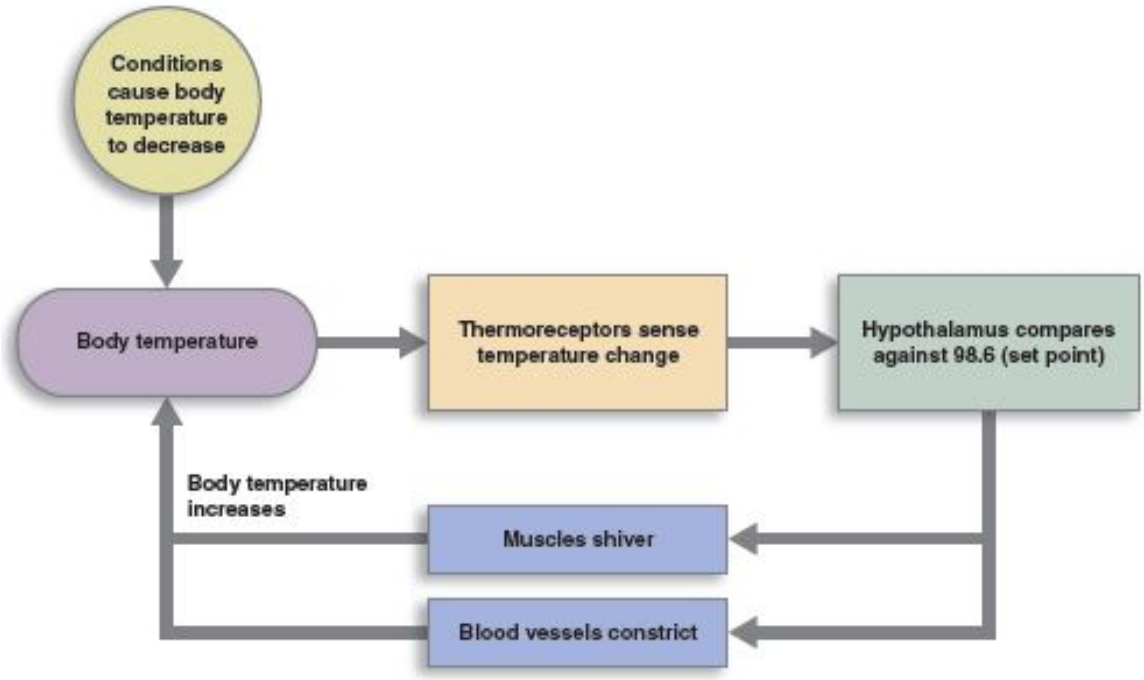


You saw an example of a feedback loop applied to temperature and identified the components involved. This is an important example of how a negative feedback loop maintains homeostasis is the body's thermoregulation mechanism. The body maintains a relatively constant internal temperature to optimize chemical processes. Neural impulses from heat-sensitive thermoreceptors in the body signal the hypothalamus. The hypothalamus, located in the brain, compares the body temperature to a set point value.

When body temperature drops, the hypothalamus initiates several physiological responses to increase heat production and conserve heat:

- Narrowing of surface blood vessels (vasoconstriction) decreases the flow of heat to the skin.
- Shivering commences, increasing production of heat by the muscles.
- Adrenal glands secrete stimulatory hormones such as norepinephrine and epinephrine to increase metabolic rates and hence heat production.

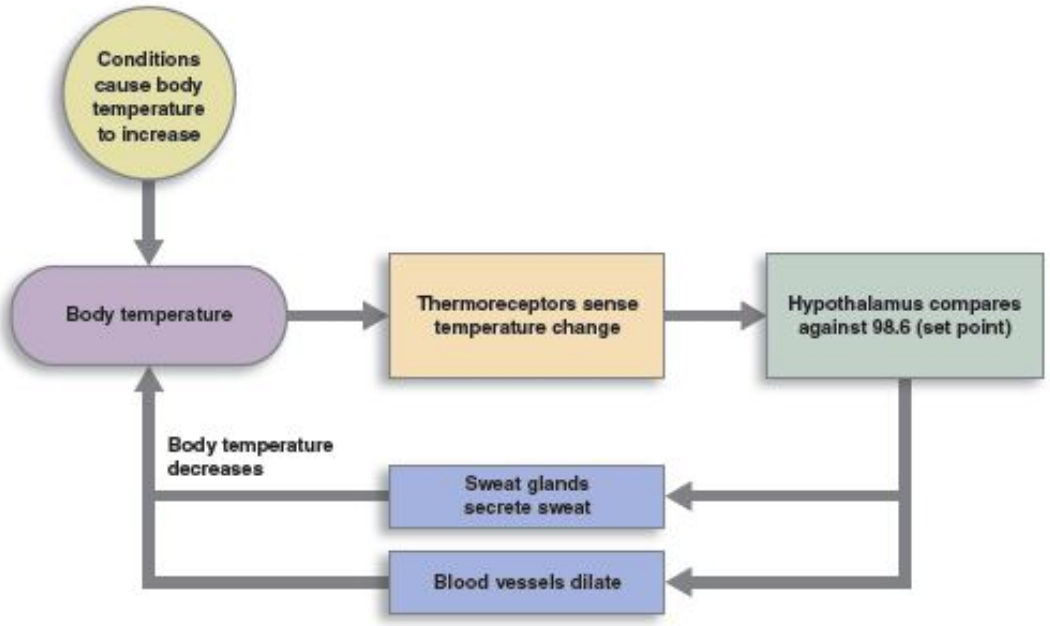
These effects cause body temperature to increase. When it returns to normal, the hypothalamus is no longer stimulated, and these effects cease.



When body temperature rises, the hypothalamus initiates several physiological responses to decrease heat production and lose heat:

- Widening of surface blood vessels (vasodilation) increases the flow of heat to the skin and get flushed.
- Sweat glands release water (sweat) and evaporation cools the skin.

These effects cause body temperature to decrease. When it returns to normal, the hypothalamus is no longer stimulated, and these effects cease.



Many homeostatic mechanisms, like temperature, have different responses if the variable is above or below the set point. When temperature increases, we sweat, when it decreases, we shiver. These responses use different effectors to adjust the variable. In other cases, a feedback loop will use the same effector to adjust the variable back toward the set point, whether the initial change of the variable was either above or below the set point. For example, pupillary diameter is adjusted to make sure an appropriate amount of light is entering the eye. If the amount of light is too low, the pupil dilates, if it is too high, the pupil constricts.

This might be compared to driving. If your speed is above the set point (the value you want it to be), you can either just decrease the level of the accelerator (i.e. coast), or you can active a second system — the brake. In both cases you slow, but it can be done by either just "backing" off on one system, or adding a second system.

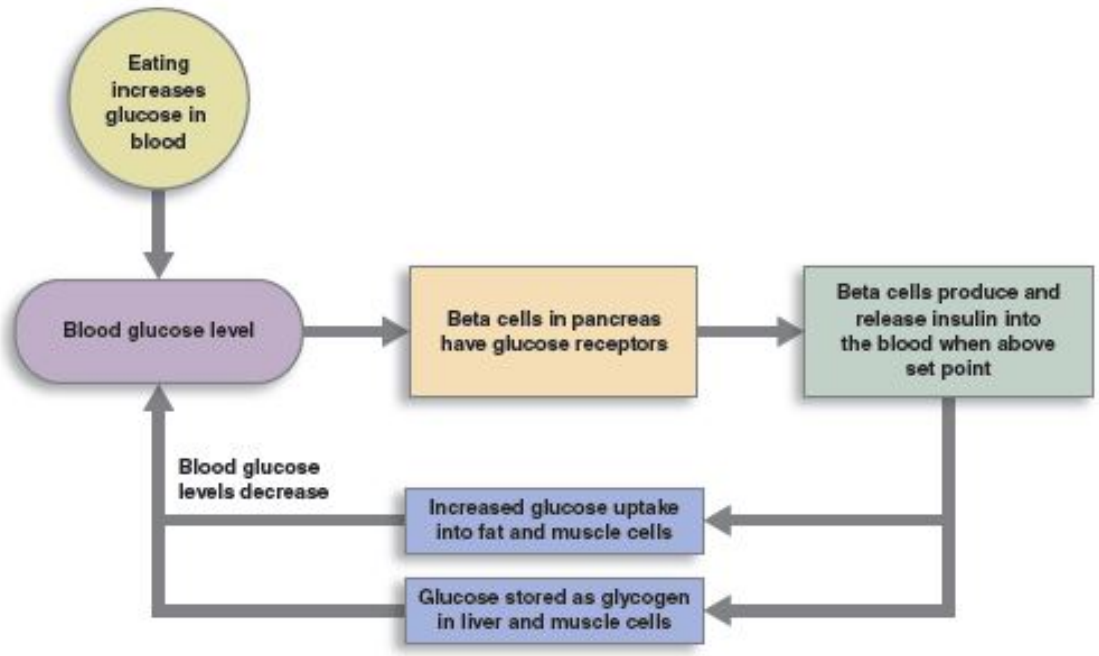
Let's look at how these two examples work related to normal blood pressure homeostasis.

Blood pressure is measured as the circulating blood puts pressure on the walls of the body's arteries. Blood pressure is created initially by the contraction of the heart. Changes in the strength and rate of contraction will be directly related to changes in blood pressure. Changes in the volume of blood would also be directly related to changes in blood pressure. Changes in the diameter of the vessels that blood travels through will change resistance and have an opposite change on blood pressure. Blood pressure homeostasis involves receptors monitoring blood pressure and control centers initiating changes in the effectors to keep it within a normal range.

Diabetes: Type 1 and Type 2

An important example of negative feedback is the control of blood sugar.

1. After a meal, the small intestine absorbs glucose from digested food. Blood glucose levels rise.
2. Increased blood glucose levels stimulate beta cells in the pancreas to produce insulin.
3. Insulin triggers liver, muscle, and fat tissue cells to absorb glucose, where it is stored. As glucose is absorbed, blood glucose levels fall.
4. Once glucose levels drop below a threshold, there is no longer a sufficient stimulus for insulin release, and the beta cells stop releasing insulin.



Due to synchronization of insulin release among the beta cells, basal insulin concentration oscillates in the blood following a meal. The oscillations are clinically important, since they are believed to help maintain sensitivity of insulin receptors in target cells. This loss of sensitivity is the basis for insulin resistance. Thus, failure of the negative feedback mechanism can result in high blood glucose levels, which have a variety of negative health effects.

Let's take a closer look at diabetes. In particular, we will discuss diabetes type 1 and type 2. Diabetes can be caused by too little insulin, resistance to insulin, or both.

Type 1 Diabetes occurs when the pancreatic beta cells are destroyed by an immune-mediated process. Because the pancreatic beta cells sense plasma glucose levels and respond by releasing insulin, individuals with type 1 diabetes have a complete lack of insulin. In this disease, daily injections of insulin are needed.

Also affected are those who lose their pancreas. Once the pancreas has been removed (because of cancer, for example), diabetes type 1 is always present.

Type 2 Diabetes is far more common than type 1. It makes up most of diabetes cases. It usually occurs in adulthood, but young people are increasingly being diagnosed with this disease. In type 2 diabetes, the pancreas still makes insulin, but the tissues do not respond effectively to normal levels of insulin, a condition termed insulin resistance. Over many years the pancreas will decrease the levels of insulin it secretes, but that is not the main problem when the disease initiates. Many people with type 2 diabetes do not know they have it, although it is a serious condition. Type 2 diabetes is becoming more common due to increasing obesity and failure to exercise, both of which contribute to insulin resistance.

Self-Check Questions

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HOMEOSTASIS TERMINOLOGY

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Feedback Loop

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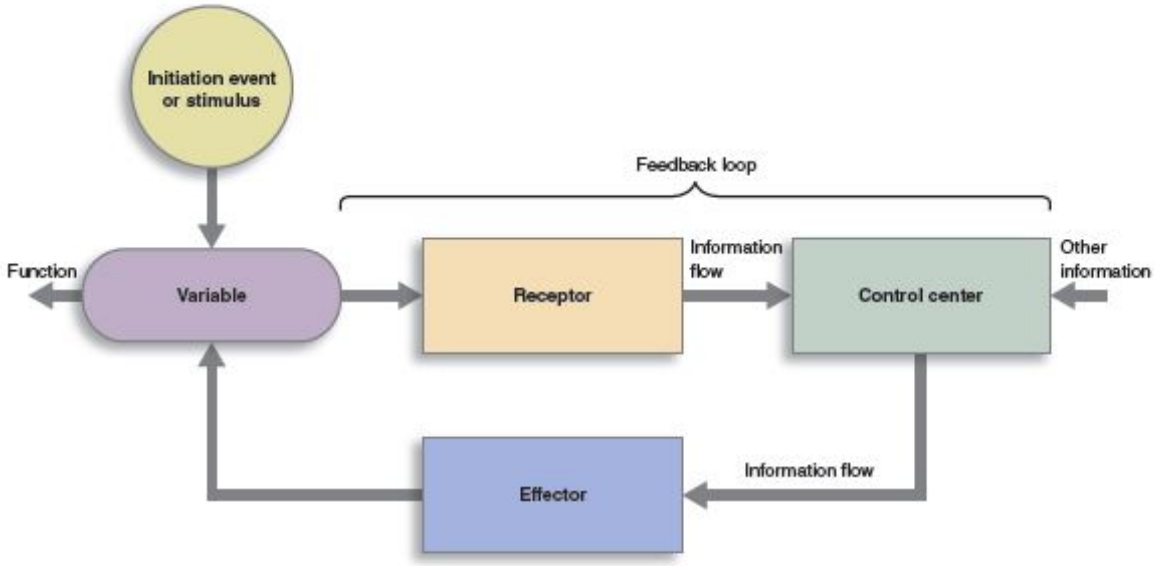

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Feedback Cycle

Any situation in which a variable is regulated and the level of the variable impacts the direction in which the variable changes (i.e. increases or decreases), even if there is not clearly identified loop components.

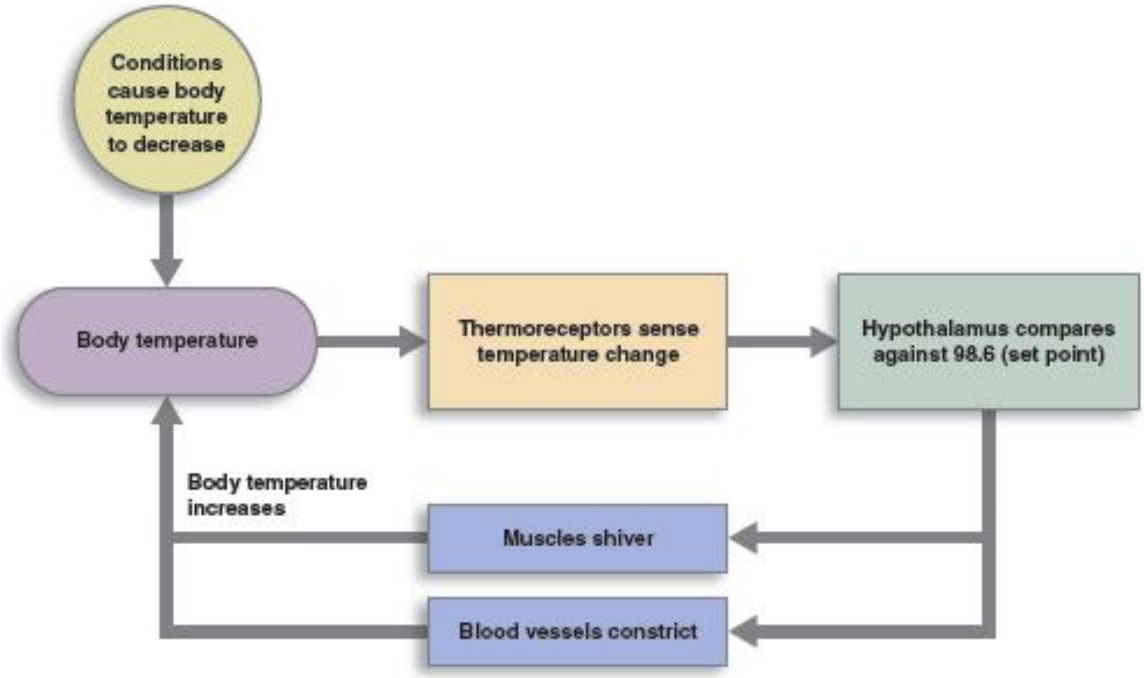
With this terminology in mind, homeostasis then can be described as the totality of the feedback loops and feedback cycles that the body incorporates to maintain a suitable functioning status.

Air conditioning is a technological system that can be described in terms of a feedback loop. The thermostat senses the temperature, an electronic interface compares the temperature against a set point (the temperature that you want it to be). If the temperature matches or is cooler, then nothing happens. If the temperature is too hot, then the electronic interface triggers the air-conditioning unit to turn on. Once the temperature is lowered sufficiently to reach the set point, the electronic interface shuts the air-conditioning unit off. For this example, identify the steps of the feedback loop.

Cruise control is another technological feedback system. The idea of cruise control is to maintain a constant speed in your car. The car's speed is determined by the speedometer and an electronic interface measures the car's speed against a set point chosen by the driver. If the speed is too slow, the interface stimulates the engine; if the speed is too fast, the interface reduces the power to the tires.

Terms Applied to Temperature

Consider one of the feedback loops that controls body temperature.



- Variable: In this instance, the variable is body temperature.

- **Receptors:** Thermoreceptors detect changes in body temperature. For example, thermoreceptors in your internal organs can detect a lowered body temperature and produce nerve impulses that travel to the control center, the hypothalamus.
- **Control Center:** The hypothalamus controls a variety of effectors that respond to a decrease in body temperature.
- **Effectors:** There are several effectors controlled by the hypothalamus.
    - blood vessels near the skin constrict, reducing blood flow (and the resultant heat loss) to the environment.
    - Skeletal muscles are also effectors in this feedback loop: they contract rapidly in response to a decrease in body temperature. This shivering helps to generate heat, which increases body temperature.

Self-Check Questions

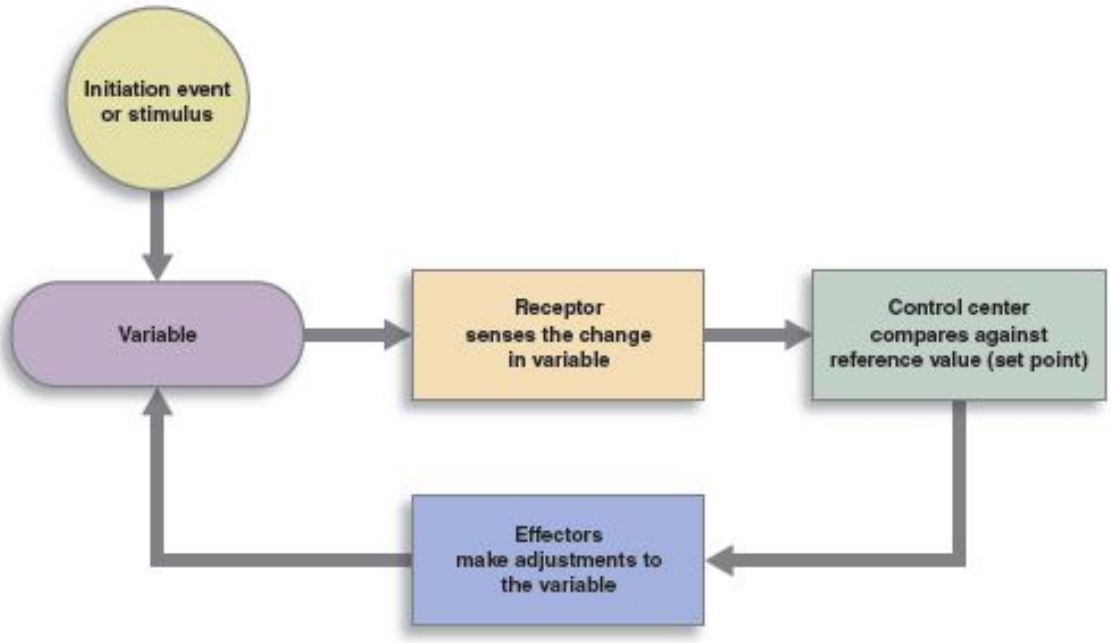
Visit your course online to take a quiz to check your understanding of Homeostasis:

FEEDBACK LOOPS

Remember that homeostasis is the maintenance of a relatively stable internal environment. When a stimulus, or change in the environment, is present, feedback loops respond to keep systems functioning near a set point, or ideal level.

Feedback

Feedback is a situation when the output or response of a loop impacts or influences the input or stimulus.



Typically, we divide feedback loops into two main types:

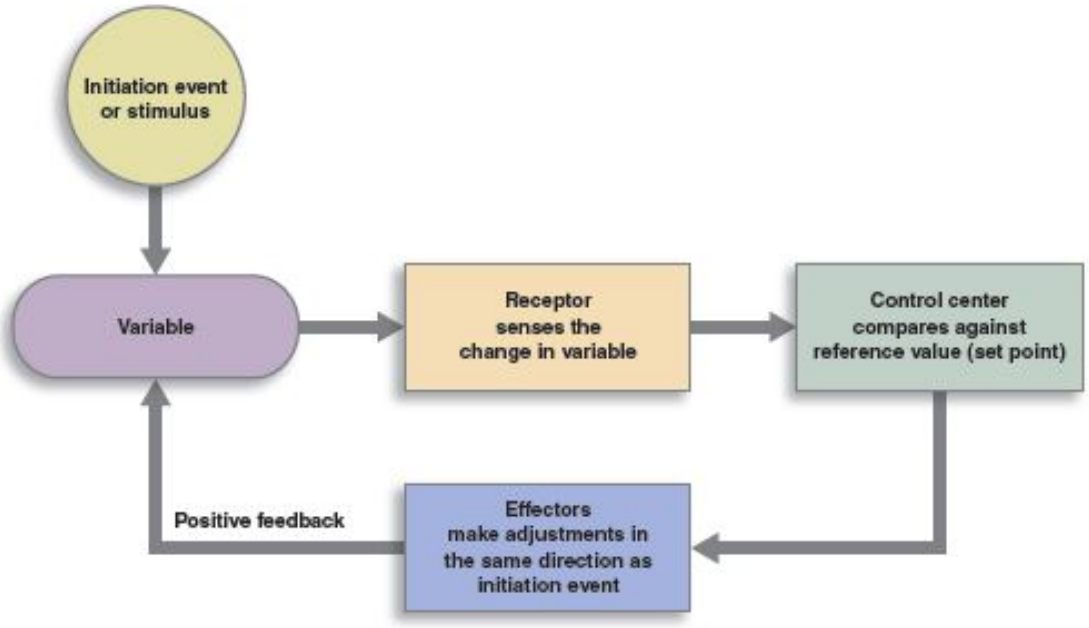
1. *positive feedback loops,* in which a change in a given direction causes additional change in the same direction.For example, an increase in the concentration of a substance causes feedback that produces continued increases in concentration.
2. *negative feedback loops*, in which a change in a given direction causes change in the opposite direction.For example, an increase in the concentration of a substance causes feedback that ultimately causes the concentration of the substance to decrease.

Positive feedback loops are inherently unstable systems. Because a change in an input causes responses that produce continued changes in the same direction, positive feedback loops can lead to runaway conditions. The term positive feedback is typically used as long as a variable has an ability to amplify itself, even if the components of a loop (receptor, control center and effector) are not easily identifiable. In most cases, positive feedback is harmful, but there are a few instances where positive feedback, when used in limited fashion, contributes to normal function. For example, during blood clotting, a cascade of enzymatic proteins activates each other, leading to the formation of a fibrin clot that prevents blood loss. One of the enzymes in the pathway, called thrombin, not only acts on the next protein in the pathway but also has an ability to activate a protein that preceded it in the cascade. This latter step leads to a positive feedback cycle, where an increase in thrombin leads to further increases in thrombin. It should be noted that there are other aspects of blood clotting that keep the overall process in check, such that thrombin levels don't rise without limit. But if we just consider the effects of thrombin on itself, it is considered a positive feedback cycle. Although some may consider this a positive feedback loop, such terminology is not universally accepted.

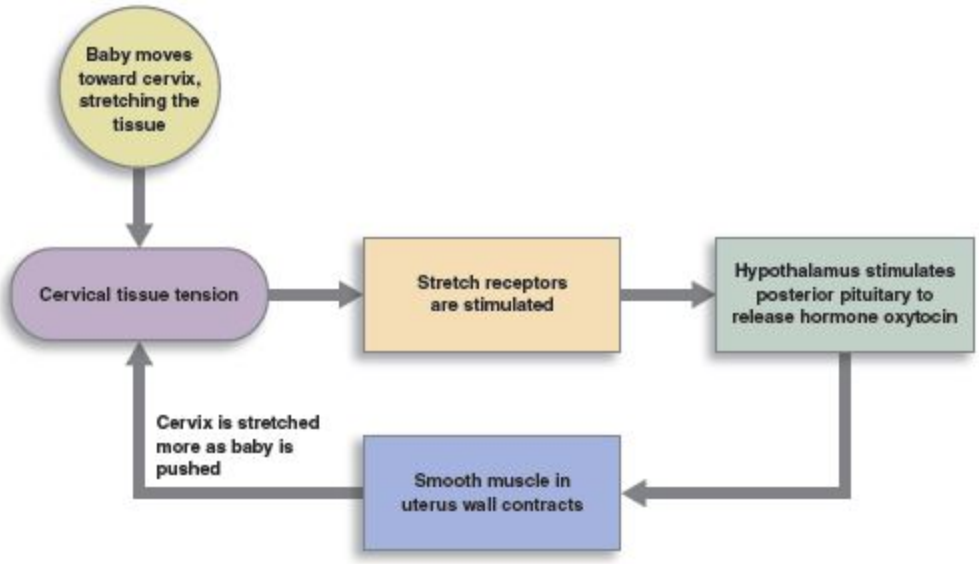
Negative feedback loops are inherently stable systems. Negative feedback loops, in conjunction with the various stimuli that can affect a variable, typically produce a condition in which the variable oscillates around the set point. For example, negative feedback loops involving insulin and glucagon help to keep blood glucose levels within a narrow concentration range. If glucose levels get too high, the body releases insulin into the bloodstream. Insulin causes the body's cells to take in and store glucose, lowering the blood glucose concentration. If blood glucose gets too low, the body releases glucagon, which causes the release of glucose from some of the body's cells.

Positive Feedback

In a positive feedback mechanism, the output of the system stimulates the system in such a way as to further increase the output. Common terms that could describe positive feedback loops or cycles include “snowballing” and “chain reaction”. Without a counter-balancing or “shut-down” reaction or process, a positive feedback mechanism has the potential to produce a runaway process. As noted, there are some physiologic processes that are commonly considered to be positive feedback, although they may not all have identifiable components of a feedback loop. In these cases, the positive feedback loop always ends with counter-signaling that suppresses the original stimulus.



A good example of positive feedback involves the amplification of labor contractions. The contractions are initiated as the baby moves into position, stretching the cervix beyond its normal position. The feedback increases the strength and frequency of the contractions until the baby is born. After birth, the stretching stops and the loop is interrupted.



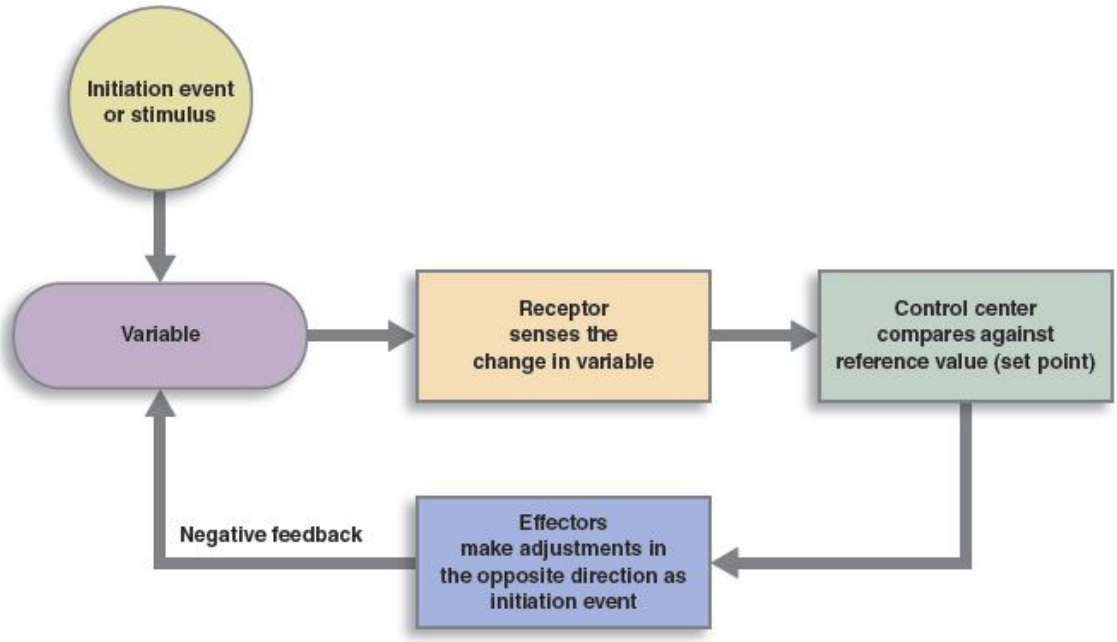
Another example of positive feedback occurs in lactation, during which a mother produces milk for her infant. During pregnancy, levels of the hormone prolactin increase. Prolactin normally stimulates milk production, but during pregnancy, progesterone inhibits milk production. At birth, when the placenta is released from the uterus, progesterone levels drop. As a result, milk production surges. As the baby feeds, its suckling stimulates the breast, promoting further release of prolactin, resulting in yet more milk production. This positive feedback ensures the baby has sufficient milk during feeding. When the baby is weaned and no longer nurses from the mother, stimulation ceases and prolactin in the mother's blood reverts to pre-breastfeeding levels.

The above provide examples of beneficial positive feedback mechanisms. However, in many instances, positive feedback can be potentially damaging to life processes. For example, blood pressure can fall significantly if a person loses a lot of blood due to trauma.

Blood pressure is a regulated variable that leads to the heart increasing its rate (i.e. heart rate increases) and contracting more strongly. These changes to the heart cause it to need more oxygen and nutrients, but if the blood volume in the body is too low, the heart tissue itself will not receive enough blood flow to meet these increased needs. The imbalance between oxygen demands of the heart and oxygen supply can lead to further heart damage, which actually lowers blood pressure, providing a larger change in the variable (blood pressure). The loop responds by trying to stimulate the heart even more strongly, leading to further heart damage…and the loop goes on until death ensues.

Negative Feedback

Most biological feedback systems are negative feedback systems. Negative feedback occurs when a system's output acts to reduce or dampen the processes that lead to the output of that system, resulting in less output. In general, negative feedback loops allow systems to self-stabilize. Negative feedback is a vital control mechanism for the body's homeostasis.

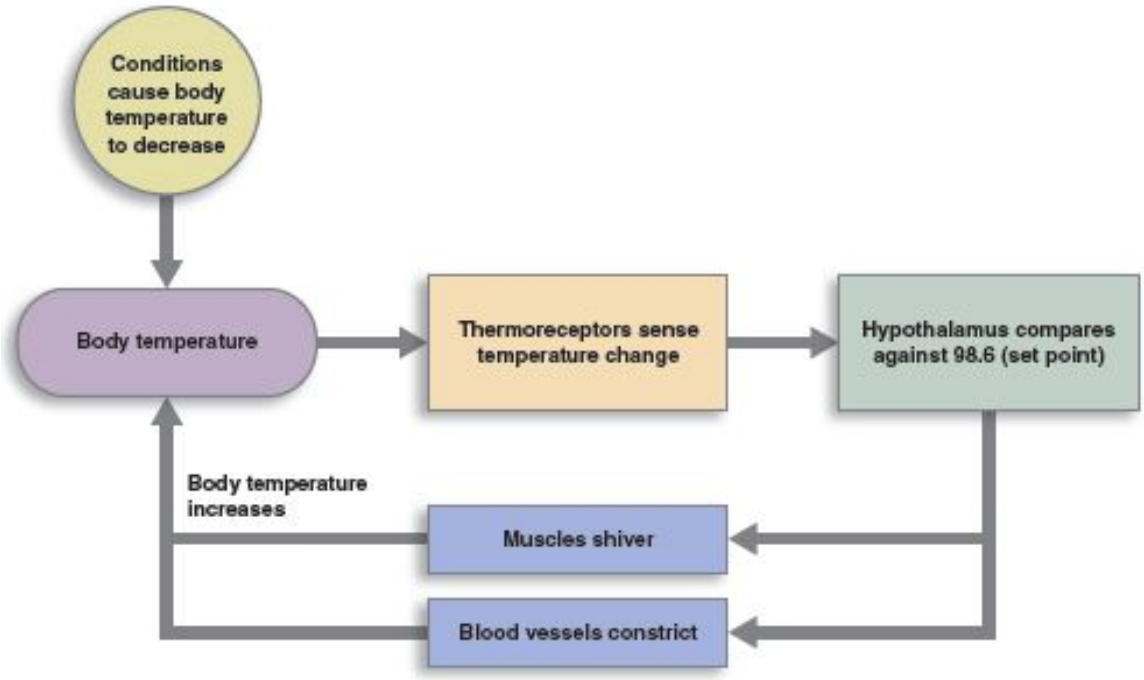


You saw an example of a feedback loop applied to temperature and identified the components involved. This is an important example of how a negative feedback loop maintains homeostasis is the body's thermoregulation mechanism. The body maintains a relatively constant internal temperature to optimize chemical processes. Neural impulses from heat-sensitive thermoreceptors in the body signal the hypothalamus. The hypothalamus, located in the brain, compares the body temperature to a set point value.

When body temperature drops, the hypothalamus initiates several physiological responses to increase heat production and conserve heat:

- Narrowing of surface blood vessels (vasoconstriction) decreases the flow of heat to the skin.
- Shivering commences, increasing production of heat by the muscles.
- Adrenal glands secrete stimulatory hormones such as norepinephrine and epinephrine to increase metabolic rates and hence heat production.

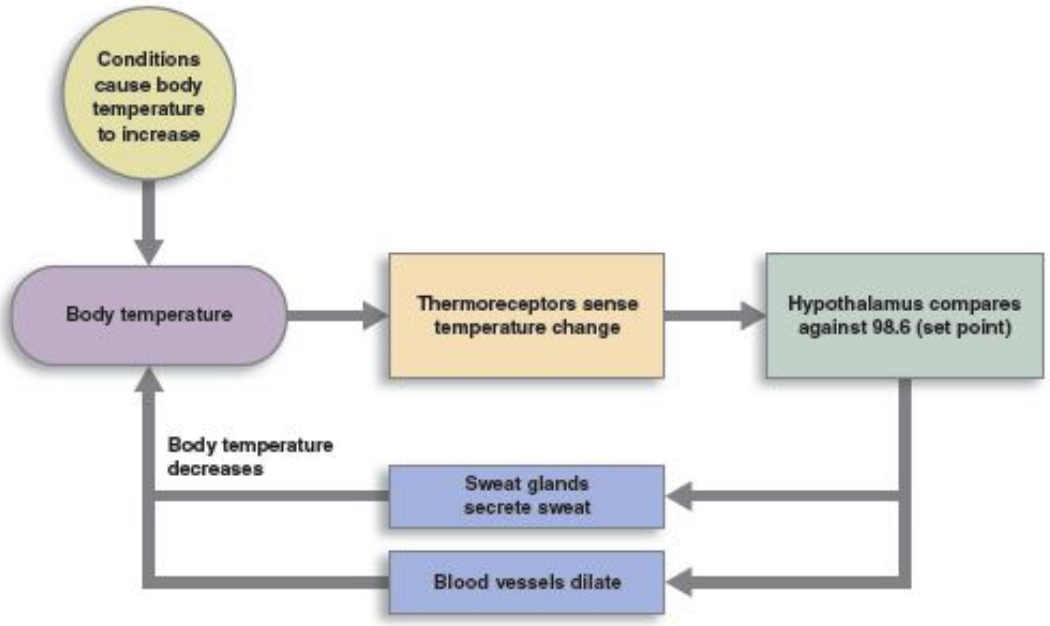
These effects cause body temperature to increase. When it returns to normal, the hypothalamus is no longer stimulated, and these effects cease.



When body temperature rises, the hypothalamus initiates several physiological responses to decrease heat production and lose heat:

- Widening of surface blood vessels (vasodilation) increases the flow of heat to the skin and get flushed.
- Sweat glands release water (sweat) and evaporation cools the skin.

These effects cause body temperature to decrease. When it returns to normal, the hypothalamus is no longer stimulated, and these effects cease.



Many homeostatic mechanisms, like temperature, have different responses if the variable is above or below the set point. When temperature increases, we sweat, when it decreases, we shiver. These responses use different effectors to adjust the variable. In other cases, a feedback loop will use the same effector to adjust the variable back toward the set point, whether the initial change of the variable was either above or below the set point. For example, pupillary diameter is adjusted to make sure an appropriate amount of light is entering the eye. If the amount of light is too low, the pupil dilates, if it is too high, the pupil constricts.

This might be compared to driving. If your speed is above the set point (the value you want it to be), you can either just decrease the level of the accelerator (i.e. coast), or you can active a second system — the brake. In both cases you slow, but it can be done by either just "backing" off on one system, or adding a second system.

Let's look at how these two examples work related to normal blood pressure homeostasis.

Blood pressure is measured as the circulating blood puts pressure on the walls of the body's arteries. Blood pressure is created initially by the contraction of the heart. Changes in the strength and rate of contraction will be directly related to changes in blood pressure. Changes in the volume of blood would also be directly related to changes in blood pressure. Changes in the diameter of the vessels that blood travels through will change resistance and have an opposite change on blood pressure. Blood pressure homeostasis involves receptors monitoring blood pressure and control centers initiating changes in the effectors to keep it within a normal range.

Self-Check Questions

Visit your course online to take a quiz to check your understanding of Homeostasis:

HOMEOSTATIC MAINTENANCE

Homeostatic Maintenance in the Body

You have read about general and specific examples of homeostasis, including positive and negative feedback, and have learned the terminology that is used to describe parts of the feedback loops. It is important to become comfortable with the terminology since it will be used to introduce new concepts in upcoming sections of this course.

Maintaining homeostasis within the body is important for proper physiological function. It is important to recognize the mechanisms of homeostasis in the body, as well as the consequences of homeostasis dysfunction.

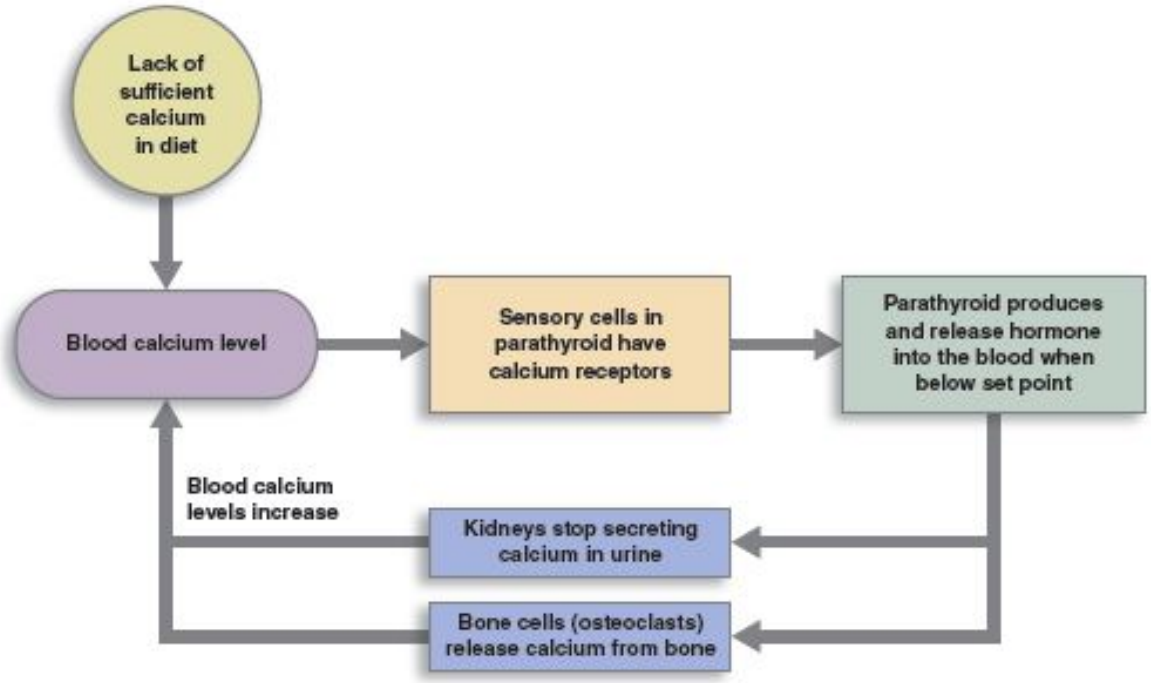
In the following examples, you will learn to identify homeostasis at different levels of organization, such as how the body maintains tight control over small molecules, and the importance of maintaining cell number.

Homeostasis of Ions

Body functions such as regulation of the heartbeat, contraction of muscles, activation of enzymes, and cellular communication require tightly regulated calcium levels. Normally, we get a lot of calcium from our diet. The small intestine absorbs calcium from digested food.

The endocrine system is the control center for regulating blood calcium homeostasis. The parathyroid and thyroid glands contain receptors that respond to levels of calcium in the blood. In this feedback system, blood calcium level is the variable, because it changes in response to the environment. Changes in blood calcium level have the following effects:

- When blood calcium is low, the parathyroid gland secretes parathyroid hormone. This hormone causes effector organs (the kidneys and bones) to respond. The kidneys prevent calcium from being excreted in the urine. Osteoclasts in bones breakdown bone tissue and release calcium. When blood calcium levels are high, less parathyroid hormone is released. Parathyroid hormone is the main controller of blood plasma calcium levels in adults.



- Children have a second hormone that contributes to calcium regulation, called calcitonin. It is released from the thyroid gland when blood calcium levels are high. Calcitonin prevents bone breakdown and causes the kidneys to reabsorb less calcium from the filtrate, allowing excess calcium to be removed from the body in urine.

Calcium imbalance in the blood can lead to disease or even death. Hypocalcemia refers to low blood calcium levels. Signs of hypocalcemia include muscle spasms and heart malfunctions. Hypercalcemia occurs when blood calcium levels are higher than normal. Hypercalcemia can also cause heart malfunction as well as muscle weakness and kidney stones.

Homeostasis of Molecules

Glucose is an important energy source used by most cells in the body, especially muscles. Without glucose, the body “starves”, but if there is too much glucose, problems occur in the kidneys, eyes, and even with the immune response. Insulin is a hormone produced by the pancreas in response to increased blood glucose levels. When the pancreas releases insulin, it acts as a key to open passageways for glucose to enter all body cells, where it is used for energy production. The liver also plays an important role in this feedback loop. Excess glucose is used by liver and muscle cells to synthesize glycogen for storage. The pancreas also produces the hormone glucagon. Glucagon is released when blood glucose levels decrease and stimulates liver cells to catabolize glycogen back to glucose, which is then released into the blood to bring blood glucose levels back up.

Control of Cell Number

Although homeostasis is often carried out by a negative feedback loop with an identifiable receptor, control center and effectors, it more broadly means maintaining variables in a range suitable for optimal function. This includes the regulation of cell number in our tissues so that we don’t have too few or too many. It may be hard to identify specific components of a feedback loop, but it is clear that there are at least negative feedback cycles that help maintain cell numbers. This negative feedback is known to occur through cell-to-cell communications of neighboring cells and an ability to sense the levels of nutrients and matrix in the area they are growing in. Normally cells will stop dividing when there is an appropriate number of cells in a tissue or space. If a neighboring

cell is lost or if there is an inadequate number of cells, cells may be stimulated to divide. Cells with too many neighbors trigger an internal response to die in a regulated programmed way called apoptosis. When cells sense they have no neighbors, signals in the nucleus cause division of the cell.

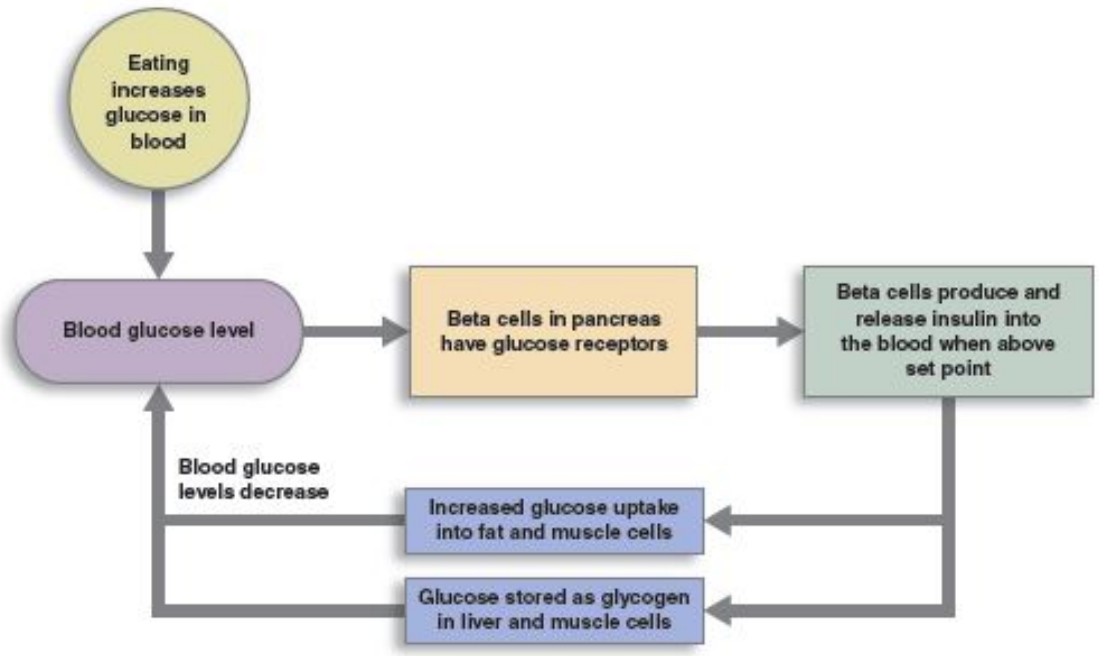
Self-Check Questions

Visit your course online to take a quiz to check your understanding of Homeostasis:

DIABETES: TYPE 1 AND TYPE 2

An important example of negative feedback is the control of blood sugar.

1. After a meal, the small intestine absorbs glucose from digested food. Blood glucose levels rise.
2. Increased blood glucose levels stimulate beta cells in the pancreas to produce insulin.
3. Insulin triggers liver, muscle, and fat tissue cells to absorb glucose, where it is stored. As glucose is absorbed, blood glucose levels fall.
4. Once glucose levels drop below a threshold, there is no longer a sufficient stimulus for insulin release, and the beta cells stop releasing insulin.



Due to synchronization of insulin release among the beta cells, basal insulin concentration oscillates in the blood following a meal. The oscillations are clinically important, since they are believed to help maintain sensitivity of insulin receptors in target cells. This loss of sensitivity is the basis for insulin resistance. Thus, failure of the

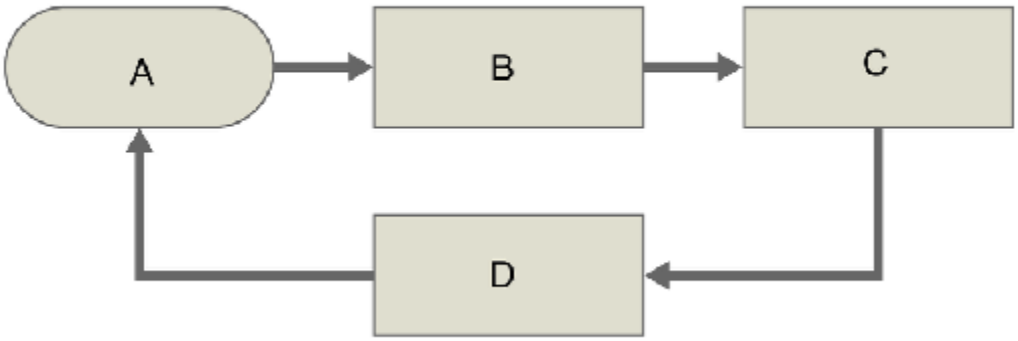
negative feedback mechanism can result in high blood glucose levels, which have a variety of negative health effects.

Let's take a closer look at diabetes. In particular, we will discuss diabetes type 1 and type 2. Diabetes can be caused by too little insulin, resistance to insulin, or both.

Type 1 Diabetes occurs when the pancreatic beta cells are destroyed by an immune-mediated process. Because the pancreatic beta cells sense plasma glucose levels and respond by releasing insulin, individuals with type 1 diabetes have a complete lack of insulin. In this disease, daily injections of insulin are needed.

Also affected are those who lose their pancreas. Once the pancreas has been removed (because of cancer, for example), diabetes type 1 is always present.

Type 2 Diabetes is far more common than type 1. It makes up most of diabetes cases. It usually occurs in adulthood, but young people are increasingly being diagnosed with this disease. In type 2 diabetes, the pancreas still makes insulin, but the tissues do not respond effectively to normal levels of insulin, a condition termed insulin resistance. Over many years the pancreas will decrease the levels of insulin it secretes, but that is not the main problem when the disease initiates. Many people with type 2 diabetes do not know they have it, although it is a serious condition. Type 2 diabetes is becoming more common due to increasing obesity and failure to exercise, both of which contribute to insulin resistance.



Self-Check Questions

Visit your course online to take a quiz to check your understanding of Homeostasis:

INTEGRATION OF SYSTEMS

Each organ system performs specific functions for the body, and each organ system is typically studied independently. However, the organ systems also work together to help the body maintain homeostasis.

For example, the cardiovascular, urinary, and lymphatic systems all help the body control water balance. The cardiovascular and lymphatic systems transport fluids throughout the body and help sense both solute and water

levels and regulate pressure. If the water level gets too high, the urinary system produces more dilute urine (urine with a higher water content) to help eliminate the excess water. If the water level gets too low, more concentrated urine is produced so that water is conserved. The digestive system also plays a role with variable water absorption. Water can be lost through the integumentary and respiratory systems, but that loss is not directly involved in maintaining body fluids and is usually associated with other homeostatic mechanisms.

Similarly, the cardiovascular, integumentary, respiratory, and muscular systems work together to help the body maintain a stable internal temperature. If body temperature rises, blood vessels in the skin dilate, allowing more blood to flow near the skin's surface. This allows heat to dissipate through the skin and into the surrounding air. The skin may also produce sweat if the body gets too hot; when the sweat evaporates, it helps to cool the body. Rapid breathing can also help the body eliminate excess heat. Together, these responses to increased body temperature explain why you sweat, pant, and become red in the face when you exercise hard. (Heavy breathing during exercise is also one way the body gets more oxygen to your muscles, and gets rid of the extra carbon dioxide produced by the muscles.)

Conversely, if your body is too cold, blood vessels in the skin contract, and blood flow to the extremities (arms and legs) slows. Muscles contract and relax rapidly, which generates heat to keep you warm. The hair on your skin rises, trapping more air, which is a good insulator, near your skin. These responses to decreased body temperature explain why you shiver, get "goose bumps," and have cold, pale extremities when you are cold.

Click on this link and move the slider to see a simulation of homeostatic temperature control.

As you have learned, blood glucose homeostasis is regulated by two hormones from the pancreas. This glucose provides the fuel for ATP production by all body cells. But the endocrine system is not the only system involved.

Many body cells respond to insulin and glucagon, but the liver of the digestive system plays in important role in ensuring the availability of fuel in-between meals. Under the influence of insulin, the anabolic process of glycogenesis (-genesis means "origin" or "birth") in the liver converts excess glucose entering liver cells to polymerize into glycogen for storage. Under the influence of glucagon, the reverse catabolic reaction of glycogenolysis (-lysis means "break up") will convert the glycogen back into glucose for release into the blood stream. The liver cells can also perform gluconeogenesis (-neo means "new"), which creates glucose from non-carbohydrate sources, mainly from specific amino acids.

The nervous system also plays a role in maintaining blood glucose levels. When the stomach is empty and blood glucose levels are low, the digestive system receptors and the brain respond by making you feel hungry—your stomach may "growl," and you may feel pain or discomfort in your midsection. These sensations prompt you to eat, which provides new nutrient sources to raise blood glucose levels. The exocrine part of the pancreas is also part of the digestive system. It produces enzymes that help digest the nutrients you have eaten so they can be absorbed by the small intestine into the blood. The circulatory system is important in transporting the glucose and pancreatic hormones in blood to all body cells.

Blood Calcium Levels

As you have learned, proper calcium levels are important for normal function of several systems. Calcium ions are used for blood clotting, the contraction of muscles, the activation of enzymes, and cellular communication. The parathyroid gland of the endocrine system is the main receptor and control center for blood calcium levels. When the parathyroid glands detect low blood calcium levels, they communicate with several organ systems and alter their function to restore blood calcium levels back to normal. The skeletal, urinary, and digestive systems all act as effectors to achieve this goal through negative feedback.

The release of parathyroid hormone from the endocrine system triggers osteoclasts of the skeletal system to breakdown (resorb) bone and release calcium into the blood. Similarly, this hormone causes the kidneys of the urinary system to reabsorb calcium and return it to the blood instead of excreting calcium into the urine. Through altered function of the kidneys to form active vitamin D, the small intestine of the digestive system increases the absorption of calcium.

When blood calcium levels are elevated, the parathyroid gland senses that as well. But in this case, instead of increasing its secretion of parathyroid hormone, it decreases secretion of the hormone. This decreases bone reabsorbtion, increases calcium levels in the urine and decreases calcium absorption in the intestines.

Blood Glucose Levels

The endocrine functions of the pancreas and liver coordinate efforts to maintain normal blood glucose levels. When pancreatic cells detect low blood glucose levels, the pancreas synthesizes and secretes the hormone glucagon. Glucagon causes the liver to convert the polymerized sugar glycogen into glucose through a process known as glycogenolysis. Glucose then travels through the blood to allow all cells of the body to use it.

If pancreatic cells detect high blood glucose levels, the pancreas synthesizes and releases the hormone insulin. Insulin causes polymerization of glucose into glycogen, which is then stored in the liver through a process known as glycogenesis.

The nervous and digestive systems also play a role in maintaining blood glucose levels. When the stomach is empty and blood glucose levels are low, the digestive system and the brain respond by making you feel hungry—your stomach may “growl,” and you may feel pain or discomfort in your midsection. These sensations prompt you to eat, which raises blood glucose levels.

Cell Count

All organ systems require a balance of cell division and apoptosis during development, growth, and repair to maintain tissue structure and function. The endocrine and immune systems are important regulators for cell populations. The endocrine system delivers steroids and growth hormones that send survival signals to specific tissues so that apoptosis is prevented. Additionally, the endocrine system delivers some hormones that work to induce apoptosis under some physiological conditions.

The cells of the immune system screen the blood for cells that divide at inappropriate times. Immune cells produce antibodies to mark these out-of-control cells for destruction. A breakdown in these processes can lead to the formation of tumors.

Self-Check Questions

Visit your course online to take a quiz to check your understanding of Homeostasis:

PRACTICE TEST: HOMEOSTASIS

MODULE 3: THE CHEMICAL LEVEL OF ORGANIZATION

INTRODUCTION TO THE CHEMICAL LEVEL OF ORGANIZATION

Learning Objectives

- Describe the fundamental composition of matter
- Identify the three subatomic particles
- Identify the four most abundant elements in the body
- Explain the relationship between an atom's number of electrons and its relative stability
- Distinguish between ionic bonds, covalent bonds, and hydrogen bonds
- Explain how energy is invested, stored, and released via chemical reactions, particularly those reactions that are critical to life
- Explain the importance of the inorganic compounds that contribute to life, such as water, salts, acids, and bases
- Compare and contrast the four important classes of organic (carbon-based) compounds—proteins, carbohydrates, lipids and nucleic acids—according to their composition and functional importance to human life

The smallest, most fundamental material components of the human body are basic chemical elements. In fact, chemicals called nucleotide bases are the foundation of the genetic code with the instructions on how to build and maintain the human body from conception through old age. There are about three billion of these base pairs in human DNA.

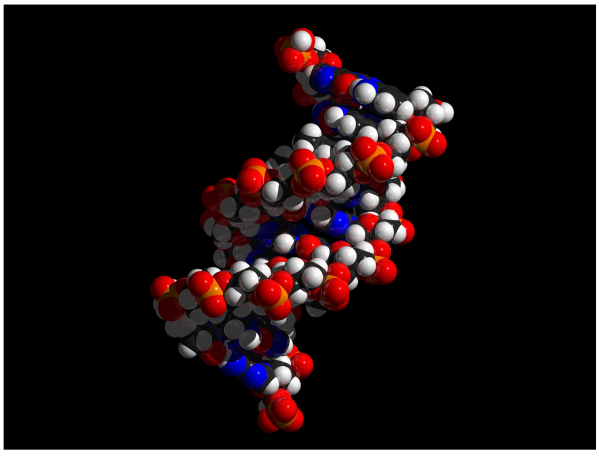


Figure 1. Human DNA. *Human DNA is described as a double helix that resembles a molecular spiral staircase. In humans the DNA is organized into 46 chromosomes.*

Human chemistry includes organic molecules (carbon-based) and biochemicals (those produced by the body). Human chemistry also includes elements. In fact, life cannot exist without many of the elements that are part of the earth. All of the elements that contribute to chemical reactions, to the transformation of energy, and to electrical activity and muscle contraction—elements that include phosphorus, carbon, sodium, and calcium, to name a few—originated in stars.

These elements, in turn, can form both the inorganic and organic chemical compounds important to life, including, for example, water, glucose, and proteins. This chapter begins by examining elements and how the structures of

atoms, the basic units of matter, determine the characteristics of elements by the number of protons, neutrons, and electrons in the atoms. The chapter then builds the framework of life from there.

CHEMISTRY

Look around you. Everything is made of chemicals of one sort or another. Life is chemistry organized into astonishing complexity and intricacy. To make sense of this organization we can look at life's chemistry as a hierarchy—levels of organization. From simple elemental ions, to simple organic molecules, complexity rises with increasingly larger macromolecules.

A person is between 1–2 meters (m) tall, but there are many length scales and biological levels of detail which are important for understanding anatomy and physiology. For perspective on size difference, consider an atom

Atoms are basic units of matter. Atoms contain a positive center (nucleus) surrounded by a cloud of electrons that allow interatomic interactions.

We can't really grasp how small atoms are, but think big instead of small. A length of 10^{10} m is more than the distance from the Earth to the moon.

Table 1. Units of Measurement

	Unit
Atoms and ions	Å = 10^{-10} m
Molecules	nm = 10^{-9} m
Cells	µm 10^{-6} m
Tissues	mm= 10^{-3} m
Organs	cm = 10^{-2} m

The smallest length scale that we will cover is the size of individual atoms, but the movement of subatomic particles called electrons, can change atomic charge. Ions are atoms that carry either a positive or negative charge from altered numbers of electrons, and many atoms and molecules exist in the body as ions.

Ionic chemistry is important in human medicine and health. Ions play an essential role in physiological processes, particularly as they move across cell membranes. Appropriate intracellular and extracellular concentrations of sodium, potassium and calcium ions are required for nerve impulses and heart beats, enable cell-to-cell communication and initiate cellular processes. For example, release of insulin by beta cells of the pancreas is mediated by ions. Transport of ions across membranes may occur by passive diffusion, through ion channels, or through pumps. Pumps often move ions against a concentration gradient. Ionic chemistry is important in human medicine. Anesthetic drugs such as Novocain block sodium channels. Neurotoxins from some snakes and puffer fish work by blocking ion movements that mormally occur in nerve transmission. Malfunctions in ionic channel or pump molecules can result in serious physiological ailments, including cystic fibrosis (mutation in a gene that codes for cell membrane chloride channel) and epilepsy.

Even subatomic particles, which are too small to see with the best microscopes in the world, play an extremely important role in maintaining proper physiology.

ELEMENTS AND ATOMS: THE BUILDING BLOCKS OF MATTER

Learning Objectives

- Discuss the relationships between matter, mass, elements, compounds, atoms, and subatomic particles
- Distinguish between atomic number and mass number
- Identify the key distinction between isotopes of the same element
- Explain how electrons occupy electron shells and their contribution to an atom's relative stability

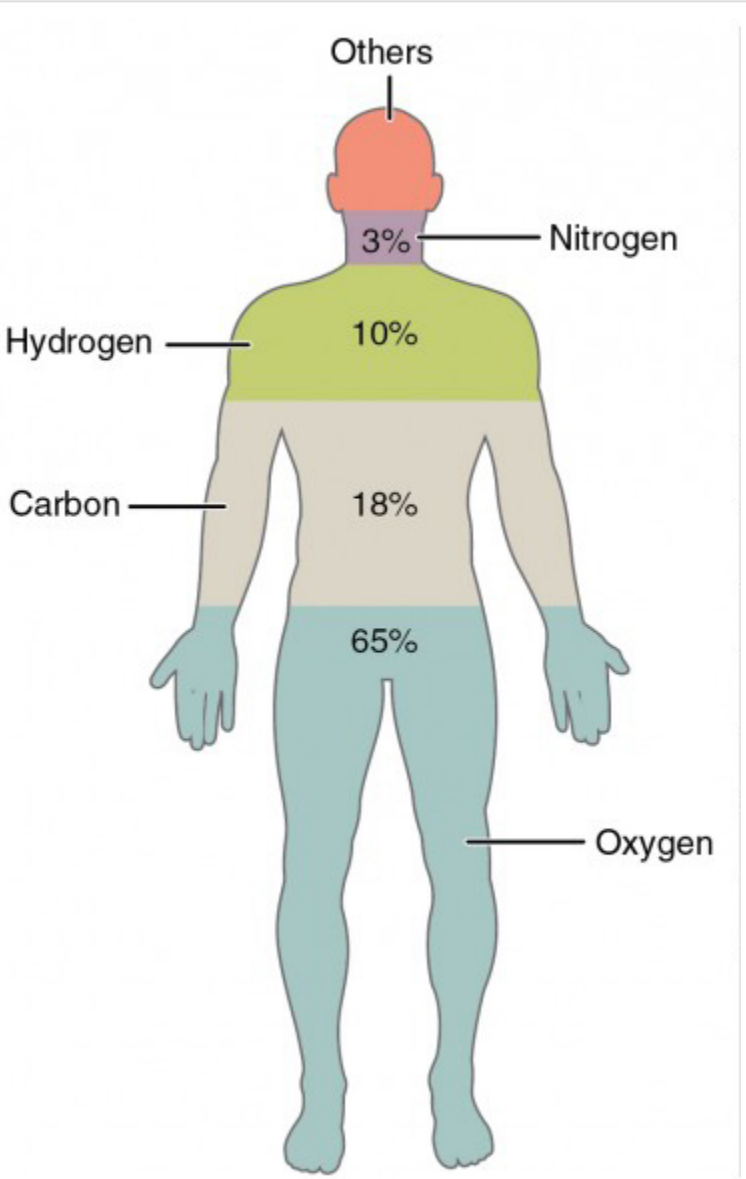
The substance of the universe—from a grain of sand to a star—is called **matter**. Scientists define matter as anything that occupies space and has mass. An object's mass and its weight are related concepts, but not quite the same. An object's mass is the amount of matter contained in the object, and the object's mass is the same whether that object is on Earth or in the zero-gravity environment of outer space. An object's weight, on the other hand, is its mass as affected by the pull of gravity. Where gravity strongly pulls on an object's mass its weight is greater than it is where gravity is less strong. An object of a certain mass weighs less on the moon, for example, than it does on Earth because the gravity of the moon is less than that of Earth. In other words, weight is variable, and is influenced by gravity. A piece of cheese that weighs a pound on Earth weighs only a few ounces on the moon.

Elements and Compounds

All matter in the natural world is composed of one or more of the 92 fundamental substances called elements. An **element** is a pure substance that is distinguished from all other matter by the fact that it cannot be created or broken down by ordinary chemical means. While your body can assemble many of the chemical compounds needed for life from their constituent elements, it cannot make elements. They must come from the environment.

A familiar example of an element that you must take in is calcium (Ca^{++}). Calcium is essential to the human body; it is absorbed and used for a number of processes, including strengthening bones. When you consume dairy products your digestive system breaks down the food into components small enough to cross into the bloodstream. Among these is calcium, which, because it is an element, cannot be broken down further. The elemental calcium in cheese, therefore, is the same as the calcium that forms your bones. Some other elements you might be familiar with are oxygen, sodium, and iron. The elements in the human body are shown in Table 1, beginning with the most abundant: oxygen (O), carbon (C), hydrogen (H), and nitrogen (N). Each element's name can be replaced by a one- or two-letter symbol; you will become familiar with some of these during this course. All the elements in your body are derived from the foods you eat and the air you breathe.

Table 1. Elements of the Human Body. The main elements that compose the human body are shown from most abundant to least abundant.

Element	Symbol	Percentage in Body	At a Look
Oxygen	O	65.0	
Carbon	C	18.5	
Hydrogen	H	9.5	
Nitrogen	N	3.2	
Calcium	Ca	1.5	
Phosphorus	P	1.0	
Potassium	K	0.4	
Sulfur	S	0.3	
Sodium	Na	0.2	
Chlorine	Cl	0.2	
Magnesium	Mg	0.1	
Trace elements include boron (B), chromium (Cr), cobalt (Co), copper (Cu), fluorine (F), iodine (I), iron (Fe), manganese (Mn), molybdenum (Mo), selenium (Se), silicon (Si), tin (Sn), vanadium (V), and zinc (Zn)		less than 1.0	

In nature, elements rarely occur alone. Instead, they combine to form compounds. A *compound* is a substance composed of two or more elements joined by chemical bonds. For example, the compound glucose is an important body fuel. It is always composed of the same three elements: carbon, hydrogen, and oxygen. Moreover, the elements that make up any given compound always occur in the same relative amounts. In glucose, there are always six carbon and six oxygen units for every twelve hydrogen units. But what, exactly, are these “units” of elements?

Atoms and Subatomic Particles

An **atom** is the smallest quantity of an element that retains the unique properties of that element. In other words, an atom of hydrogen is a unit of hydrogen—the smallest amount of hydrogen that can exist. As you might guess, atoms are almost unfathomably small. The period at the end of this sentence is millions of atoms wide.

Atomic Structure and Energy

Atoms are made up of even smaller subatomic particles, three types of which are important: the **proton**, **neutron**, and ***electron***. The number of positively-charged protons and non-charged ("neutral") neutrons, gives mass to the atom, and the number of each in the nucleus of the atom determine the element. The number of negatively-charged electrons that "spin" around the nucleus at close to the speed of light equals the number of protons. An electron has about 1/2000th the mass of a proton or neutron.

Figure 1 shows two models that can help you imagine the structure of an atom—in this case, helium (He). In the planetary model, helium's two electrons are shown circling the nucleus in a fixed orbit depicted as a ring. Although this model is helpful in visualizing atomic structure, in reality, electrons do not travel in fixed orbits, but whiz around the nucleus erratically in a so-called electron cloud.

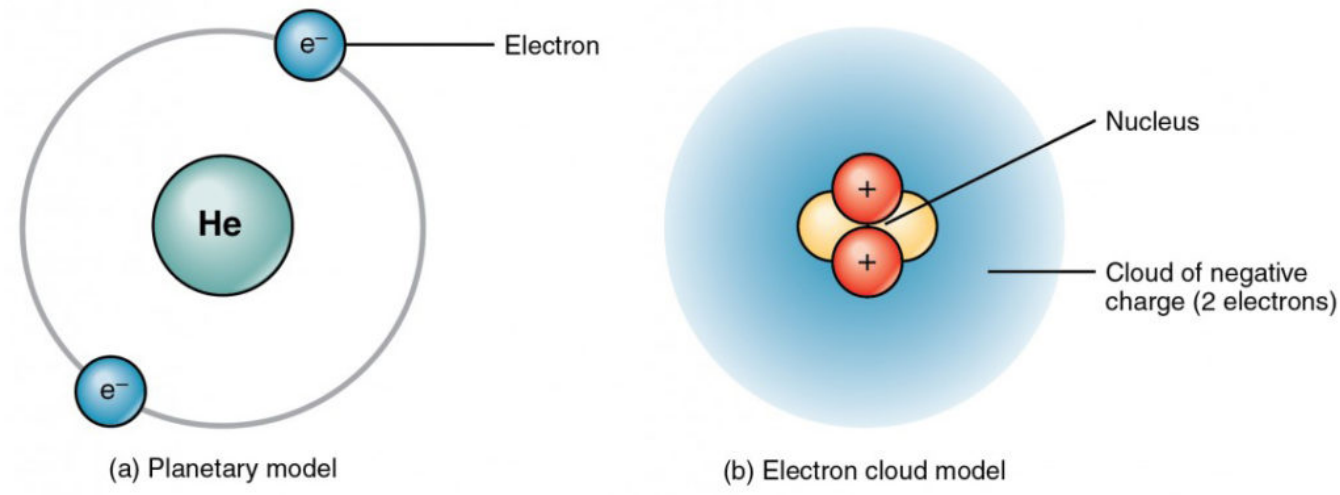


Figure 1. Two Models of Atomic Structure. *(a) In the planetary model, the electrons of helium are shown in fixed orbits, depicted as rings, at a precise distance from the nucleus, somewhat like planets orbiting the sun. (b) In the electron cloud model, the electrons of carbon are shown in the variety of locations they would have at different distances from the nucleus over time.*

An atom's protons and electrons carry electrical charges. Protons, with their positive charge, are designated p^+. Electrons, which have a negative charge, are designated e^-. An atom's neutrons have no charge: they are electrically neutral. Just as a magnet sticks to a steel refrigerator because their opposite charges attract, the positively charged protons attract the negatively charged electrons. This mutual attraction gives the atom some structural stability. The attraction by the positively charged nucleus helps keep electrons from straying far. The number of protons and electrons within a neutral atom are equal, thus, the atom's overall charge is balanced.

Atomic Number and Mass Number

An atom of carbon is unique to carbon, but a proton of carbon is not. One proton is the same as another, whether it is found in an atom of carbon, sodium (Na), or iron (Fe). The same is true for neutrons and electrons. So, what gives an element its distinctive properties—what makes carbon so different from sodium or iron? The answer is the unique quantity of protons each contains. Carbon by definition is an element whose atoms contain six protons. No other element has exactly six protons in its atoms. Moreover, *all* atoms of carbon, whether found in your liver or in a lump of coal, contain six protons. Thus, the ***atomic number***, which is the number of protons in the nucleus

of the atom, identifies the element. Because an atom usually has the same number of electrons as protons, the atomic number identifies the usual number of electrons as well.

In their most common form, many elements also contain the same number of neutrons as protons. The most common form of carbon, for example, has six neutrons as well as six protons, for a total of 12 subatomic particles in its nucleus. An element's **mass number** is the sum of the number of protons and neutrons in its nucleus. So the most common form of carbon's mass number is 12. (Electrons have so little mass that they do not appreciably contribute to the mass of an atom.) Carbon is a relatively light element. Uranium (U), in contrast, has a mass number of 238 and is referred to as a heavy metal. Its atomic number is 92 (it has 92 protons) but it contains 146 neutrons; it has the most mass of all the naturally occurring elements.

The **periodic table of the elements**, shown in Figure 2, is a chart identifying the 92 elements found in nature, as well as several larger, unstable elements discovered experimentally. The elements are arranged in order of their atomic number, with hydrogen and helium at the top of the table, and the more massive elements below. The periodic table is a useful device because for each element, it identifies the chemical symbol, the atomic number, and the mass number, while organizing elements according to their propensity to react with other elements. The number of protons and electrons in an element are equal. The number of protons and neutrons may be equal for some elements, but are not equal for all.

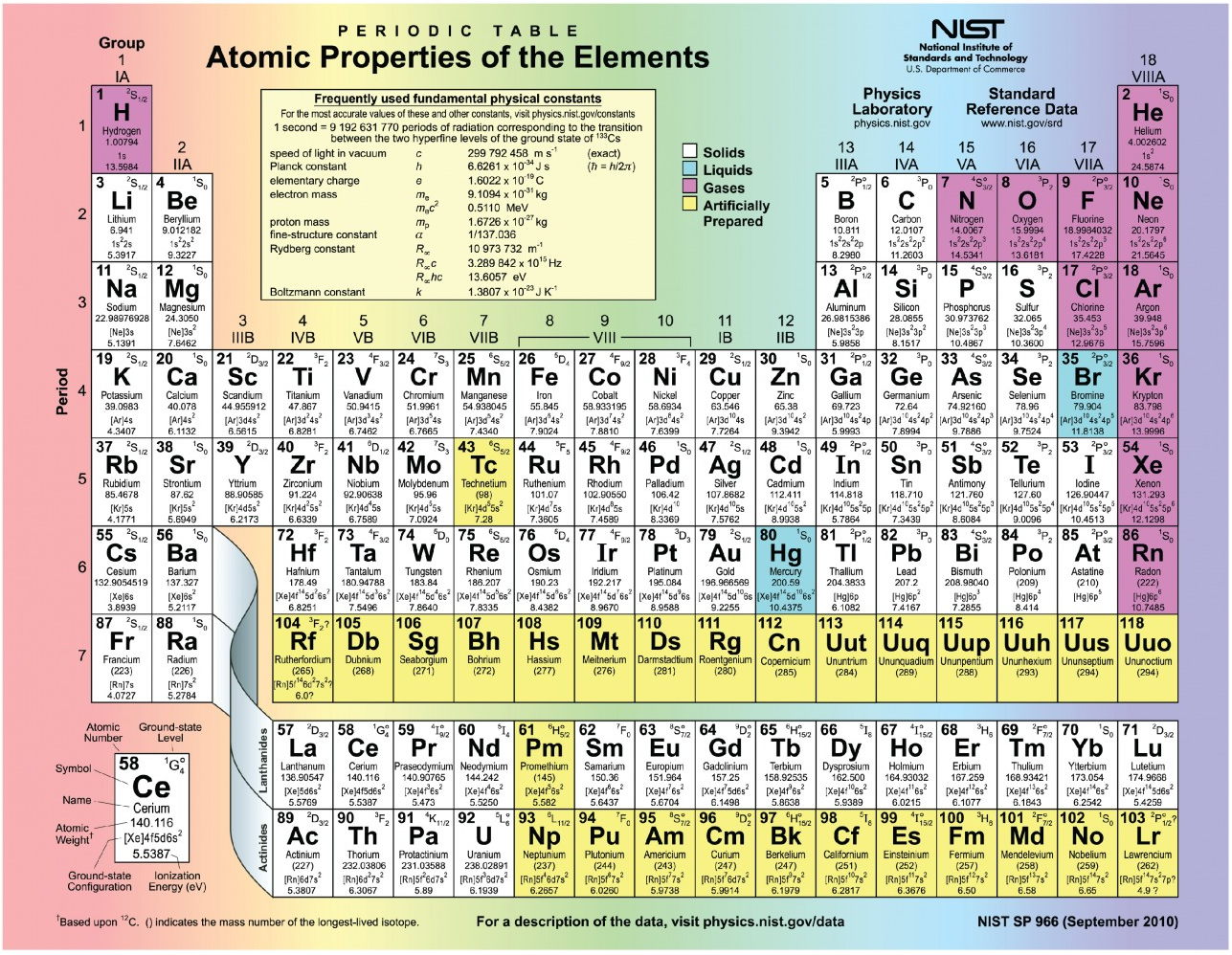


Figure 2. The Periodic Table of the Elements. *(credit: R.A. Dragoset, A. Musgrove, C.W. Clark, W.C. Martin)*

Visit this website to view the periodic table. In the periodic table of the elements, elements in a single row have the same number of electrons that can participate in a chemical reaction. These electrons are known as "valence electrons." For example, the elements in the first row all have a single valence electron, an electron

that can be “donated” in a chemical reaction with another atom. What is the meaning of a mass number shown in parentheses?

Isotopes

Although each element has a unique number of protons, it can exist as different isotopes. An *isotope* is one of the different forms of an element, distinguished from one another by different numbers of neutrons. The standard isotope of carbon is ^{12}C, commonly called carbon twelve. ^{12}C has six protons and six neutrons, for a mass number of twelve. All of the isotopes of carbon have the same number of protons; therefore, ^{13}C has seven neutrons, and ^{14}C has eight neutrons. The different isotopes of an element can also be indicated with the mass number hyphenated (for example, C-12 instead of ^{12}C). Hydrogen has three common isotopes, (see Figure 3).

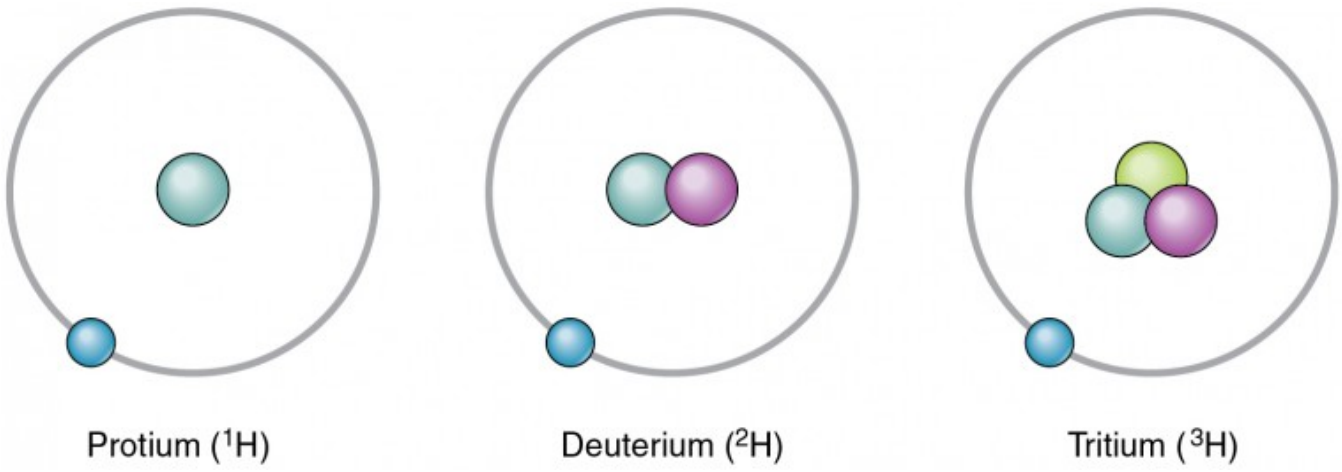


Figure 3. Isotopes of Hydrogen. *Protium, designated ^{1}H, has one proton and no neutrons. It is by far the most abundant isotope of hydrogen in nature. Deuterium, designated ^{2}H, has one proton and one neutron. Tritium, designated ^{3}H, has two neutrons.*

An isotope that contains more than the usual number of neutrons is referred to as a heavy isotope. An example is ^{14}C. Heavy isotopes tend to be unstable, and unstable isotopes are radioactive. A *radioactive isotope* is an isotope whose nucleus readily decays, giving off subatomic particles and electromagnetic energy. Different radioactive isotopes (also called radioisotopes) differ in their half-life, the time it takes for half of any size sample of an isotope to decay. For example, the half-life of tritium—a radioisotope of hydrogen—is about 12 years, indicating it takes 12 years for half of the tritium nuclei in a sample to decay. Excessive exposure to radioactive isotopes can damage human cells and even cause cancer and birth defects, but when exposure is controlled, some radioactive isotopes can be useful in medicine. For more information, see the Career Connections.

Career Connection: Interventional Radiologist

The controlled use of radioisotopes has advanced medical diagnosis and treatment of disease. Interventional radiologists are physicians who treat disease by using minimally invasive techniques involving radiation. Many conditions that could once only be treated with a lengthy and traumatic operation can now be treated non-surgically, reducing the cost, pain, length of hospital stay, and recovery time for patients. For example, in the past, the only options for a patient with one or more tumors in the liver were surgery and chemotherapy (the administration of drugs to treat cancer). Some liver tumors, however, are difficult to access surgically, and others could require the surgeon to remove too much of the liver. Moreover, chemotherapy is highly toxic to the liver, and certain tumors do not respond well to it anyway. In some such cases, an interventional radiologist can treat the tumors by disrupting their blood supply, which they need if they are to continue to grow. In this procedure, called radioembolization, the radiologist accesses the liver with a fine needle, threaded through one of the patient’s blood vessels. The radiologist then inserts tiny radioactive “seeds” into

the blood vessels that supply the tumors. In the days and weeks following the procedure, the radiation emitted from the seeds destroys the vessels and directly kills the tumor cells in the vicinity of the treatment.

Radioisotopes emit subatomic particles that can be detected and tracked by imaging technologies. One of the most advanced uses of radioisotopes in medicine is the positron emission tomography (PET) scanner, which detects the activity in the body of a very small injection of radioactive glucose, the simple sugar that cells use for energy. The PET camera reveals to the medical team which of the patient's tissues are taking up the most glucose. Thus, the most metabolically active tissues show up as bright "hot spots" on the images (Figure 4). PET can reveal some cancerous masses because cancer cells consume glucose at a high rate to fuel their rapid reproduction.

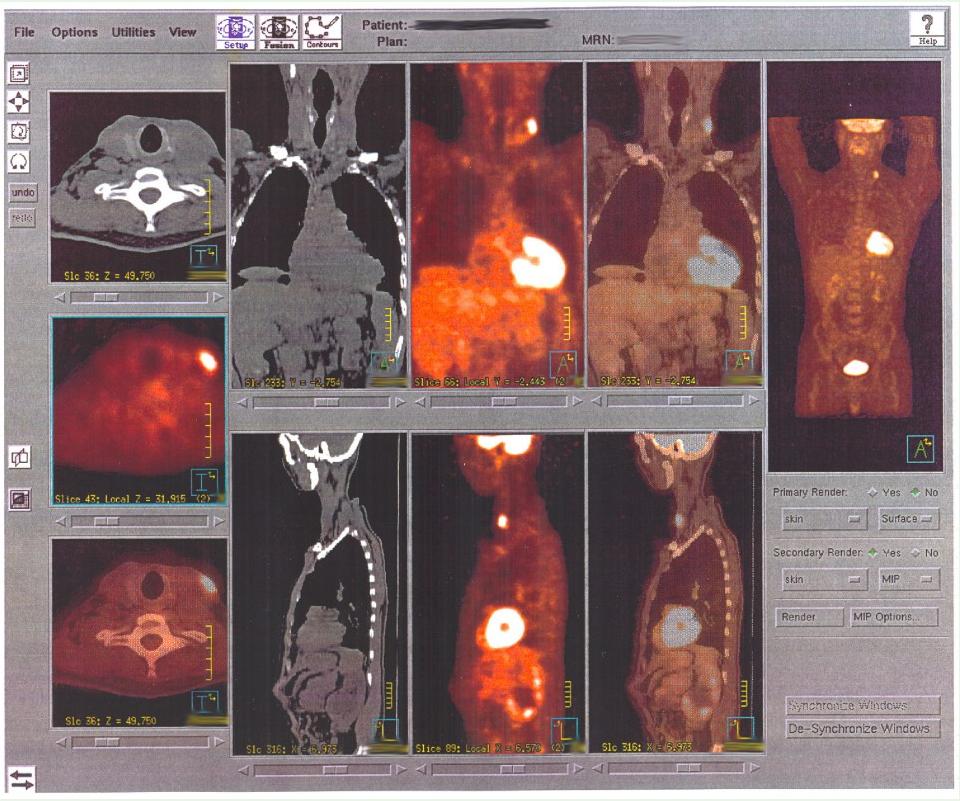


Figure 4. PET Scan. *PET highlights areas in the body where there is relatively high glucose use, which is characteristic of cancerous tissue. This PET scan shows sites of the spread of a large primary tumor to other sites.*

The Behavior of Electrons

In the human body, atoms do not exist as independent entities. Rather, they are constantly reacting with other atoms to form and to break down more complex substances. To fully understand anatomy and physiology you must grasp how atoms participate in such reactions. The key is understanding the behavior of electrons.

Although electrons do not follow rigid orbits a set distance away from the atom's nucleus, they do tend to stay within certain regions of space called electron shells. An *electron shell* is a layer of electrons that encircle the nucleus at a distinct energy level.

The atoms of the elements found in the human body have from one to five electron shells, and all electron shells hold eight electrons except the first shell, which can only hold two. This configuration of electron shells is the same for all atoms. The precise number of shells depends on the number of electrons in the atom. Hydrogen and helium have just one and two electrons, respectively. If you take a look at the periodic table of the elements, you will notice that hydrogen and helium are placed alone on either sides of the top row; they are the only elements that have just one electron shell (Figure 5). A second shell is necessary to hold the electrons in all elements larger than hydrogen and helium.

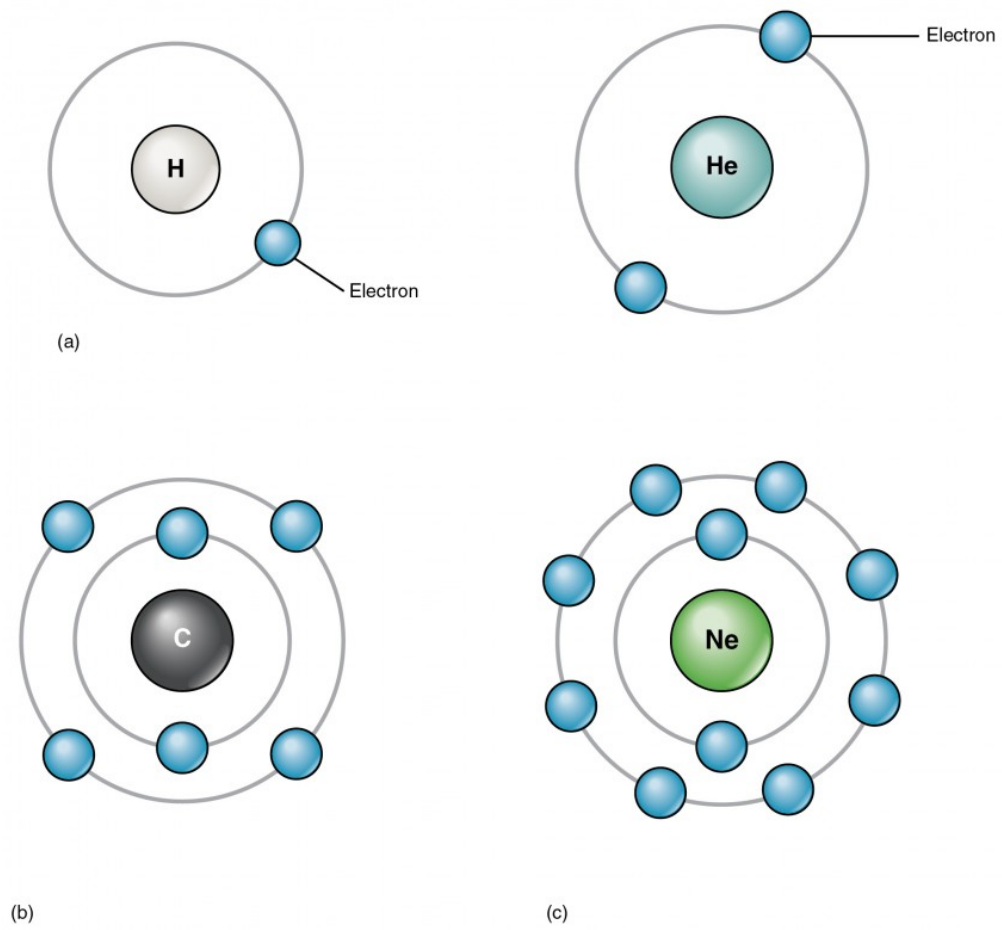


Figure 5. Electron Shells. *Electrons orbit the atomic nucleus at distinct levels of energy called electron shells. (a) With one electron, hydrogen only half-fills its electron shell. Helium also has a single shell, but its two electrons completely fill it. (b) The electrons of carbon completely fill its first electron shell, but only half-fills its second. (c) Neon, an element that does not occur in the body, has 10 electrons, filling both of its electron shells.*

Lithium (Li), whose atomic number is 3, has three electrons. Two of these fill the first electron shell, and the third spills over into a second shell. The second electron shell can accommodate as many as eight electrons. Carbon, with its six electrons, entirely fills its first shell, and half-fills its second. With ten electrons, neon (Ne) entirely fills its two electron shells. Again, a look at the periodic table reveals that all of the elements in the second row, from lithium to neon, have just two electron shells. Atoms with more than ten electrons require more than two shells. These elements occupy the third and subsequent rows of the periodic table.

The factor that most strongly governs the tendency of an atom to participate in chemical reactions is the number of electrons in its valence shell. A *valence shell* is an atom's outermost electron shell. If the valence shell is full, the atom is stable; meaning its electrons are unlikely to be pulled away from the nucleus by the electrical charge of other atoms. If the valence shell is not full, the atom is reactive; meaning it will tend to react with other atoms in ways that make the valence shell full. Consider hydrogen, with its one electron only half-filling its valence shell. This single electron is likely to be drawn into relationships with the atoms of other elements, so that hydrogen's single valence shell can be stabilized.

All atoms (except hydrogen and helium with their single electron shells) are most stable when there are exactly eight electrons in their valence shell. This principle is referred to as the octet rule, and it states that an atom will give up, gain, or share electrons with another atom so that it ends up with eight electrons in its own valence shell. For example, oxygen, with six electrons in its valence shell, is likely to react with other atoms in a way that results in the addition of two electrons to oxygen's valence shell, bringing the number to eight. When two hydrogen atoms each share their single electron with oxygen, covalent bonds are formed, resulting in a molecule of water, H_2O.

In nature, atoms of one element tend to join with atoms of other elements in characteristic ways. For example, carbon commonly fills its valence shell by linking up with four atoms of hydrogen. In so doing, the two elements

form the simplest of organic molecules, methane, which also is one of the most abundant and stable carbon-containing compounds on Earth. As stated above, another example is water; oxygen needs two electrons to fill its valence shell. It commonly interacts with two atoms of hydrogen, forming H_2O. Incidentally, the name “hydrogen” reflects its contribution to water (hydro- = “water”; -gen = “maker”). Thus, hydrogen is the “water maker.”

CHEMICAL BONDS

Learning Objectives

- Explain the relationship between molecules and compounds
- Distinguish between ions, cations, and anions
- Identify the key difference between ionic and covalent bonds
- Distinguish between nonpolar and polar covalent bonds
- Explain how water molecules link via hydrogen bonds

Atoms separated by a great distance cannot link; rather, they must come close enough for the electrons in their valence shells to interact. But do atoms ever actually touch one another? Most physicists would say no, because the negatively charged electrons in their valence shells repel one another. No force within the human body—or anywhere in the natural world—is strong enough to overcome this electrical repulsion. So when you read about atoms linking together or colliding, bear in mind that the atoms are not merging in a physical sense.

Instead, atoms link by forming a chemical bond. A *bond* is a weak or strong electrical attraction that holds atoms in the same vicinity. The new grouping is typically more stable—less likely to react again—than its component atoms were when they were separate. A more or less stable grouping of two or more atoms held together by chemical bonds is called a **molecule**. The bonded atoms may be of the same element, as in the case of H_2, which is called molecular hydrogen or hydrogen gas. When a molecule is made up of two or more atoms of different elements, it is called a chemical **compound**. Thus, a unit of water, or H_2O, is a compound, as is a single molecule of the gas methane, or CH_4.

Three types of chemical bonds are important in human physiology, because they hold together substances that are used by the body for critical aspects of homeostasis, signaling, and energy production, to name just a few important processes. These are ionic bonds, covalent bonds, and hydrogen bonds.

Ions and Ionic Bonds

Recall that an atom typically has the same number of positively charged protons and negatively charged electrons. As long as this situation remains, the atom is electrically neutral. But when an atom participates in a chemical reaction that results in the donation or acceptance of one or more electrons, the atom will then become positively or negatively charged. This happens frequently for most atoms in order to have a full valence shell, as described previously. This can happen either by gaining electrons to fill a shell that is more than half-full, or by giving away electrons to empty a shell than is less than half-full, thereby leaving the next smaller electron shell as the new, full, valence shell. An atom that has an electrical charge—whether positive or negative—is an **ion**.

Watch this video to learn about electrical energy and the attraction/repulsion of charges. What happens to the charged electroscope when a conductor is moved between its plastic sheets, and why?

Watch this video online: https://youtu.be/F6v8wm7_vdQ

Potassium (K), for instance, is an important element in all body cells. Its atomic number is 19. It has just one electron in its valence shell. This characteristic makes potassium highly likely to participate in chemical reactions in which it donates one electron. (It is easier for potassium to donate one electron than to gain seven electrons.) The loss will cause the positive charge of potassium's protons to be more influential than the negative charge of potassium's electrons. In other words, the resulting potassium ion will be slightly positive. A potassium ion is written K^+, indicating that it has lost a single electron. A positively charged ion is known as a **cation**.

Now consider fluorine (F), a component of bones and teeth. Its atomic number is nine, and it has seven electrons in its valence shell. Thus, it is highly likely to bond with other atoms in such a way that fluorine accepts one electron (it is easier for fluorine to gain one electron than to donate seven electrons). When it does, its electrons will outnumber its protons by one, and it will have an overall negative charge. The ionized form of fluorine is called fluoride, and is written as F^-. A negatively charged ion is known as an **anion**.

Atoms that have more than one electron to donate or accept will end up with stronger positive or negative charges. A cation that has donated two electrons has a net charge of +2. Using magnesium (Mg) as an example, this can be written Mg^{++} or Mg^{2+}. An anion that has accepted two electrons has a net charge of –2. The ionic form of selenium (Se), for example, is typically written Se^{2-}.

The opposite charges of cations and anions exert a moderately strong mutual attraction that keeps the atoms in close proximity forming an ionic bond. An **ionic bond** is an ongoing, close association between ions of opposite charge. The table salt you sprinkle on your food owes its existence to ionic bonding. As shown in Figure 1, sodium commonly donates an electron to chlorine, becoming the cation Na^+. When chlorine accepts the electron, it becomes the chloride anion, Cl^-. With their opposing charges, these two ions strongly attract each other.

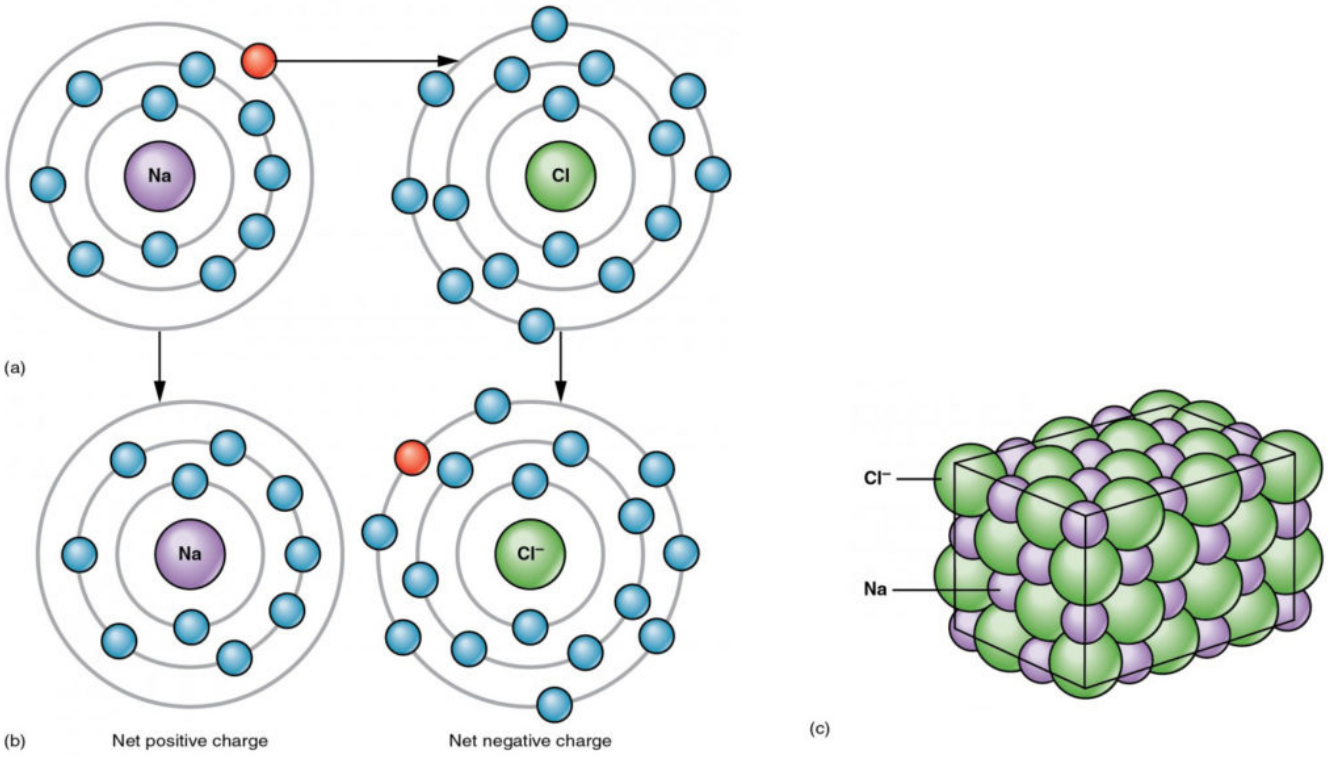


Figure 1. Ionic Bonding. *(a) Sodium readily donates the solitary electron in its valence shell to chlorine, which needs only one electron to have a full valence shell. (b) The opposite electrical charges of the resulting sodium cation and chloride anion result in the formation of a bond of attraction called an ionic bond. (c) The attraction of many sodium and chloride ions results in the formation of large groupings called crystals.*

Water is an essential component of life because it is able to break the ionic bonds in salts to free the ions. In fact, in biological fluids, most individual atoms exist as ions. These dissolved ions produce electrical charges within the body. The behavior of these ions produces the tracings of heart and brain function observed as waves on an electrocardiogram (EKG or ECG) or an electroencephalogram (EEG). The electrical activity that derives from the interactions of the charged ions is why they are also called electrolytes.

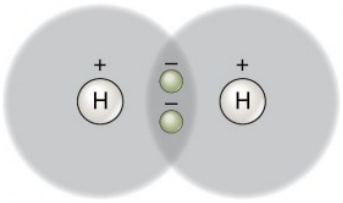
Covalent Bonds

Unlike ionic bonds formed by the attraction between a cation's positive charge and an anion's negative charge, molecules formed by a **covalent bond** share electrons in a mutually stabilizing relationship. Like next-door neighbors whose kids hang out first at one home and then at the other, the atoms do not lose or gain electrons permanently. Instead, the electrons move back and forth between the elements. Because of the close sharing of pairs of electrons (one electron from each of two atoms), covalent bonds are stronger than ionic bonds.

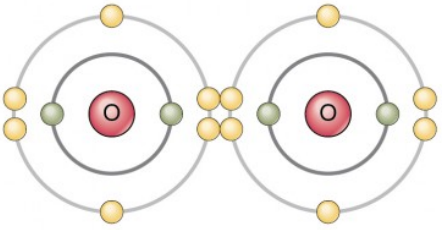
Nonpolar Covalent Bonds

Figure 2 shows several common types of covalent bonds. Notice that the two covalently bonded atoms typically share just one or two electron pairs, though larger sharings are possible. The important concept to take from this is that in covalent bonds, electrons in the outermost valence shell are shared to fill the valence shells of both atoms, ultimately stabilizing both of the atoms involved. In a single covalent bond, a single electron is shared between two atoms, while in a double covalent bond, two pairs of electrons are shared between two atoms. There even are triple covalent bonds, where three atoms are shared.

(a) A single covalent bond: hydrogen gas (H—H). Two atoms of hydrogen each share their solitary electron in a single covalent bond.



(b) A double covalent bond: oxygen gas (O═O). An atom of oxygen has six electrons in its valence shell; thus, two more would make it stable. Two atoms of oxygen achieve stability by sharing two pairs of electrons in a double covalent bond.



Molecule of oxygen gas (O_2)

(c) Two double covalent bonds: carbon dioxide (O═C═O). An atom of carbon has four electrons in its valence shell; thus, four more would make it stable. An atom of carbon and two atoms of oxygen achieve stability by sharing two electron pairs each, in two double covalent bonds.

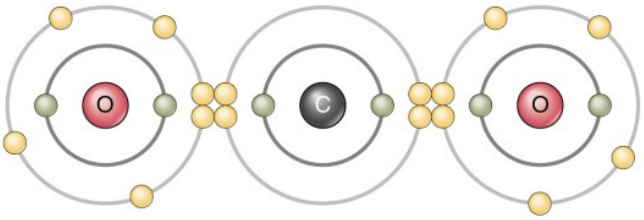


Figure 2. Covalent Bonding

You can see that the covalent bonds shown in Figure 2 are balanced. The sharing of the negative electrons is relatively equal, as is the electrical pull of the positive protons in the nucleus of the atoms involved. This is why covalently bonded molecules that are electrically balanced in this way are described as nonpolar; that is, no region of the molecule is either more positive or more negative than any other.

Polar Covalent Bonds

Groups of legislators with completely opposite views on a particular issue are often described as “polarized” by news writers. In chemistry, a *polar molecule* is a molecule that contains regions that have opposite electrical charges. Polar molecules occur when atoms share electrons unequally, in polar covalent bonds.

The most familiar example of a polar molecule is water (Figure 3). The molecule has three parts: one atom of oxygen, the nucleus of which contains eight protons, and two hydrogen atoms, whose nuclei each contain only one proton. Because every proton exerts an identical positive charge, a nucleus that contains eight protons exerts a charge eight times greater than a nucleus that contains one proton. This means that the negatively charged electrons present in the water molecule are more strongly attracted to the oxygen nucleus than to the hydrogen nuclei. Each hydrogen atom’s single negative electron therefore migrates toward the oxygen atom, making the oxygen end of their bond slightly more negative than the hydrogen end of their bond.

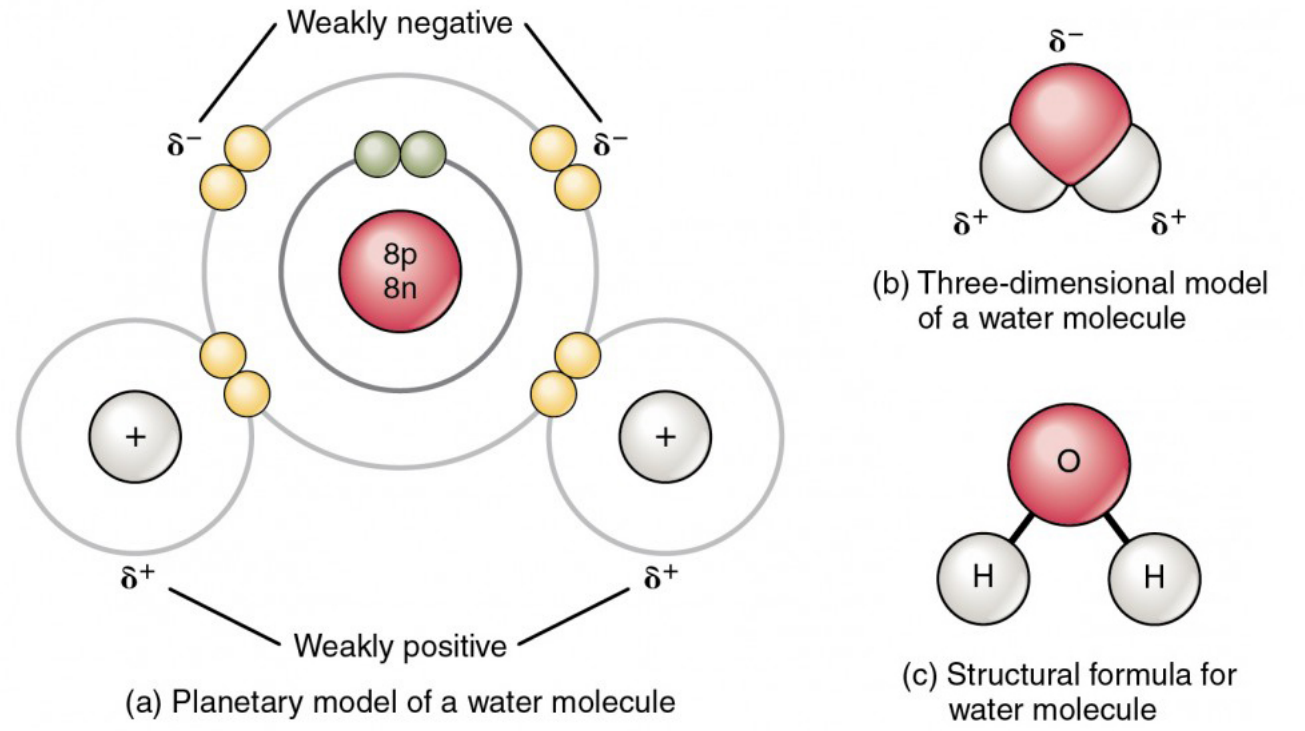


Figure 3. Polar Covalent Bonds in a Water Molecule

What is true for the bonds is true for the water molecule as a whole; that is, the oxygen region has a slightly negative charge and the regions of the hydrogen atoms have a slightly positive charge. These charges are often referred to as “partial charges” because the strength of the charge is less than one full electron, as would occur in an ionic bond. As shown in Figure 3, regions of weak polarity are indicated with the Greek letter delta (∂) and a plus (+) or minus (–) sign.

Even though a single water molecule is unimaginably tiny, it has mass, and the opposing electrical charges on the molecule pull that mass in such a way that it creates a shape somewhat like a triangular tent (see Figure 3b). This dipole, with the positive charges at one end formed by the hydrogen atoms at the “bottom” of the tent and the negative charge at the opposite end (the oxygen atom at the “top” of the tent) makes the charged regions highly likely to interact with charged regions of other polar molecules. For human physiology, the resulting bond is one of the most important formed by water—the hydrogen bond.

Hydrogen Bonds

A **hydrogen bond** is formed when a weakly positive hydrogen atom already bonded to one electronegative atom (for example, the oxygen in the water molecule) is attracted to another electronegative atom from another molecule. In other words, hydrogen bonds always include hydrogen that is already part of a polar molecule.

The most common example of hydrogen bonding in the natural world occurs between molecules of water. It happens before your eyes whenever two raindrops merge into a larger bead, or a creek spills into a river. Hydrogen bonding occurs because the weakly negative oxygen atom in one water molecule is attracted to the weakly positive hydrogen atoms of two other water molecules (Figure 4).

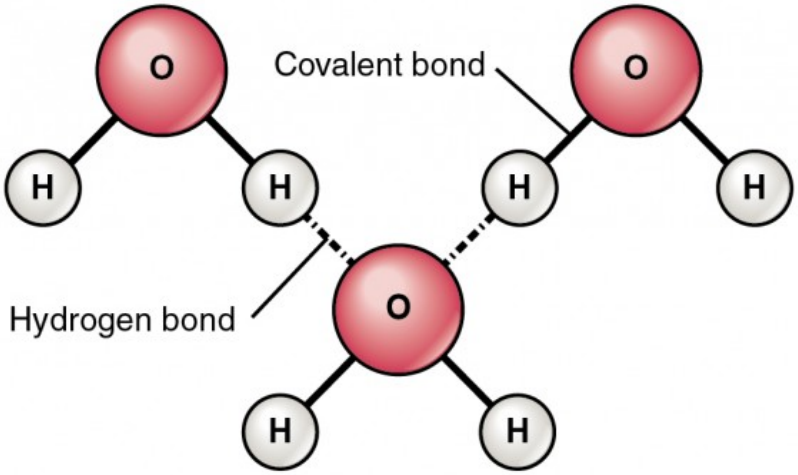


Figure 4. Hydrogen Bonds between Water Molecules. *Notice that the bonds occur between the weakly positive charge on the hydrogen atoms and the weakly negative charge on the oxygen atoms. Hydrogen bonds are relatively weak, and therefore are indicated with a dotted (rather than a solid) line.*

Water molecules also strongly attract other types of charged molecules as well as ions. This explains why "table salt," for example, actually is a molecule called a "salt" in chemistry, which consists of equal numbers of positively-charged sodium (Na^+) and negatively-charged chloride (Cl^-), dissolves so readily in water, in this case forming dipole-ion bonds between the water and the electrically-charged ions (electrolytes). Water molecules also repel molecules with nonpolar covalent bonds, like fats, lipids, and oils. You can demonstrate this with a simple kitchen experiment: pour a teaspoon of vegetable oil, a compound formed by nonpolar covalent bonds, into a glass of water. Instead of instantly dissolving in the water, the oil forms a distinct bead because the polar water molecules repel the nonpolar oil.

CHEMICAL REACTIONS

Learning Objectives

- Distinguish between kinetic and potential energy, and between exergonic and endergonic chemical reactions
- Identify four forms of energy important in human functioning
- Describe the three basic types of chemical reactions
- Identify several factors influencing the rate of chemical reactions

One characteristic of a living organism is metabolism, which is the sum total of all of the chemical reactions that go on to maintain that organism's health and life. The bonding processes you have learned thus far are anabolic chemical reactions; that is, they form larger molecules from smaller molecules or atoms. But recall that metabolism can proceed in another direction: in catabolic chemical reactions, bonds between components of

larger molecules break, releasing smaller molecules or atoms. Both types of reaction involve exchanges not only of matter, but of energy.

The Role of Energy in Chemical Reactions

Chemical reactions require a sufficient amount of energy to cause the matter to collide with enough precision and force that old chemical bonds can be broken and new ones formed. In general, **kinetic energy** is the form of energy powering any type of matter in motion. Imagine you are building a brick wall. The energy it takes to lift and place one brick atop another is kinetic energy—the energy matter possesses because of its motion. Once the wall is in place, it stores potential energy. **Potential energy** is the energy of position, or the energy matter possesses because of the positioning or structure of its components. If the brick wall collapses, the stored potential energy is released as kinetic energy as the bricks fall.

In the human body, potential energy is stored in the bonds between atoms and molecules. **Chemical energy** is the form of potential energy in which energy is stored in chemical bonds. When those bonds are formed, chemical energy is invested, and when they break, chemical energy is released. Notice that chemical energy, like all energy, is neither created nor destroyed; rather, it is converted from one form to another. When you eat an energy bar before heading out the door for a hike, the honey, nuts, and other foods the bar contains are broken down and rearranged by your body into molecules that your muscle cells convert to kinetic energy.

Chemical reactions that release more energy than they absorb are characterized as exergonic. The catabolism of the foods in your energy bar is an example. Some of the chemical energy stored in the bar is absorbed into molecules your body uses for fuel, but some of it is released—for example, as heat. In contrast, chemical reactions that absorb more energy than they release are endergonic. These reactions require energy input, and the resulting molecule stores not only the chemical energy in the original components, but also the energy that fueled the reaction. Because energy is neither created nor destroyed, where does the energy needed for endergonic reactions come from? In many cases, it comes from exergonic reactions.

Forms of Energy Important in Human Functioning

You have already learned that chemical energy is absorbed, stored, and released by chemical bonds. In addition to chemical energy, mechanical, radiant, and electrical energy are important in human functioning.

- Mechanical energy, which is stored in physical systems such as machines, engines, or the human body, directly powers the movement of matter. When you lift a brick into place on a wall, your muscles provide the mechanical energy that moves the brick.
- Radiant energy is energy emitted and transmitted as waves rather than matter. These waves vary in length from long radio waves and microwaves to short gamma waves emitted from decaying atomic nuclei. The full spectrum of radiant energy is referred to as the electromagnetic spectrum. The body uses the ultraviolet energy of sunlight to convert a compound in skin cells to vitamin D, which is essential to human functioning. The human eye evolved to see the wavelengths that comprise the colors of the rainbow, from red to violet, so that range in the spectrum is called “visible light.”
- Electrical energy, supplied by electrolytes in cells and body fluids, contributes to the voltage changes that help transmit impulses in nerve and muscle cells.

Characteristics of Chemical Reactions

All chemical reactions begin with a **reactant**, the general term for the one or more substances that enter into the reaction. Sodium and chloride ions, for example, are the reactants in the production of table salt. The one or more substances produced by a chemical reaction are called the **product**.

In chemical reactions, the components of the reactants—the elements involved and the number of atoms of each—are all present in the product(s). Similarly, there is nothing present in the products that are not present in the reactants. This is because chemical reactions are governed by the law of conservation of mass, which states that matter cannot be created or destroyed in a chemical reaction.

Just as you can express mathematical calculations in equations such as 2 + 7 = 9, you can use chemical equations to show how reactants become products. As in math, chemical equations proceed from left to right, but instead of an equal sign, they employ an arrow or arrows indicating the direction in which the chemical reaction proceeds. For example, the chemical reaction in which one atom of nitrogen and three atoms of hydrogen produce ammonia would be written as $N + 3H \rightarrow NH_3$. Correspondingly, the breakdown of ammonia into its components would be written as $NH_3 \rightarrow N + 3H$.

Notice that, in the first example, a nitrogen (N) atom and three hydrogen (H) atoms bond to form a compound. This anabolic reaction requires energy, which is then stored within the compound's bonds. Such reactions are referred to as synthesis reactions. A **synthesis reaction** is a chemical reaction that results in the synthesis (joining) of components that were formerly separate (Figure 1a). Again, nitrogen and hydrogen are reactants in a synthesis reaction that yields ammonia as the product. The general equation for a synthesis reaction is $A + B \rightarrow AB$.

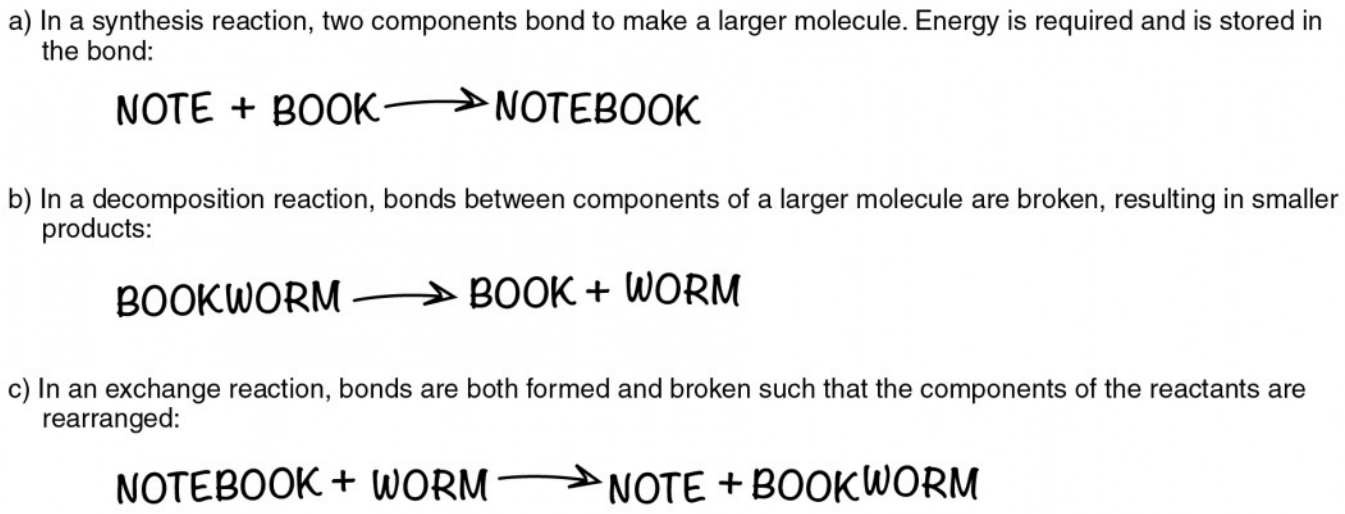


Figure 1. The Three Fundamental Chemical Reactions. *The atoms and molecules involved in the three fundamental chemical reactions can be imagined as words.*

In the second example, ammonia is catabolized into its smaller components, and the potential energy that had been stored in its bonds is released. Such reactions are referred to as decomposition reactions. A *decomposition reaction* is a chemical reaction that breaks down or "de-composes" something larger into its constituent parts (see Figure 1b). The general equation for a decomposition reaction is: $AB \rightarrow A+B$.

An **exchange reaction** is a chemical reaction in which both synthesis and decomposition occur, chemical bonds are both formed and broken, and chemical energy is absorbed, stored, and released (see Figure 1c). The simplest form of an exchange reaction might be: $A+BC \rightarrow AB+C$. Notice that, to produce these products, B and C had to break apart in a decomposition reaction, whereas A and B had to bond in a synthesis reaction. A more complex exchange reaction might be: $AB+CD \rightarrow AC+BD$. Another example might be: $AB+CD \rightarrow AD+BC$.

In theory, any chemical reaction can proceed in either direction under the right conditions. Reactants may synthesize into a product that is later decomposed. Reversibility is also a quality of exchange reactions. For instance, $A+BC \rightarrow AB+C$ could then reverse to $AB+C \rightarrow A+BC$. This reversibility of a chemical reaction is indicated with a double arrow: $A+BC \rightleftarrows AB+C$. Still, in the human body, many chemical reactions do proceed in a predictable direction, either one way or the other. You can think of this more predictable path as the path of least resistance because, typically, the alternate direction requires more energy.

Factors Influencing the Rate of Chemical Reactions

If you pour vinegar into baking soda, the reaction is instantaneous; the concoction will bubble and fizz. But many chemical reactions take time. A variety of factors influence the rate of chemical reactions. This section, however, will consider only the most important in human functioning.

Properties of the Reactants

If chemical reactions are to occur quickly, the atoms in the reactants have to have easy access to one another. Thus, the greater the surface area of the reactants, the more readily they will interact. When you pop a cube of cheese into your mouth, you chew it before you swallow it. Among other things, chewing increases the surface area of the food so that digestive chemicals can more easily get at it. As a general rule, gases tend to react faster than liquids or solids, again because it takes energy to separate particles of a substance, and gases by definition already have space between their particles. Similarly, the larger the molecule, the greater the number of total bonds, so reactions involving smaller molecules, with fewer total bonds, would be expected to proceed faster.

In addition, recall that some elements are more reactive than others. Reactions that involve highly reactive elements like hydrogen proceed more quickly than reactions that involve less reactive elements. Reactions involving stable elements like helium are not likely to happen at all.

Temperature

Nearly all chemical reactions occur at a faster rate at higher temperatures. Recall that kinetic energy is the energy of matter in motion. The kinetic energy of subatomic particles increases in response to increases in thermal energy. The higher the temperature, the faster the particles move, and the more likely they are to come in contact and react.

Concentration and Pressure

If just a few people are dancing at a club, they are unlikely to step on each other's toes. But as more and more people get up to dance—especially if the music is fast—collisions are likely to occur. It is the same with chemical reactions: the more particles present within a given space, the more likely those particles are to bump into one another. This means that chemists can speed up chemical reactions not only by increasing the **concentration** of particles—the number of particles in the space—but also by decreasing the volume of the space, which would correspondingly increase the pressure. If there were 100 dancers in that club, and the manager abruptly moved the party to a room half the size, the concentration of the dancers would double in the new space, and the likelihood of collisions would increase accordingly.

Enzymes and Other Catalysts

For two chemicals in nature to react with each other they first have to come into contact, and this occurs through random collisions. Because heat helps increase the kinetic energy of atoms, ions, and molecules, it promotes their collision. But in the body, extremely high heat—such as a very high fever—can damage body cells and be life-threatening. On the other hand, normal body temperature is not high enough to promote the chemical reactions that sustain life. That is where catalysts come in.

In chemistry, a **catalyst** is a substance that increases the rate of a chemical reaction without itself undergoing any change. You can think of a catalyst as a chemical change agent. They help increase the rate and force at which atoms, ions, and molecules collide, thereby increasing the probability that their valence shell electrons will interact.

The most important catalysts in the human body are enzymes. An **enzyme** is a catalyst composed of protein or ribonucleic acid (RNA), both of which will be discussed later in this chapter. Like all catalysts, enzymes work by lowering the level of energy that needs to be invested in a chemical reaction. A chemical reaction's **activation energy** is the "threshold" level of energy needed to break the bonds in the reactants. Once those bonds are broken, new arrangements can form. Without an enzyme to act as a catalyst, a much larger investment of energy is needed to ignite a chemical reaction (Figure 2).

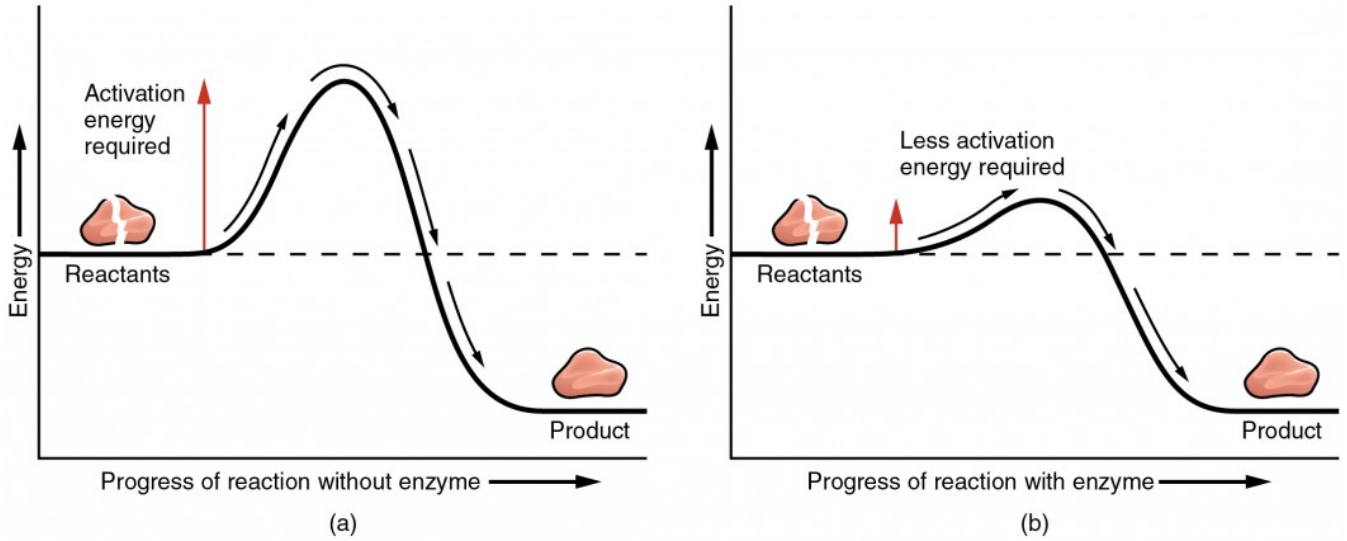


Figure 2. Enzymes. *Enzymes decrease the activation energy required for a given chemical reaction to occur. (a) Without an enzyme, the energy input needed for a reaction to begin is high. (b) With the help of an enzyme, less energy is needed for a reaction to begin.*

Enzymes are critical to the body's healthy functioning. They assist, for example, with the breakdown of food and its conversion to energy. In fact, most of the chemical reactions in the body are facilitated by enzymes.

INORGANIC COMPOUNDS ESSENTIAL TO HUMAN FUNCTIONING

Learning Objectives

- Compare and contrast inorganic and organic compounds
- Identify the properties of water that make it essential to life
- Explain the role of salts in body functioning
- Distinguish between acids and bases, and explain their role in pH
- Discuss the role of buffers in helping the body maintain pH homeostasis

The concepts you have learned so far in this chapter govern all forms of matter, and would work as a foundation for geology as well as biology. This section of the chapter narrows the focus to the chemistry of human life; that is, the compounds important for the body's structure and function. In general, these compounds are either inorganic or organic.

- An **inorganic compound** is a substance that does not contain both carbon and hydrogen. A great many inorganic compounds do contain hydrogen atoms, such as water (H_2O) and the hydrochloric acid (HCl) produced by your stomach. In contrast, only a handful of inorganic compounds contain carbon atoms. Carbon dioxide (CO_2) is one of the few examples.

- An **organic compound**, then, is a substance that contains both carbon and hydrogen. Organic compounds are synthesized via covalent bonds within living organisms, including the human body. Recall that carbon and hydrogen are the second and third most abundant elements in your body. You will soon discover how these two elements combine in the foods you eat, in the compounds that make up your body structure, and in the chemicals that fuel your functioning.

The following section examines the three groups of inorganic compounds essential to life: water, salts, acids, and bases. Organic compounds are covered later in the chapter.

Water

As much as 70 percent of an adult's body weight is water. This water is contained both within the cells and between the cells that make up tissues and organs. Its several roles make water indispensable to human functioning.

Water as a Lubricant and Cushion

Water is a major component of many of the body's lubricating fluids. Just as oil lubricates the hinge on a door, water in synovial fluid lubricates the actions of body joints, and water in pleural fluid helps the lungs expand and recoil with breathing. Watery fluids help keep food flowing through the digestive tract, and ensure that the movement of adjacent abdominal organs is friction free.

Water also protects cells and organs from physical trauma, cushioning the brain within the skull, for example, and protecting the delicate nerve tissue of the eyes. Water cushions a developing fetus in the mother's womb as well.

Water as a Heat Sink

A heat sink is a substance or object that absorbs and dissipates heat but does not experience a corresponding increase in temperature. In the body, water absorbs the heat generated by chemical reactions without greatly increasing in temperature. Moreover, when the environmental temperature soars, the water stored in the body helps keep the body cool. This cooling effect happens as warm blood from the body's core flows to the blood vessels just under the skin and is transferred to the environment. At the same time, sweat glands release warm water in sweat. As the water evaporates into the air, it carries away heat, and then the cooler blood from the periphery circulates back to the body core.

Water as a Component of Liquid Mixtures

A mixture is a combination of two or more substances, each of which maintains its own chemical identity. In other words, the constituent substances are not chemically bonded into a new, larger chemical compound. The concept is easy to imagine if you think of powdery substances such as flour and sugar; when you stir them together in a bowl, they obviously do not bond to form a new compound. The room air you breathe is a gaseous mixture, containing three discrete elements—nitrogen, oxygen, and argon—and one compound, carbon dioxide. There are three types of liquid mixtures, all of which contain water as a key component. These are solutions, colloids, and suspensions.

For cells in the body to survive, they must be kept moist in a water-based liquid called a solution. In chemistry, a liquid **solution** consists of a solvent that dissolves a substance called a solute. An important characteristic of solutions is that they are homogeneous; that is, the solute molecules are distributed evenly throughout the solution. If you were to stir a teaspoon of sugar into a glass of water, the sugar would dissolve into sugar molecules separated by water molecules. The ratio of sugar to water in the left side of the glass would be the same as the ratio of sugar to water in the right side of the glass. If you were to add more sugar, the ratio of sugar to water would change, but the distribution—provided you had stirred well—would still be even.

Water is considered the "universal solvent" and it is believed that life cannot exist without water because of this. Water is certainly the most abundant solvent in the body; essentially all of the body's chemical reactions occur among compounds dissolved in water. Because water molecules are polar, with regions of positive and negative

electrical charge, water readily dissolves ionic compounds and polar covalent compounds. Such compounds are referred to as hydrophilic, or “water-loving.” As mentioned above, sugar dissolves well in water. This is because sugar molecules contain regions of hydrogen-oxygen polar bonds, making it hydrophilic. Nonpolar molecules, which do not readily dissolve in water, are called hydrophobic, or “water-fearing.”

Concentrations of Solutes

Various mixtures of solutes and water are described in chemistry. The concentration of a given solute is the number of particles of that solute in a given space (oxygen makes up about 21 percent of atmospheric air). In the bloodstream of humans, glucose concentration is usually measured in milligram (mg) per deciliter (dL), and in a healthy adult averages about 100 mg/dL. Another method of measuring the concentration of a solute is by its molarilty—which is moles (M) of the molecules per liter (L). The mole of an element is its atomic weight, while a mole of a compound is the sum of the atomic weights of its components, called the molecular weight. An often-used example is calculating a mole of glucose, with the chemical formula $C_6H_{12}O_6$. Using the periodic table, the atomic weight of carbon (C) is 12.011 grams (g), and there are six carbons in glucose, for a total atomic weight of 72.066 g. Doing the same calculations for hydrogen (H) and oxygen (O), the molecular weight equals 180.156g (the “gram molecular weight” of glucose). When water is added to make one liter of solution, you have one mole (1M) of glucose. This is particularly useful in chemistry because of the relationship of moles to “Avogadro’s number.” A mole of any solution has the same number of particles in it: 6.02×10^{23}. Many substances in the bloodstream and other tissue of the body are measured in thousandths of a mole, or millimoles (mM).

A **colloid** is a mixture that is somewhat like a heavy solution. The solute particles consist of tiny clumps of molecules large enough to make the liquid mixture opaque (because the particles are large enough to scatter light). Familiar examples of colloids are milk and cream. In the thyroid glands, the thyroid hormone is stored as a thick protein mixture also called a colloid.

A **suspension** is a liquid mixture in which a heavier substance is suspended temporarily in a liquid, but over time, settles out. This separation of particles from a suspension is called sedimentation. An example of sedimentation occurs in the blood test that establishes sedimentation rate, or sed rate. The test measures how quickly red blood cells in a test tube settle out of the watery portion of blood (known as plasma) over a set period of time. Rapid sedimentation of blood cells does not normally happen in the healthy body, but aspects of certain diseases can cause blood cells to clump together, and these heavy clumps of blood cells settle to the bottom of the test tube more quickly than do normal blood cells.

The Role of Water in Chemical Reactions

Two types of chemical reactions involve the creation or the consumption of water: dehydration synthesis and hydrolysis.

- In dehydration synthesis, one reactant gives up an atom of hydrogen and another reactant gives up a hydroxyl group (OH) in the synthesis of a new product. In the formation of their covalent bond, a molecule of water is released as a byproduct (Figure 1). This is also sometimes referred to as a condensation reaction.
- In hydrolysis, a molecule of water disrupts a compound, breaking its bonds. The water is itself split into H and OH. One portion of the severed compound then bonds with the hydrogen atom, and the other portion bonds with the hydroxyl group.

These reactions are reversible, and play an important role in the chemistry of organic compounds (which will be discussed shortly).

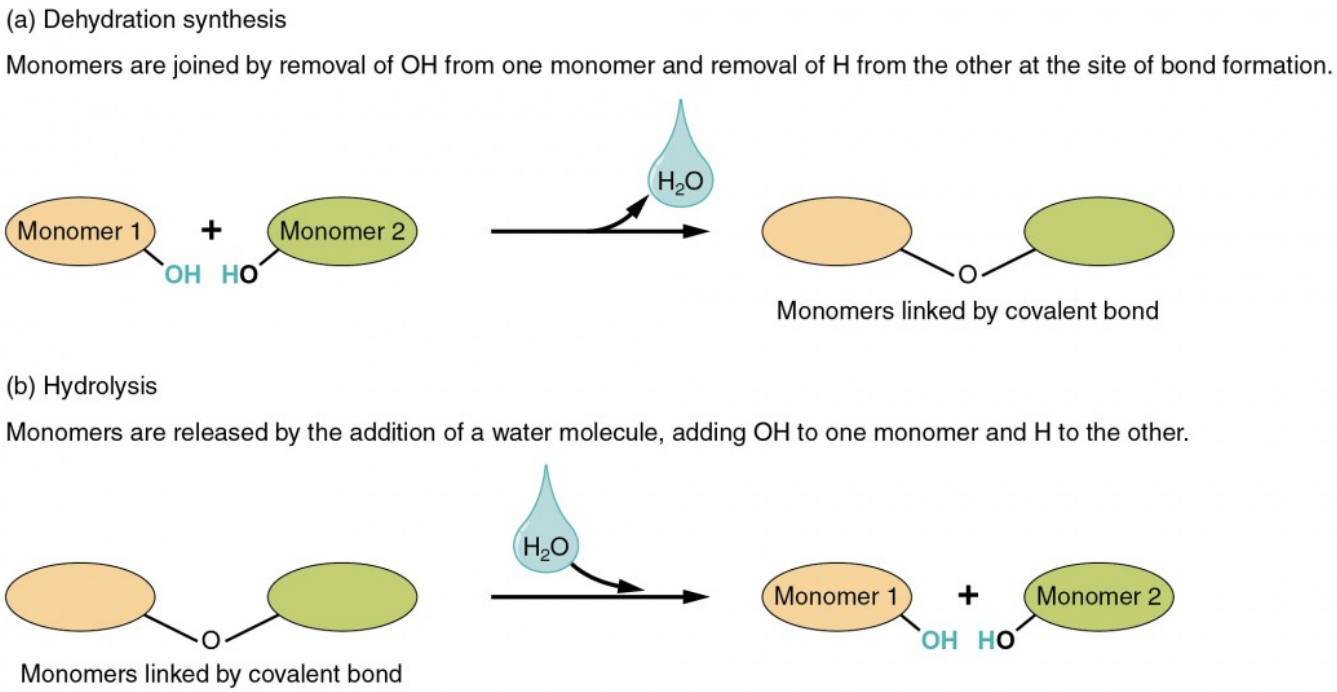


Figure 1. Dehydration Synthesis and Hydrolysis. *Monomers, the basic units for building larger molecules, form polymers (two or more chemically-bonded monomers). (a) In dehydration synthesis, two monomers are covalently bonded in a reaction in which one gives up a hydroxyl group and the other a hydrogen atom. A molecule of water is released as a byproduct during dehydration reactions. (b) In hydrolysis, the covalent bond between two monomers is split by the addition of a hydrogen atom to one and a hydroxyl group to the other, which requires the contribution of one molecule of water.*

Salts

Recall that salts are formed when ions form ionic bonds. In these reactions, one atom gives up one or more electrons, and thus becomes positively charged, whereas the other accepts one or more electrons and becomes negatively charged. You can now define a salt as a substance that, when dissolved in water, dissociates into ions other than H^+ or OH^-. This fact is important in distinguishing salts from acids and bases, discussed next.

A typical salt, NaCl, dissociates completely in water (Figure 2). The positive and negative regions on the water molecule (the hydrogen and oxygen ends respectively) attract the negative chloride and positive sodium ions, pulling them away from each other. Again, whereas nonpolar and polar covalently bonded compounds break apart into molecules in solution, salts dissociate into ions. These ions are electrolytes; they are capable of conducting an electrical current in solution. This property is critical to the function of ions in transmitting nerve impulses and prompting muscle contraction.

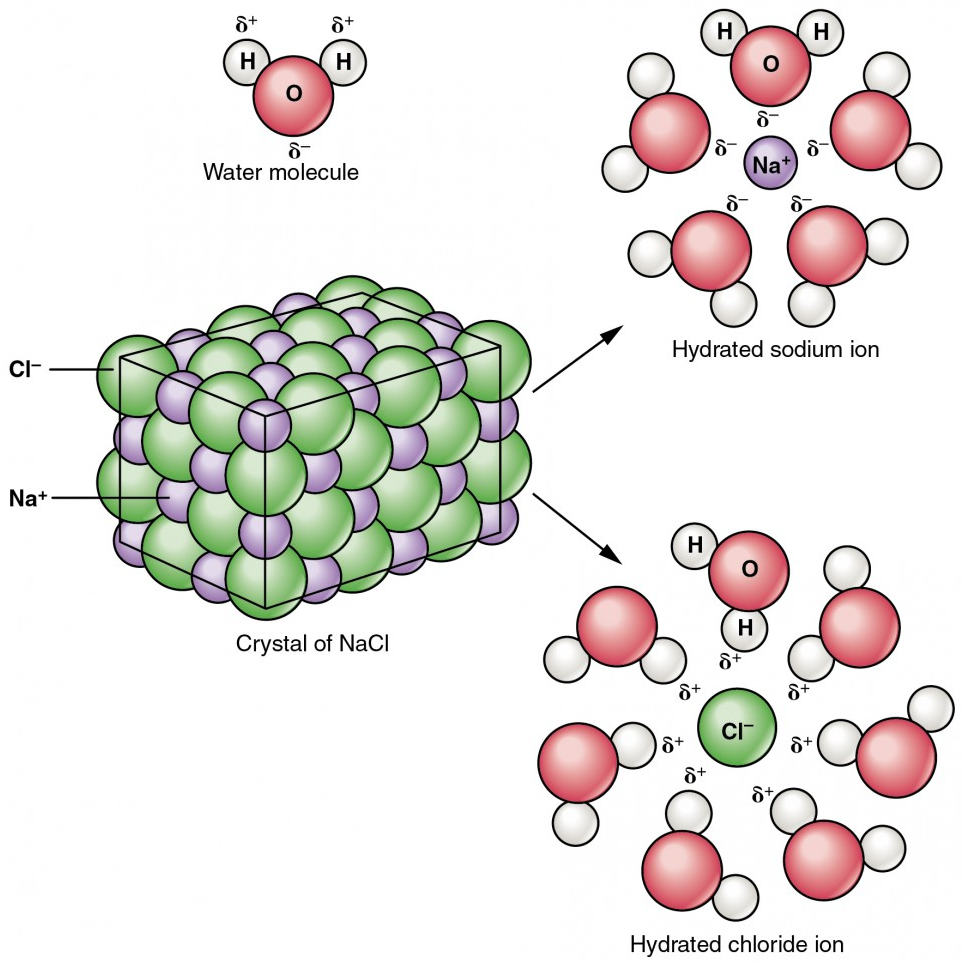


Figure 2. Dissociation of Sodium Chloride in Water. *Notice that the crystals of sodium chloride dissociate not into molecules of NaCl, but into Na^+ cations and Cl^- anions, each completely surrounded by water molecules.*

Many other salts are important in the body. For example, bile salts produced by the liver help break apart dietary fats, and calcium phosphate salts form the mineral portion of teeth and bones.

Acids and Bases

Acids and bases, like salts, dissociate in water into electrolytes. Acids and bases can very much change the properties of the solutions in which they are dissolved.

Acids

An **acid** is a substance that releases hydrogen ions (H^+) in solution (Figure 3a). Because an atom of hydrogen has just one proton and one electron, a positively charged hydrogen ion is simply a proton. This solitary proton is highly likely to participate in chemical reactions. Strong acids are compounds that release all of their H^+ in solution; that is, they ionize completely. Hydrochloric acid (HCl), which is released from cells in the lining of the stomach, is a strong acid because it releases all of its H^+ in the stomach's watery environment. This strong acid aids in digestion and kills ingested microbes. Weak acids do not ionize completely; that is, some of their hydrogenionsremain bonded within a compound in solution. An example of a weak acid is vinegar, or acetic acid; it is called acetate after it gives up a proton.

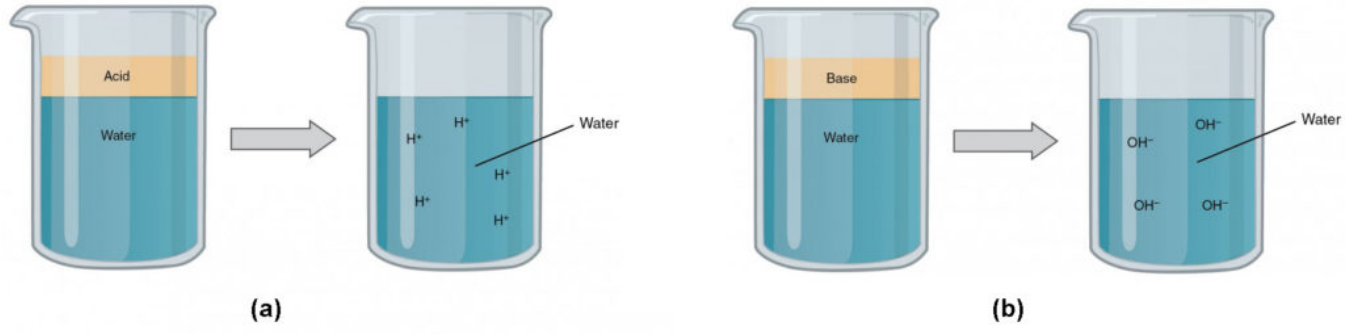


Figure 3. Acids and Bases. *(a) In aqueous solution, an acid dissociates into hydrogen ions (H^+) and anions. Nearly every molecule of a strong acid dissociates, producing a high concentration of H^+. (b) In aqueous solution, a base dissociates into hydroxyl ions (OH^-) and cations. Nearly every molecule of a strong base dissociates, producing a high concentration of OH^-.*

Bases

A **base** is a substance that releases hydroxyl ions (OH^-) in solution, or one that accepts H^+ already present in solution (see Figure 3b). The hydroxyl ions or other base combine with H^+ present to form a water molecule, thereby removing H^+ and reducing the solution's acidity. Strong bases release most or all of their hydroxyl ions; weak bases release only some hydroxyl ions or absorb only a few H^+. Food mixed with hydrochloric acid from the stomach would burn the small intestine, the next portion of the digestive tract after the stomach, if it were not for the release of bicarbonate (HCO_3^-), a weak base that attracts H^+. Bicarbonate accepts some of the H^+ protons, thereby reducing the acidity of the solution.

The Concept of pH

The relative acidity or alkalinity of a solution can be indicated by its pH. A solution's **pH** is the negative, base-10 logarithm of the hydrogen ion (H^+) concentration of the solution. As an example, a pH 4 solution has an H^+ concentration that is ten times greater than that of a pH 5 solution. That is, a solution with a pH of 4 is ten times more acidic than a solution with a pH of 5. The concept of pH will begin to make more sense when you study the pH scale, like that shown in Figure 4. The scale consists of a series of increments ranging from 0 to 14. A solution with a pH of 7 is considered neutral—neither acidic nor basic. Pure water has a pH of 7. The lower the number below 7, the more acidic the solution, or the greater the concentration of H^+. The concentration of hydrogen ions at each pH value is 10 times different than the next pH. For instance, a pH value of 4 corresponds to a proton concentration of 10^{-4} M, or 0.0001M, while a pH value of 5 corresponds to a proton concentration of 10^{-5} M, or 0.00001M. The higher the number above 7, the more basic (alkaline) the solution, or the lower the concentration of H^+. Human urine, for example, is ten times more acidic than pure water, and HCl is 10,000,000 times more acidic than water.

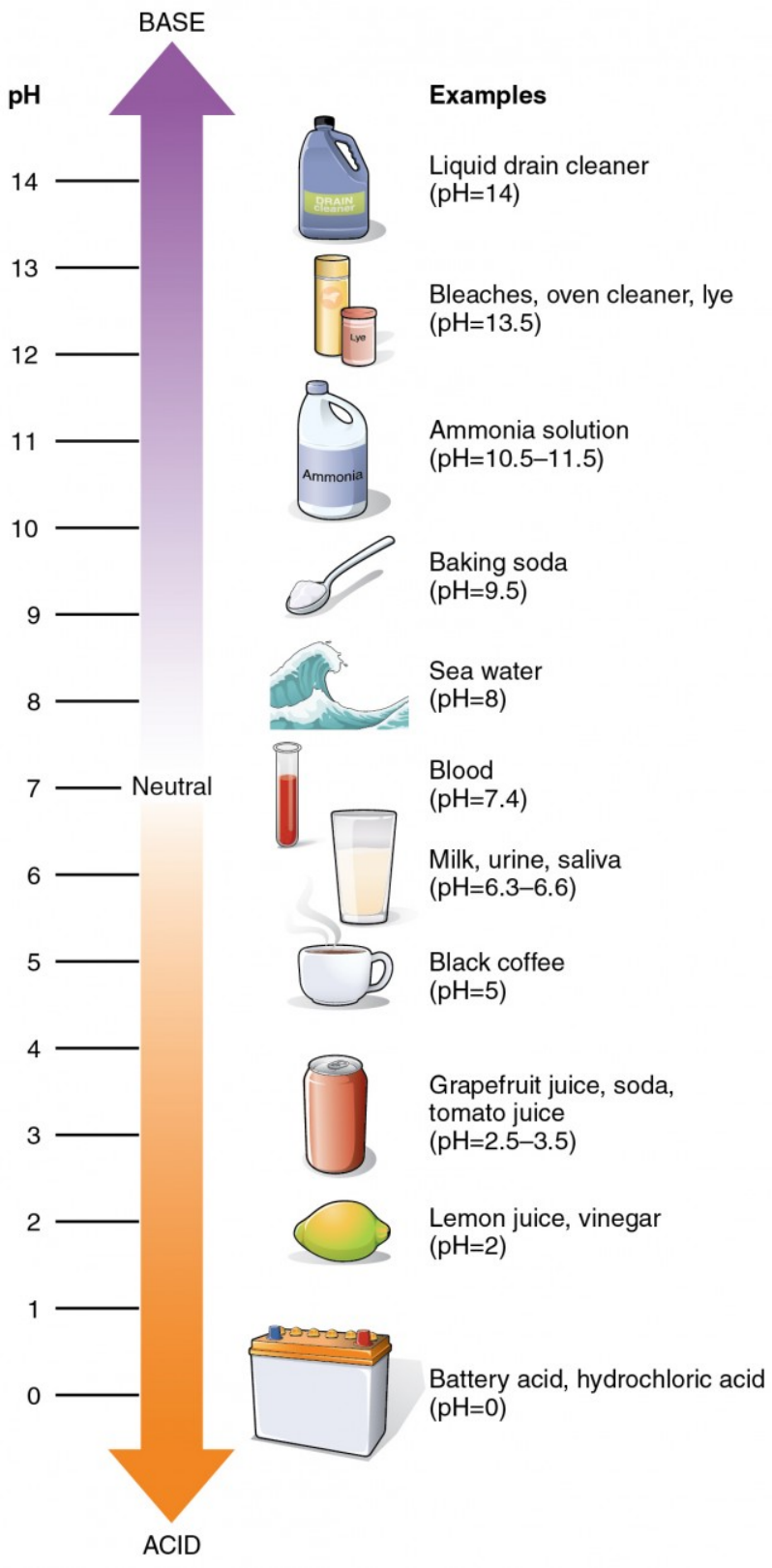


Figure 4. The pH Scale

Buffers

The pH of human blood normally ranges from 7.35 to 7.45, although it is typically identified as pH 7.4. At this slightly basic pH, blood can reduce the acidity resulting from the carbon dioxide (CO_2) constantly being released into the bloodstream by the trillions of cells in the body. Homeostatic mechanisms (along with exhaling CO_2 while breathing) normally keep the pH of blood within this narrow range. This is critical, because fluctuations—either too acidic or too alkaline—can lead to life-threatening disorders.

All cells of the body depend on homeostatic regulation of acid–base balance at a pH of approximately 7.4. The body therefore has several mechanisms for this regulation, involving breathing, the excretion of chemicals in urine, and the internal release of chemicals collectively called buffers into body fluids. A **buffer** is a solution of a weak acid and its conjugate base. A buffer can neutralize small amounts of acids or bases in body fluids. For example, if there is even a slight decrease below 7.35 in the pH of a bodily fluid, the buffer in the fluid—in this case, acting as a weak base—will bind the excess hydrogen ions. In contrast, if pH rises above 7.45, the buffer will act as a weak acid and contribute hydrogen ions.

Homeostatic Imbalances: Acids and Bases

Excessive acidity of the blood and other body fluids is known as acidosis. Common causes of acidosis are situations and disorders that reduce the effectiveness of breathing, especially the person's ability to exhale fully, which causes a buildup of CO_2 (and H^+) in the bloodstream. Acidosis can also be caused by metabolic problems that reduce the level or function of buffers that act as bases, or that promote the production of acids. For instance, with severe diarrhea, too much bicarbonate can be lost from the body, allowing acids to build up in body fluids. In people with poorly managed diabetes (ineffective regulation of blood sugar), acids called ketones are produced as a form of body fuel. These can build up in the blood, causing a serious condition called diabetic ketoacidosis. Kidney failure, liver failure, heart failure, cancer, and other disorders also can prompt metabolic acidosis.

In contrast, alkalosis is a condition in which the blood and other body fluids are too alkaline (basic). As with acidosis, respiratory disorders are a major cause; however, in respiratory alkalosis, carbon dioxide levels fall too low. Lung disease, aspirin overdose, shock, and ordinary anxiety can cause respiratory alkalosis, which reduces the normal concentration of H^+.

Metabolic alkalosis often results from prolonged, severe vomiting, which causes a loss of hydrogen and chloride ions (as components of HCl). Medications also can prompt alkalosis. These include diuretics that cause the body to lose potassium ions, as well as antacids when taken in excessive amounts, for instance by someone with persistent heartburn or an ulcer.

ORGANIC COMPOUNDS ESSENTIAL TO HUMAN FUNCTIONING

Learning Objectives

- Identify four types of organic molecules essential to human functioning

- Explain the chemistry behind carbon's affinity for covalently bonding in organic compounds
- Provide examples of three types of carbohydrates, and identify the primary functions of carbohydrates in the body
- Discuss four types of lipids important in human functioning
- Describe the structure of proteins, and discuss their importance to human functioning
- Identify the building blocks of nucleic acids, and the roles of DNA, RNA, and ATP in human functioning

Organic compounds typically consist of groups of carbon atoms covalently bonded to hydrogen, usually oxygen, and often other elements as well. Created by living things, they are found throughout the world, in soils and seas, commercial products, and every cell of the human body. The four types most important to human structure and function are carbohydrates, lipids, proteins, and nucleotides. Before exploring these compounds, you need to first understand the chemistry of carbon.

The Chemistry of Carbon

What makes organic compounds ubiquitous is the chemistry of their carbon core. Recall that carbon atoms have four electrons in their valence shell, and that the octet rule dictates that atoms tend to react in such a way as to complete their valence shell with eight electrons. Carbon atoms do not complete their valence shells by donating or accepting four electrons. Instead, they readily share electrons via covalent bonds.

Commonly, carbon atoms share with other carbon atoms, often forming a long carbon chain referred to as a carbon skeleton. When they do share, however, they do not share all their electrons exclusively with each other. Rather, carbon atoms tend to share electrons with a variety of other elements, one of which is always hydrogen. Carbon and hydrogen groupings are called hydrocarbons. If you study the figures of organic compounds in the remainder of this chapter, you will see several with chains of hydrocarbons in one region of the compound.

Many combinations are possible to fill carbon's four "vacancies." Carbon may share electrons with oxygen or nitrogen or other atoms in a particular region of an organic compound. Moreover, the atoms to which carbon atoms bond may also be part of a functional group. A **functional group** is a group of atoms linked by strong covalent bonds and tending to function in chemical reactions as a single unit. You can think of functional groups as tightly knit "cliques" whose members are unlikely to be parted. Five functional groups are important in human physiology; these are the hydroxyl, carboxyl, amino, methyl and phosphate groups (Table 1).

Table 1. Functional Groups Important in Human Physiology

Functional group	Structural formula	Importance
Hydroxyl	—O—H	Hydroxyl groups are polar. They are components of all four types of organic compounds discussed in this chapter. They are involved in dehydration synthesis and hydrolysis reactions.
Carboxyl	O—C—OH	Carboxyl groups are found within fatty acids, amino acids, and many other acids.
Amino	—N—H_2	Amino groups are found within amino acids, the building blocks of proteins.
Methyl	—C—H_3	Methyl groups are found within amino acids.
Phosphate	—P—O_4^{2-}	Phosphate groups are found within phospholipids and nucleotides.

Carbon's affinity for covalent bonding means that many distinct and relatively stable organic molecules nevertheless readily form larger, more complex molecules. Any large molecule is referred to as **macromolecule** (macro- = "large"), and the organic compounds in this section all fit this description. However, some macromolecules are made up of several "copies" of single units called monomer (mono- = "one"; -mer = "part"). Like beads in a long necklace, these monomers link by covalent bonds to form long polymers (poly- = "many"). There are many examples of monomers and polymers among the organic compounds.

Monomers form polymers by engaging in dehydration synthesis. As was noted earlier, this reaction results in the release of a molecule of water. Each monomer contributes: One gives up a hydrogen atom and the other gives up a hydroxyl group. Polymers are split into monomers by hydrolysis (-lysis = "rupture"). The bonds between their monomers are broken, via the donation of a molecule of water, which contributes a hydrogen atom to one monomer and a hydroxyl group to the other.

Carbohydrates

The term carbohydrate means "hydrated carbon." Recall that the root hydro- indicates water. A **carbohydrate** is a molecule composed of carbon, hydrogen, and oxygen; in most carbohydrates, hydrogen and oxygen are found in the same two-to-one relative proportions they have in water. In fact, the chemical formula for a "generic" molecule of carbohydrate is $(CH_2O)_n$. Carbohydrates are referred to as saccharides, a word meaning "sugars." Three forms are important in the body. Monosaccharides are the monomers of carbohydrates. Disaccharides (di- = "two") are made up of two monomers. **Polysaccharides** are the polymers, and can consist of hundreds to thousands of monomers.

Monosaccharides

A **monosaccharide** is a monomer of carbohydrates. Five monosaccharides are important in the body. Three of these are the hexose sugars, so called because they each contain six atoms of carbon. These are glucose, fructose, and galactose, shown in Figure 1a. The remaining monosaccharides are the two pentose sugars, each of which contains five atoms of carbon. They are ribose and deoxyribose, shown in Figure 1b.

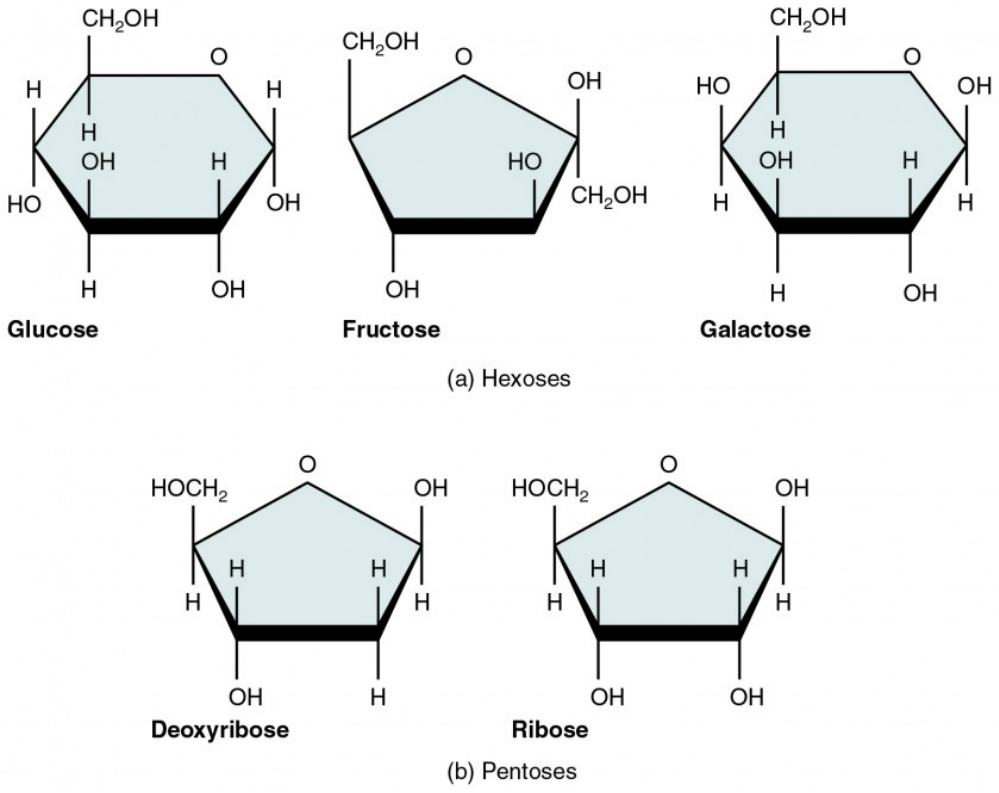


Figure 1. Five Important Monosaccharides.

Disaccharides

A **disaccharide** is a pair of monosaccharides. Disaccharides are formed via dehydration synthesis, and the bond linking them is referred to as a glycosidic bond (glyco- = "sugar"). Three disaccharides (shown in Figure 2) are important to humans. These are sucrose, commonly referred to as table sugar; lactose, or milk sugar; and maltose, or malt sugar. As you can tell from their common names, you consume these in your diet; however, your body cannot use them directly. Instead, in the digestive tract, they are split into their component monosaccharides via hydrolysis.

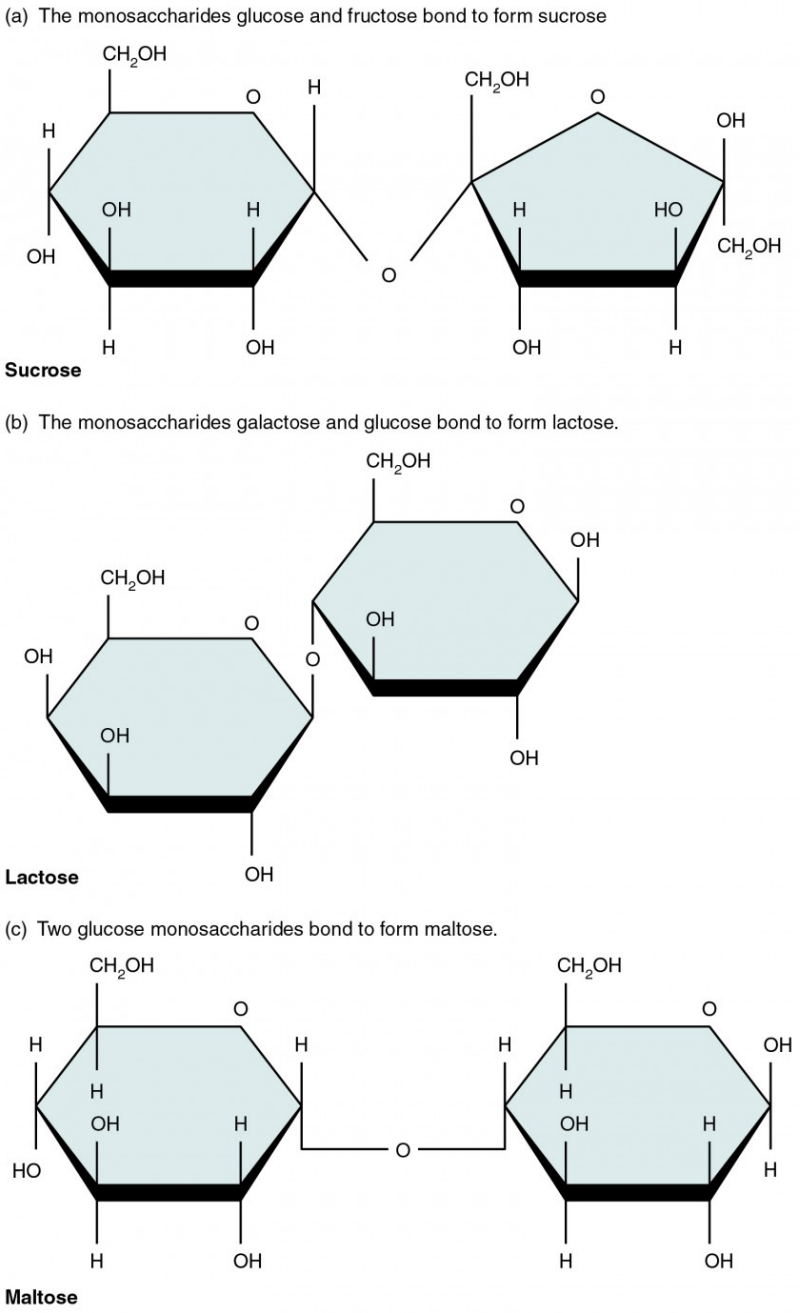


Figure 2. Three Important Disaccharides. *All three important disaccharides form by dehydration synthesis.*

Watch this video to observe the formation of a disaccharide. What happens when water encounters a glycosidic bond?

Watch this video online: https://youtu.be/b7TdWLNhMtM

Polysaccharides

Polysaccharides can contain a few to a thousand or more monosaccharides. Three are important to the body (Figure 3):

- Starches are polymers of glucose. They occur in long chains called amylose or branched chains called amylopectin, both of which are stored in plant-based foods and are relatively easy to digest.
- Glycogen is also a polymer of glucose, but it is stored in the tissues of animals, especially in the muscles and liver. It is not considered a dietary carbohydrate because very little glycogen remains in animal tissues after slaughter; however, the human body stores excess glucose as glycogen, again, in the muscles and liver.
- Cellulose, a polysaccharide that is the primary component of the cell wall of green plants, is the component of plant food referred to as “fiber”. In humans, cellulose/fiber is not digestible; however, dietary fiber has many health benefits. It helps you feel full so you eat less, it promotes a healthy digestive tract, and a diet high in fiber is thought to reduce the risk of heart disease and possibly some forms of cancer.

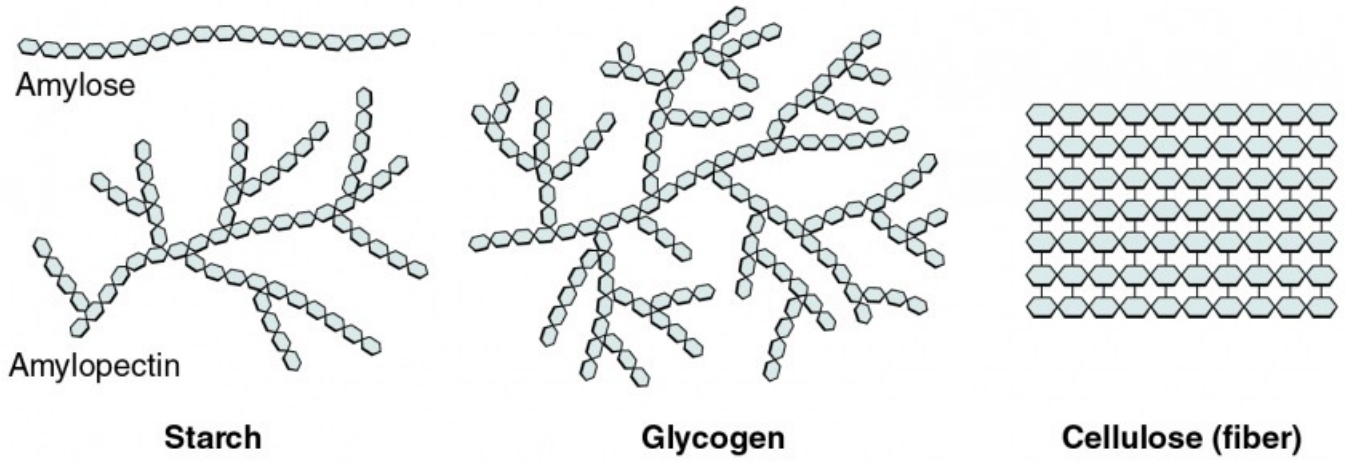


Figure 3. Three Important Polysaccharides. *Three important polysaccharides are starches, glycogen, and fiber.*

Functions of Carbohydrates

The body obtains carbohydrates from plant-based foods. Grains, fruits, and legumes and other vegetables provide most of the carbohydrate in the human diet, although lactose is found in dairy products.

Although most body cells can break down other organic compounds for fuel, all body cells can use glucose. Moreover, nerve cells (neurons) in the brain, spinal cord, and through the peripheral nervous system, as well as red blood cells, can use only glucose for fuel. In the breakdown of glucose for energy, molecules of adenosine triphosphate, better known as ATP, are produced. **Adenosine triphosphate (ATP)** is composed of a ribose sugar, an adenine base, and three phosphate groups. ATP releases free energy when its phosphate bonds are broken, and thus supplies ready energy to the cell. More ATP is produced in the presence of oxygen (O_2) than in pathways that do not use oxygen. The overall reaction for the conversion of the energy in glucose to energy stored in ATP can be written:

$C_6H_{12}O_6 + 6\ O_2 \rightarrow 6\ CO_2 + 6\ H_2O + ATP$

In addition to being a critical fuel source, carbohydrates are present in very small amounts in cells’ structure. For instance, some carbohydrate molecules bind with proteins to produce glycoproteins, and others combine with lipids to produce glycolipids, both of which are found in the membrane that encloses the contents of body cells.

Lipids

A **lipid** is one of a highly diverse group of compounds made up mostly of hydrocarbons. The few oxygen atoms they contain are often at the periphery of the molecule. Their nonpolar hydrocarbons make all lipids hydrophobic. In water, lipids do not form a true solution, but they may form an emulsion, which is the term for a mixture of solutions that do not mix well.

Triglycerides

A **triglyceride** is one of the most common dietary lipid groups, and the type found most abundantly in body tissues. This compound, which is commonly referred to as a fat, is formed from the synthesis of two types of molecules (Figure 4):

- A glycerol backbone at the core of triglycerides, consists of three carbon atoms.
- Three fatty acids, long chains of hydrocarbons with a carboxyl group and a methyl group at opposite ends, extend from each of the carbons of the glycerol.

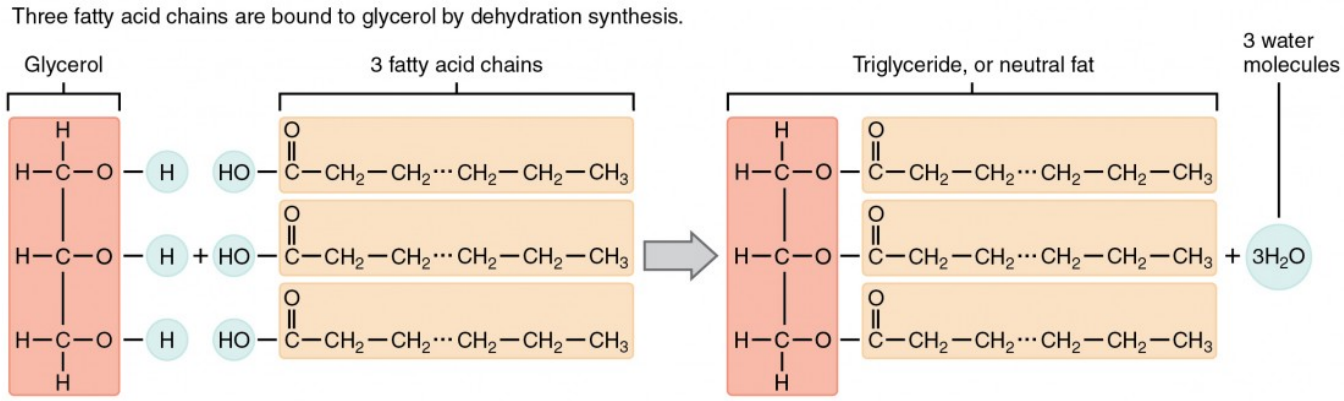


Figure 4. Triglycerides. *Triglycerides are composed of glycerol attached to three fatty acids via dehydration synthesis. Notice that glycerol gives up a hydrogen atom, and the carboxyl groups on the fatty acids each give up a hydroxyl group.*

Triglycerides form via dehydration synthesis. Glycerol gives up hydrogen atoms from its hydroxyl groups at each bond, and the carboxyl group on each fatty acid chain gives up a hydroxyl group. A total of three water molecules are thereby released.

Fatty acid chains that have no double carbon bonds anywhere along their length and therefore contain the maximum number of hydrogen atoms are called saturated fatty acids. These straight, rigid chains pack tightly together and are solid or semi-solid at room temperature (Figure 5a). Butter and lard are examples, as is the fat found on a steak or in your own body. In contrast, fatty acids with one double carbon bond are kinked at that bond (Figure 5b). These monounsaturated fatty acids are therefore unable to pack together tightly, and are liquid at room temperature. Polyunsaturated fatty acids contain two or more double carbon bonds, and are also liquid at room temperature. Plant oils such as olive oil typically contain both mono- and polyunsaturated fatty acids.

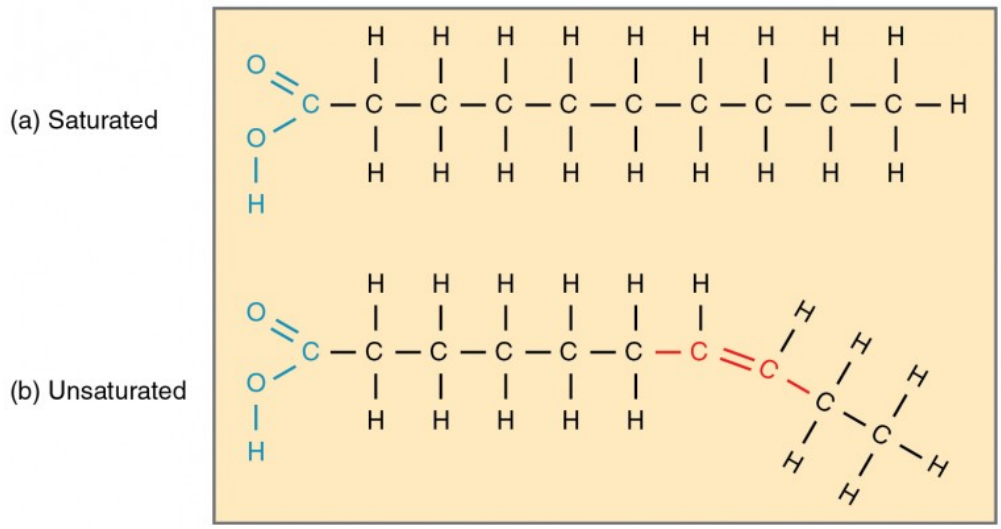


Figure 5. Fatty Acid Shapes. The level of saturation of a fatty acid affects its shape. (a) Saturated fatty acid chains are straight. (b) Unsaturated fatty acid chains are kinked.

Whereas a diet high in saturated fatty acids increases the risk of heart disease, a diet high in unsaturated fatty acids is thought to reduce the risk. This is especially true for the omega-3 unsaturated fatty acids found in cold-water fish such as salmon. These fatty acids have their first double carbon bond at the third hydrocarbon from the methyl group (referred to as the omega end of the molecule).

Finally, *trans* fatty acids found in some processed foods, including some stick and tub margarines, are thought to be even more harmful to the heart and blood vessels than saturated fatty acids. *Trans* fats are created from unsaturated fatty acids (such as corn oil) when chemically treated to produce partially hydrogenated fats.

As a group, triglycerides are a major fuel source for the body. When you are resting or asleep, a majority of the energy used to keep you alive is derived from triglycerides stored in your fat (adipose) tissues. Triglycerides also fuel long, slow physical activity such as gardening or hiking, and contribute a modest percentage of energy for vigorous physical activity. Dietary fat also assists the absorption and transport of the nonpolar fat-soluble vitamins A, D, E, and K. Additionally, stored body fat protects and cushions the body's bones and internal organs, and acts as insulation to retain body heat.

Fatty acids are also components of glycolipids, which are sugar-fat compounds found in the cell membrane. Lipoproteins are compounds in which the hydrophobic triglycerides are packaged in protein envelopes for transport in body fluids.

Phospholipids

As its name suggests, a **phospholipid** is a bond between the glycerol component of a lipid and a phosphorous molecule. In fact, phospholipids are similar in structure to triglycerides. However, instead of having three fatty acids, a phospholipid is generated from a diglyceride, a glycerol with just two fatty acid chains (Figure 6). The third binding site on the glycerol is taken up by the phosphate group, which in turn is attached to a polar "head" region of the molecule. Recall that triglycerides are nonpolar and hydrophobic. This still holds for the fatty acid portion of a phospholipid compound. However, the phosphate-containing group at the head of the compound is polar and thereby hydrophilic. In other words, one end of the molecule can interact with oil, and the other end with water. This makes phospholipids ideal emulsifiers, compounds that help disperse fats in aqueous liquids, and enables them to interact with both the watery interior of cells and the watery solution outside of cells as components of the cell membrane.

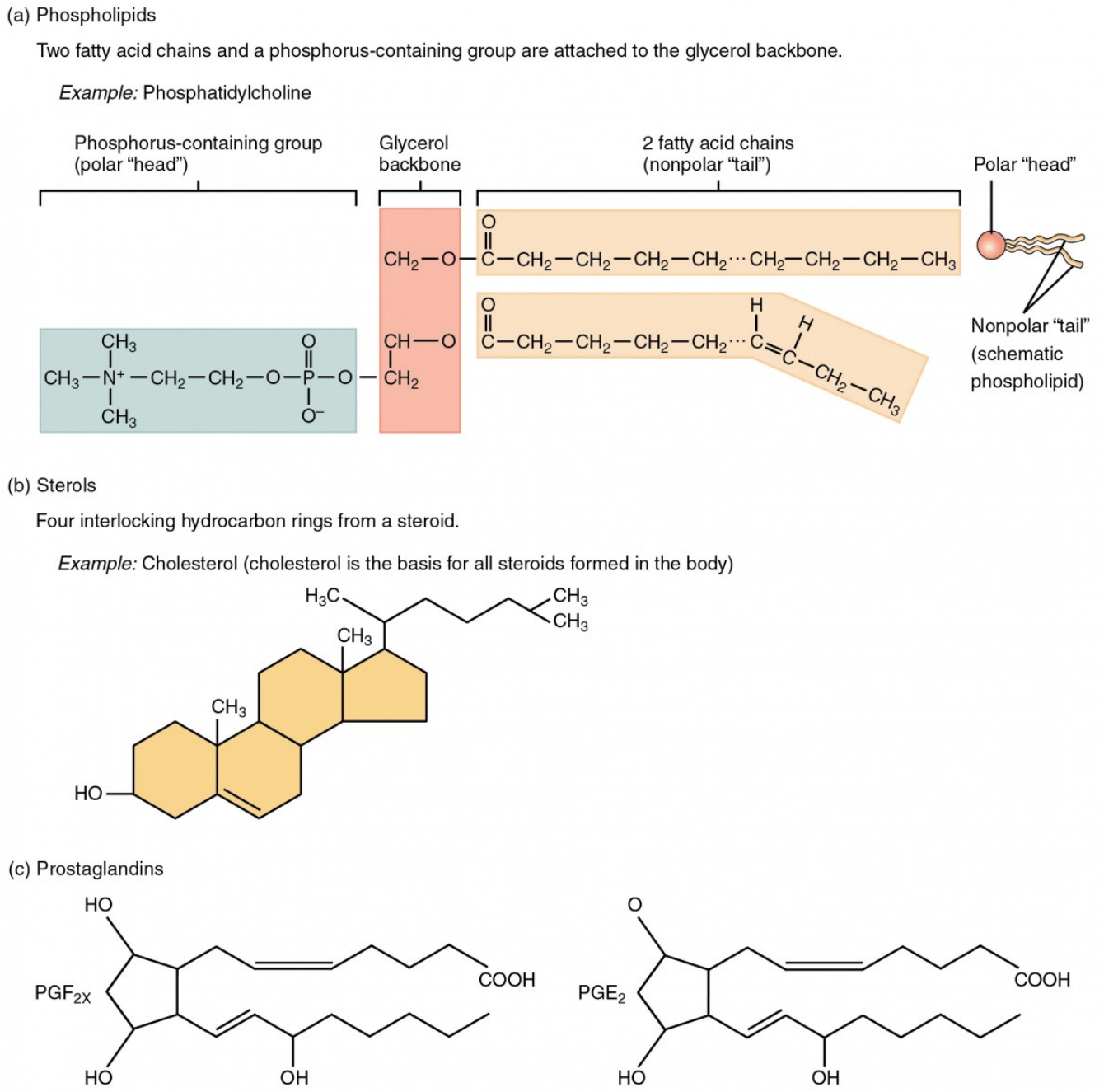


Figure 6. Other Important Lipids. *(a) Phospholipids are composed of two fatty acids, glycerol, and a phosphate group. (b) Sterols are ring-shaped lipids. Shown here is cholesterol. (c) Prostaglandins are derived from unsaturated fatty acids. Prostaglandin E2 (PGE2) includes hydroxyl and carboxyl groups.*

Steroids

A **steroid** compound (referred to as a sterol) has as its foundation a set of four hydrocarbon rings bonded to a variety of other atoms and molecules (see Figure 6b). Although both plants and animals synthesize sterols, the type that makes the most important contribution to human structure and function is cholesterol, which is synthesized by the liver in humans and animals and is also present in most animal-based foods. Like other lipids, cholesterol's hydrocarbons make it hydrophobic; however, it has a polar hydroxyl head that is hydrophilic. Cholesterol is an important component of bile acids, compounds that help emulsify dietary fats. In fact, the word root *chole–* refers to bile. Cholesterol is also a building block of many hormones, signaling molecules that the body releases to regulate processes at distant sites. Finally, like phospholipids, cholesterol molecules are found in

the cell membrane, where their hydrophobic and hydrophilic regions help regulate the flow of substances into and out of the cell.

Prostaglandins

Like a hormone, a **prostaglandin** is one of a group of signaling molecules, but prostaglandins are derived from unsaturated fatty acids (see Figure 6c). One reason that the omega-3 fatty acids found in fish are beneficial is that they stimulate the production of certain prostaglandins that help regulate aspects of blood pressure and inflammation, and thereby reduce the risk for heart disease. Prostaglandins also sensitize nerves to pain. One class of pain-relieving medications called nonsteroidal anti-inflammatory drugs (NSAIDs) works by reducing the effects of prostaglandins.

Proteins

You might associate proteins with muscle tissue, but in fact, proteins are critical components of all tissues and organs. A **protein** is an organic molecule composed of amino acids linked by peptide bonds. Proteins include the keratin in the epidermis of skin that protects underlying tissues, the collagen found in the dermis of skin, in bones, and in the meninges that cover the brain and spinal cord. Proteins are also components of many of the body's functional chemicals, including digestive enzymes in the digestive tract, antibodies, the neurotransmitters that neurons use to communicate with other cells, and the peptide-based hormones that regulate certain body functions (for instance, growth hormone). While carbohydrates and lipids are composed of hydrocarbons and oxygen, all proteins also contain nitrogen (N), and many contain sulfur (S), in addition to carbon, hydrogen, and oxygen.

Microstructure of Proteins

Proteins are polymers made up of nitrogen-containing monomers called amino acids. An **amino acid** is a molecule composed of an amino group and a carboxyl group, together with a variable side chain. Just 20 different amino acids contribute to nearly all of the thousands of different proteins important in human structure and function. Body proteins contain a unique combination of a few dozen to a few hundred of these 20 amino acid monomers. All 20 of these amino acids share a similar structure (Figure 7). All consist of a central carbon atom to which the following are bonded:

- a hydrogen atom
- an alkaline (basic) amino group NH_2 (see Table 1)
- an acidic carboxyl group COOH (see Table 1)
- a variable group

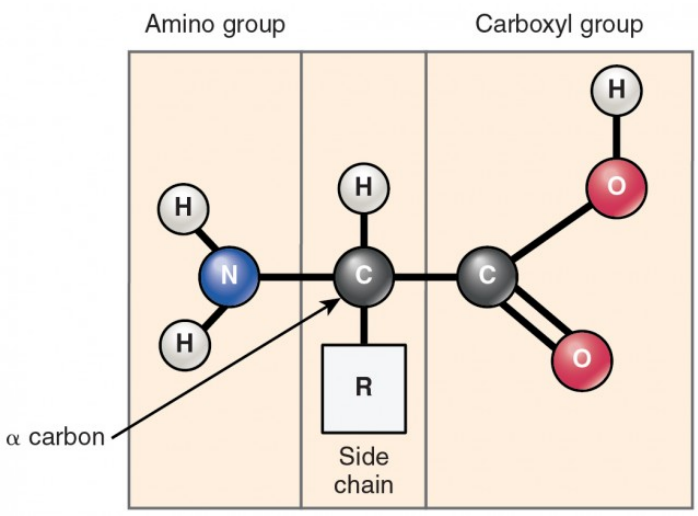


Figure 7. Structure of an Amino Acid

Notice that all amino acids contain both an acid (the carboxyl group) and a base (the amino group) (*amine* = "nitrogen-containing"). For this reason, they make excellent buffers, helping the body regulate acid–base balance. What distinguishes the 20 amino acids from one another is their variable group, which is referred to as a side chain or an R-group. This group can vary in size and can be polar or nonpolar, giving each amino acid its unique characteristics. For example, the side chains of two amino acids—cysteine and methionine—contain sulfur. Sulfur does not readily participate in hydrogen bonds, whereas all other amino acids do. This variation influences the way that proteins containing cysteine and methionine are assembled.

Amino acids join via dehydration synthesis to form protein polymers (Figure 8). The unique bond holding amino acids together is called a peptide bond. A **peptide bond** is a covalent bond between two amino acids that forms by dehydration synthesis. A peptide, in fact, is a very short chain of amino acids. Strands containing fewer than about 100 amino acids are generally referred to as polypeptides rather than proteins.

The body is able to synthesize most of the amino acids from components of other molecules; however, nine cannot be synthesized and have to be consumed in the diet. These are known as the essential amino acids.

Free amino acids available for protein construction are said to reside in the amino acid pool within cells. Structures within cells use these amino acids when assembling proteins. If a particular essential amino acid is not available in sufficient quantities in the amino acid pool, however, synthesis of proteins containing it can slow or even cease.

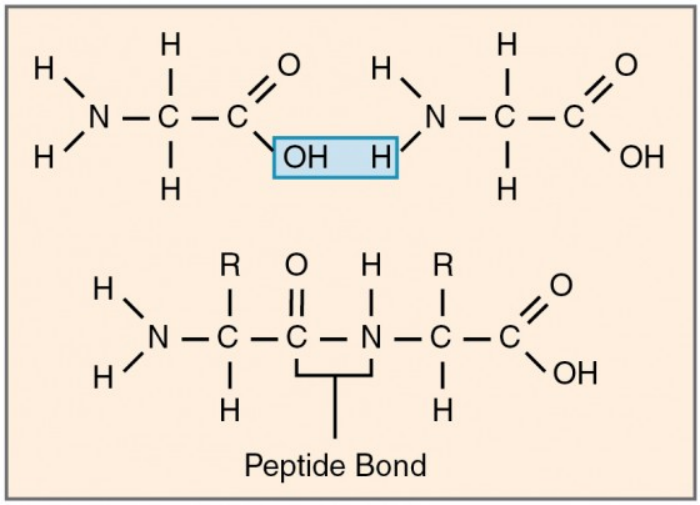


Figure 8. Peptide Bond. *Different amino acids join together to form peptides, polypeptides, or proteins via dehydration synthesis. The bonds between the amino acids are peptide bonds.*

Shape of Proteins

Just as a fork cannot be used to eat soup and a spoon cannot be used to spear meat, a protein's shape is essential to its function. A protein's shape is determined, most fundamentally, by the sequence of amino acids of which it is made (Figure 9a). The sequence is called the primary structure of the protein.

Although some polypeptides exist as linear chains, most are twisted or folded into more complex secondary structures that form when bonding occurs between amino acids with different properties at different regions of the polypeptide. The most common secondary structure is a spiral called an alpha-helix. If you were to take a length of string and simply twist it into a spiral, it would not hold the shape. Similarly, a strand of amino acids could not maintain a stable spiral shape without the help of hydrogen bonds, which create bridges between different regions of the same strand (see Figure 9b). Less commonly, a polypeptide chain can form a beta-pleated sheet, in which hydrogen bonds form bridges between different regions of a single polypeptide that has folded back upon itself, or between two or more adjacent polypeptide chains.

The secondary structure of proteins further folds into a compact three-dimensional shape, referred to as the protein's tertiary structure (see Figure 9c). In this configuration, amino acids that had been very distant in the primary chain can be brought quite close via hydrogen bonds or, in proteins containing cysteine, via disulfide bonds. A **disulfide bond** is a covalent bond between sulfur atoms in a polypeptide. Often, two or more separate polypeptides bond to form an even larger protein with a quaternary structure (see Figure 9d). The polypeptide subunits forming a quaternary structure can be identical or different. For instance, hemoglobin, the protein found in red blood cells is composed of four tertiary polypeptides, two of which are called alpha chains and two of which are called beta chains.

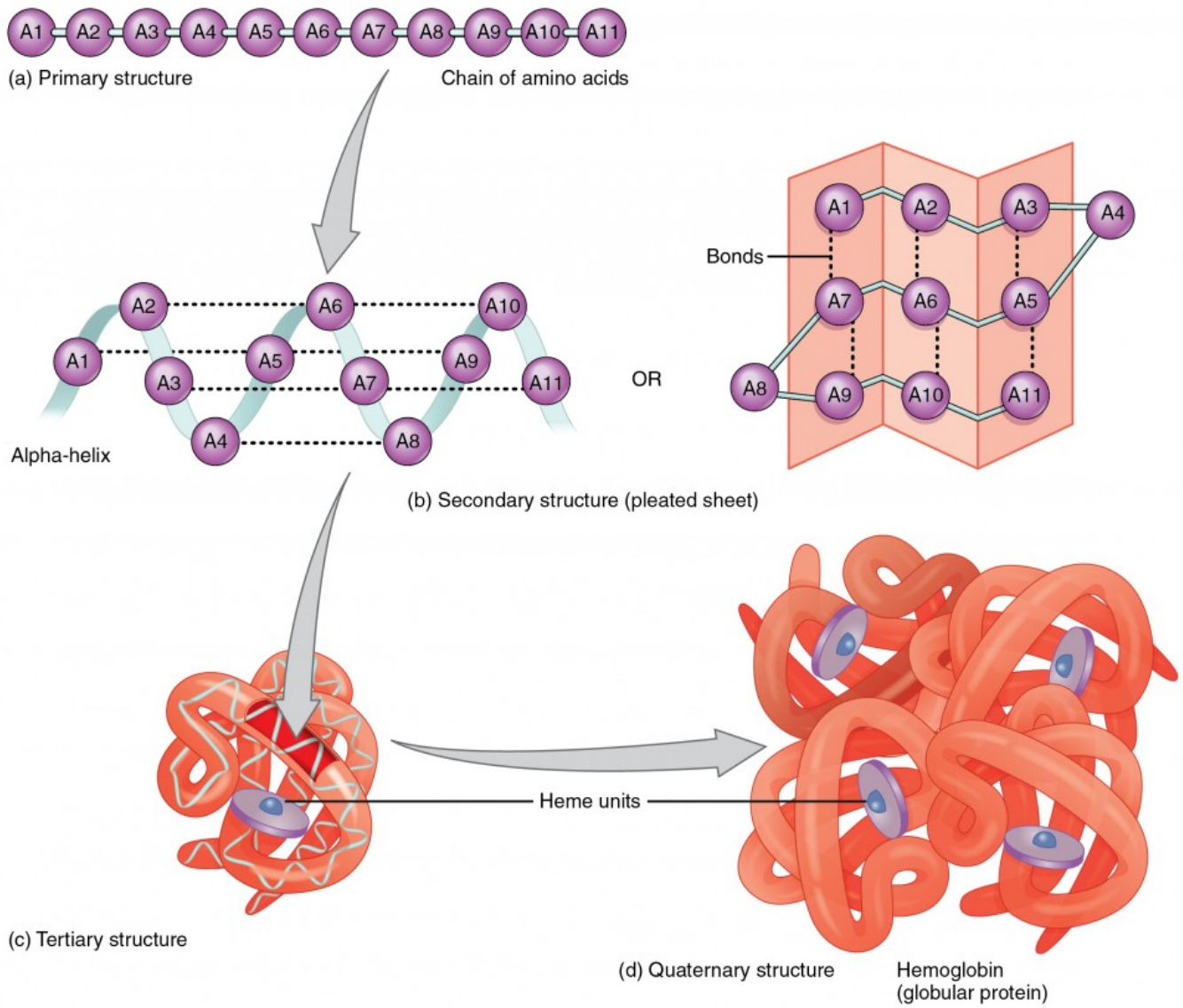


Figure 9. The Shape of Proteins. *(a) The primary structure is the sequence of amino acids that make up the polypeptide chain. (b) The secondary structure, which can take the form of an alpha-helix or a beta-pleated sheet, is maintained by hydrogen bonds between amino acids in different regions of the original polypeptide strand. (c) The tertiary structure occurs as a result of further folding and bonding of the secondary structure. (d) The quaternary structure occurs as a result of interactions between two or more tertiary subunits. The example shown here is hemoglobin, a protein in red blood cells which transports oxygen to body tissues.*

When they are exposed to extreme heat, acids, bases, and certain other substances, proteins will denature. *Denaturation* is a change in the structure of a molecule through physical or chemical means. Denatured proteins lose their functional shape and are no longer able to carry out their jobs. An everyday example of protein denaturation is the curdling of milk when acidic lemon juice is added.

The contribution of the shape of a protein to its function can hardly be exaggerated. For example, the long, slender shape of protein strands that make up muscle tissue is essential to their ability to contract (shorten) and relax (lengthen). As another example, bones contain long threads of a protein called collagen that acts as scaffolding upon which bone minerals are deposited. These elongated proteins, called fibrous proteins, are strong and durable and typically hydrophobic.

In contrast, globular proteins are globes or spheres that tend to be highly reactive and are hydrophilic. The hemoglobin proteins packed into red blood cells are an example (see Figure 9d); however, globular proteins are abundant throughout the body, playing critical roles in most body functions. Enzymes, introduced earlier as protein catalysts, are examples of this. The next section takes a closer look at the action of enzymes.

Proteins Function as Enzymes

If you were trying to type a paper, and every time you hit a key on your laptop there was a delay of six or seven minutes before you got a response, you would probably get a new laptop. In a similar way, without enzymes to catalyze chemical reactions, the human body would be nonfunctional. It functions only because enzymes function.

Enzymatic reactions—chemical reactions catalyzed by enzymes—begin when substrates bind to the enzyme. A **substrate** is a reactant in an enzymatic reaction. This occurs on regions of the enzyme known as active sites (Figure 10). Any given enzyme catalyzes just one type of chemical reaction. This characteristic, called specificity, is due to the fact that a substrate with a particular shape and electrical charge can bind only to an active site corresponding to that substrate.

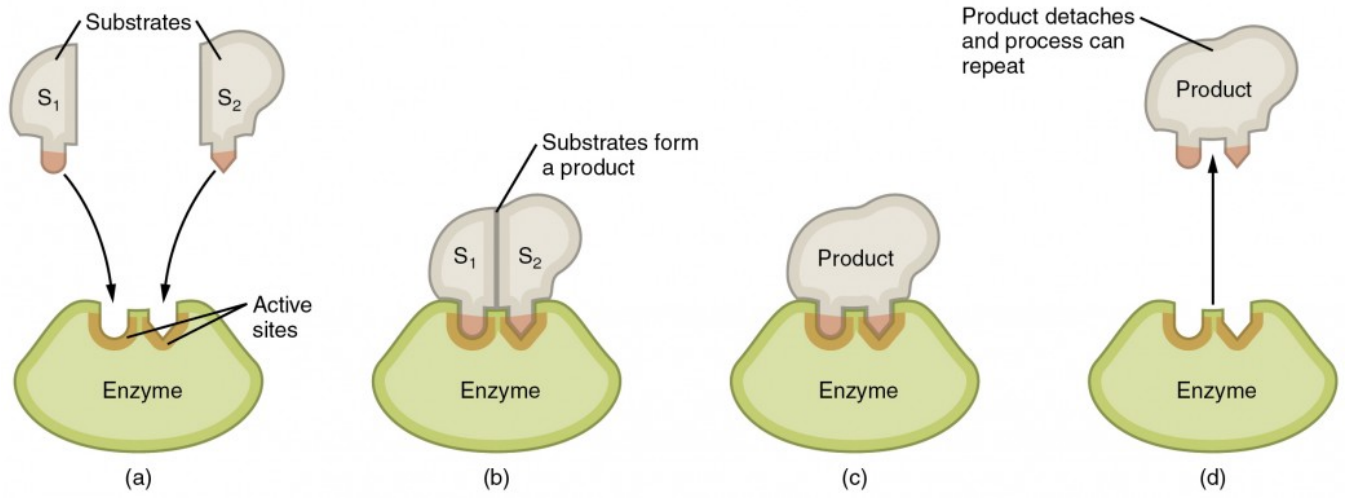


Figure 10. Steps in an Enzymatic Reaction. *(a) Substrates approach active sites on enzyme. (b) Substrates bind to active sites, producing an enzyme–substrate complex. (c) Changes internal to the enzyme–substrate complex facilitate interaction of the substrates. (d) Products are released and the enzyme returns to its original form, ready to facilitate another enzymatic reaction.*

Binding of a substrate produces an enzyme–substrate complex. It is likely that enzymes speed up chemical reactions in part because the enzyme–substrate complex undergoes a set of temporary and reversible changes that cause the substrates to be oriented toward each other in an optimal position to facilitate their interaction. This promotes increased reaction speed. The enzyme then releases the product(s), and resumes its original shape. The enzyme is then free to engage in the process again, and will do so as long as substrate remains.

Other Functions of Proteins

Advertisements for protein bars, powders, and shakes all say that protein is important in building, repairing, and maintaining muscle tissue, but the truth is that proteins contribute to all body tissues, from the skin to the brain cells. Also, certain proteins act as hormones, chemical messengers that help regulate body functions, For example, growth hormone is important for skeletal growth, among other roles.

As was noted earlier, the basic and acidic components enable proteins to function as buffers in maintaining acid–base balance, but they also help regulate fluid–electrolyte balance. Proteins attract fluid, and a healthy concentration of proteins in the blood, the cells, and the spaces between cells helps ensure a balance of fluids in these various “compartments.” Moreover, proteins in the cell membrane help to transport electrolytes in and out of the cell, keeping these ions in a healthy balance. Like lipids, proteins can bind with carbohydrates. They can thereby produce glycoproteins or proteoglycans, both of which have many functions in the body.

The body can use proteins for energy when carbohydrate and fat intake is inadequate, and stores of glycogen and adipose tissue become depleted. However, since there is no storage site for protein except functional tissues, using protein for energy causes tissue breakdown, and results in body wasting.

Nucleotides

The fourth type of organic compound important to human structure and function are the nucleotides (Figure 11). A **nucleotide** is one of a class of organic compounds composed of three subunits:

- one or more phosphate groups
- a pentose sugar: either deoxyribose or ribose
- a nitrogen-containing base: adenine, cytosine, guanine, thymine, or uracil

Nucleotides can be assembled into nucleic acids (DNA or RNA) or the energy compound adenosine triphosphate.

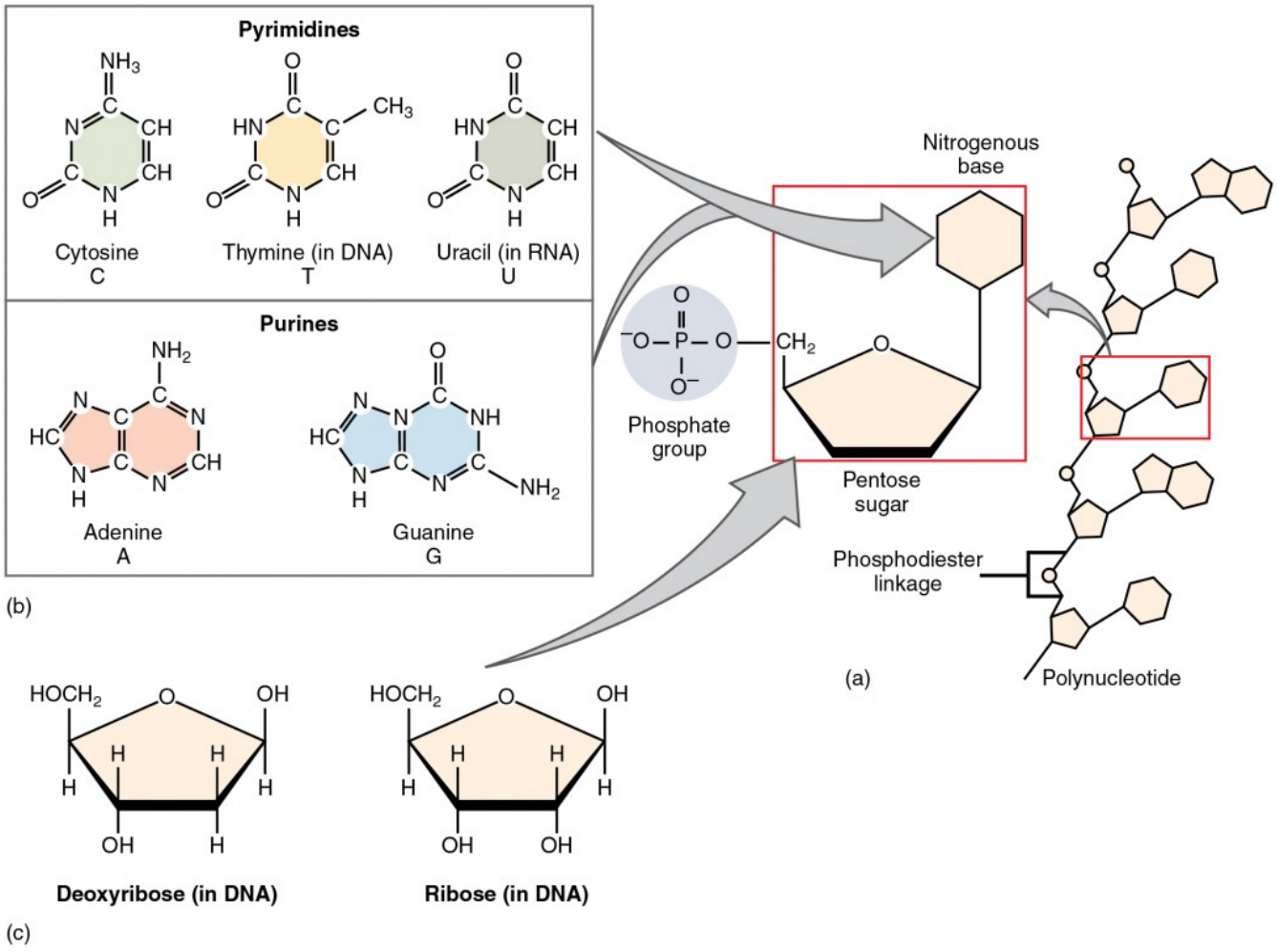


Figure 11. Nucleotides. (a) The building blocks of all nucleotides are one or more phosphate groups, a pentose sugar, and a nitrogen-containing base. (b) The nitrogen-containing bases of nucleotides. (c) The two pentose sugars of DNA and RNA.

Nucleic Acids

The nucleic acids differ in their type of pentose sugar. **Deoxyribonucleic acid (DNA)** is nucleotide that stores genetic information. DNA contains deoxyribose (so-called because it has one less atom of oxygen than ribose) plus one phosphate group and one nitrogen-containing base. The “choices” of base for DNA are adenine, cytosine, guanine, and thymine. **Ribonucleic acid (RNA)** is a ribose-containing nucleotide that helps manifest the genetic code as protein. RNA contains ribose, one phosphate group, and one nitrogen-containing base, but the “choices” of base for RNA are adenine, cytosine, guanine, and uracil.

The nitrogen-containing bases adenine and guanine are classified as purines. A **purine** is a nitrogen-containing molecule with a double ring structure, which accommodates several nitrogen atoms. The bases cytosine, thymine (found in DNA only) and uracil (found in RNA only) are pyramidines. A **pyramidine** is a nitrogen-containing base with a single ring structure

Bonds formed by dehydration synthesis between the pentose sugar of one nucleic acid monomer and the phosphate group of another form a "backbone," from which the components' nitrogen-containing bases protrude. In DNA, two such backbones attach at their protruding bases via hydrogen bonds. These twist to form a shape known as a double helix (Figure 12). The sequence of nitrogen-containing bases within a strand of DNA form the genes that act as a molecular code instructing cells in the assembly of amino acids into proteins. Humans have almost 22,000 genes in their DNA, locked up in the 46 chromosomes inside the nucleus of each cell (except red blood cells which lose their nuclei during development). These genes carry the genetic code to build one's body, and are unique for each individual except identical twins.

In contrast, RNA consists of a single strand of sugar-phosphate backbone studded with bases. Messenger RNA (mRNA) is created during protein synthesis to carry the genetic instructions from the DNA to the cell's protein manufacturing plants in the cytoplasm, the ribosomes.

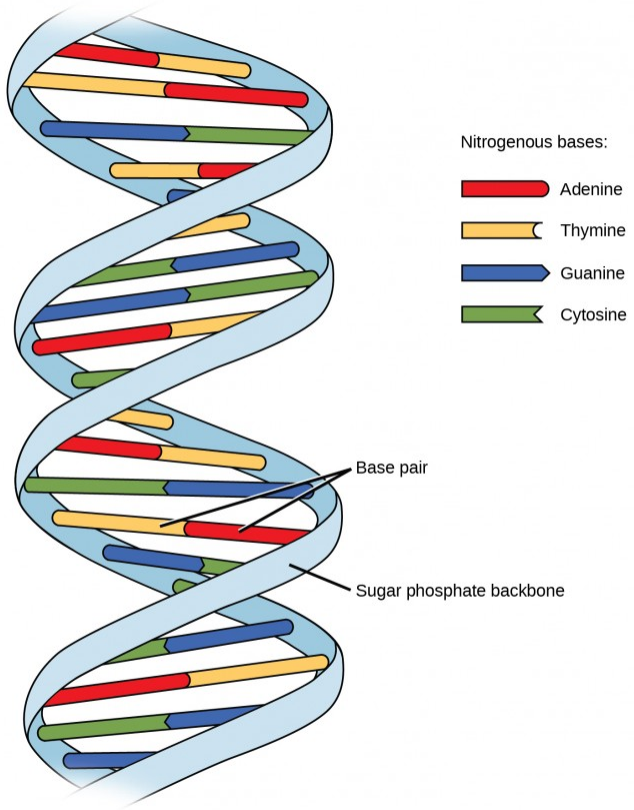


Figure 12. DNA. *In the DNA double helix, two strands attach via hydrogen bonds between the bases of the component nucleotides.*

Adenosine Triphosphate

The nucleotide adenosine triphosphate (ATP), is composed of a ribose sugar, an adenine base, and three phosphate groups (Figure 13). ATP is classified as a high energy compound because the two covalent bonds linking its three phosphates store a significant amount of potential energy. In the body, the energy released from these high energy bonds helps fuel the body's activities, from muscle contraction to the transport of substances in and out of cells to anabolic chemical reactions.

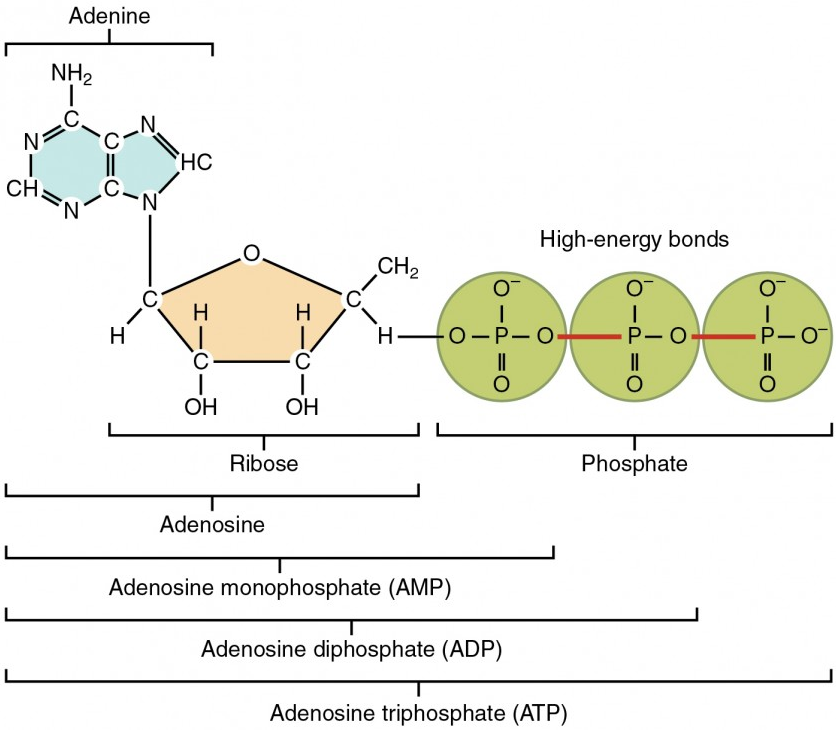


Figure 13. Structure of Adenosine Triphosphate (ATP)

When a phosphate group is cleaved from ATP, the products are adenosine diphosphate (ADP) and inorganic phosphate (P_i). This hydrolysis reaction can be written:

$ATP + H_2O \rightarrow ADP + P_i + \text{energy}$

Removal of a second phosphate leaves adenosine monophosphate (AMP) and two phosphate groups. Again, these reactions also liberate the energy that had been stored in the phosphate-phosphate bonds. They are reversible, too, as when ADP undergoes phosphorylation. **Phosphorylation** is the addition of a phosphate group to an organic compound, in this case, resulting in ATP. In such cases, the same level of energy that had been released during hydrolysis must be reinvested to power dehydration synthesis.

Cells can also transfer a phosphate group from ATP to another organic compound. For example, when glucose first enters a cell, a phosphate group is transferred from ATP, forming glucose phosphate ($C_6H_{12}O_6$—P) and ADP. Once glucose is phosphorylated in this way, it can be stored as glycogen or metabolized for immediate energy.

GLOSSARY: THE CHEMICAL LEVEL OF ORGANIZATION

acid: compound that releases hydrogen ions (H^+) in solution

activation energy: amount of energy greater than the energy contained in the reactants, which must be overcome for a reaction to proceed

adenosine triphosphate (ATP): nucleotide containing ribose and an adenine base that is essential in energy transfer

amino acid: building block of proteins; characterized by an amino and carboxyl functional groups and a variable side-chain

anion: atom with a negative charge

atom: smallest unit of an element that retains the unique properties of that element

atomic number: number of protons in the nucleus of an atom

base: compound that accepts hydrogen ions (H^+) in solution

bond: electrical force linking atoms

buffer: solution containing a weak acid or a weak base that opposes wide fluctuations in the pH of body fluids

carbohydrate: class of organic compounds built from sugars, molecules containing carbon, hydrogen, and oxygen in a 1-2-1 ratio

catalyst: substance that increases the rate of a chemical reaction without itself being changed in the process

cation: atom with a positive charge

chemical energy: form of energy that is absorbed as chemical bonds form, stored as they are maintained, and released as they are broken

colloid: liquid mixture in which the solute particles consist of clumps of molecules large enough to scatter light

compound: substance composed of two or more different elements joined by chemical bonds

concentration: number of particles within a given space

covalent bond: chemical bond in which two atoms share electrons, thereby completing their valence shells

decomposition reaction: type of catabolic reaction in which one or more bonds within a larger molecule are broken, resulting in the release of smaller molecules or atoms

denaturation: change in the structure of a molecule through physical or chemical means

deoxyribonucleic acid (DNA): deoxyribose-containing nucleotide that stores genetic information

disaccharide: pair of carbohydrate monomers bonded by dehydration synthesis via a glycosidic bond

disulfide bond: covalent bond formed within a polypeptide between sulfide groups of sulfur-containing amino acids, for example, cysteine

electron shell: area of space a given distance from an atom's nucleus in which electrons are grouped

electron: subatomic particle having a negative charge and nearly no mass; found orbiting the atom's nucleus

element: substance that cannot be created or broken down by ordinary chemical means

enzyme: protein or RNA that catalyzes chemical reactions

exchange reaction: type of chemical reaction in which bonds are both formed and broken, resulting in the transfer of components

functional group: group of atoms linked by strong covalent bonds that tends to behave as a distinct unit in chemical reactions with other atoms

hydrogen bond: dipole-dipole bond in which a hydrogen atom covalently bonded to an electronegative atom is weakly attracted to a second electronegative atom

inorganic compound: substance that does not contain both carbon and hydrogen

ionic bond: attraction between an anion and a cation

ion: atom with an overall positive or negative charge

isotope: one of the variations of an element in which the number of neutrons differ from each other

kinetic energy: energy that matter possesses because of its motion

lipid: class of nonpolar organic compounds built from hydrocarbons and distinguished by the fact that they are not soluble in water

macromolecule: large molecule formed by covalent bonding

mass number: sum of the number of protons and neutrons in the nucleus of an atom

matter: physical substance; that which occupies space and has mass

molecule: two or more atoms covalently bonded together

monosaccharide: monomer of carbohydrate; also known as a simple sugar

neutron: heavy subatomic particle having no electrical charge and found in the atom's nucleus

nucleotide: class of organic compounds composed of one or more phosphate groups, a pentose sugar, and a base

organic compound: substance that contains both carbon and hydrogen

pH: negative logarithm of the hydrogen ion (H^+) concentration of a solution

peptide bond: covalent bond formed by dehydration synthesis between two amino acids

periodic table of the elements: arrangement of the elements in a table according to their atomic number; elements having similar properties because of their electron arrangements compose columns in the table, while elements having the same number of valence shells compose rows in the table

phospholipid: a lipid compound in which a phosphate group is combined with a diglyceride

phosphorylation: addition of one or more phosphate groups to an organic compound

polar molecule: molecule with regions that have opposite charges resulting from uneven numbers of electrons in the nuclei of the atoms participating in the covalent bond

polysaccharide: compound consisting of more than two carbohydrate monomers bonded by dehydration synthesis via glycosidic bonds

potential energy: stored energy matter possesses because of the positioning or structure of its components

product: one or more substances produced by a chemical reaction

prostaglandin: lipid compound derived from fatty acid chains and important in regulating several body processes

protein: class of organic compounds that are composed of many amino acids linked together by peptide bonds

proton: heavy subatomic particle having a positive charge and found in the atom's nucleus

purine: nitrogen-containing base with a double ring structure; adenine and guanine

pyrimidine: nitrogen-containing base with a single ring structure; cytosine, thiamine, and uracil

radioactive isotope: unstable, heavy isotope that gives off subatomic particles, or electromagnetic energy, as it decays; also called radioisotopes

reactant: one or more substances that enter into the reaction

ribonucleic acid (RNA): ribose-containing nucleotide that helps manifest the genetic code as protein

solution: homogeneous liquid mixture in which a solute is dissolved into molecules within a solvent

steroid: (also, sterol) lipid compound composed of four hydrocarbon rings bonded to a variety of other atoms and molecules

substrate: reactant in an enzymatic reaction

suspension: liquid mixture in which particles distributed in the liquid settle out over time

synthesis reaction: type of anabolic reaction in which two or more atoms or molecules bond, resulting in the formation of a larger molecule

triglyceride: lipid compound composed of a glycerol molecule bonded with three fatty acid chains

valence shell: outermost electron shell of an atom

PRACTICE TEST: THE CHEMICAL LEVEL OF ORGANIZATION

Review the material from this module by completing the practice in course online.

MODULE 4: THE CELLULAR LEVEL OF ORGANIZATION

INTRODUCTION TO THE CELLULAR LEVEL OF ORGANIZATION

Learning Objectives

- Describe the structure and function of the cell membrane, including its regulation of materials into and out of the cell
- Describe the functions of the various cytoplasmic organelles
- Explain the structure and contents of the nucleus, as well as the process of DNA replication
- Explain the process by which a cell builds proteins using the DNA code
- List the stages of the cell cycle in order, including the steps of cell division in both somatic cells
- Discuss how a cell differentiates and becomes more specialized
- List the morphological and physiological characteristics of some representative cell types in the human body

You developed from a single fertilized egg cell into the complex organism containing trillions of cells that you see when you look in a mirror. During this developmental process, early, undifferentiated cells differentiate and become specialized in their structure and function. These different cell types form specialized tissues that work in concert to perform all of the functions necessary for the living organism. Cellular and developmental biologists study how the continued division of a single cell leads to such complexity and differentiation.

Consider the difference between a structural cell in the skin and a nerve cell. A structural skin cell may be shaped like a flat plate (squamous) and live only for a short time before it is shed and replaced. Packed tightly into rows and sheets, the squamous skin cells provide a protective barrier for the cells and tissues that lie beneath. A nerve cell, on the other hand, may be shaped something like a star, sending out long processes up to a meter in length and may live for the entire lifetime of the organism. With their long winding appendages, nerve cells can communicate with one another and with other types of body cells and send rapid signals that inform the organism about its environment and allow it to interact with that environment.

These differences illustrate one very important theme that is consistent at all organizational levels of biology: the form of a structure is optimally suited to perform particular functions assigned to that structure. Keep this theme in mind as you tour the inside of a cell and are introduced to the various types of cells in the body. A primary responsibility of each cell is to contribute to homeostasis.

Homeostasis is a term used in biology that refers to a dynamic state of balance within parameters that are compatible with life. For example, living cells require a water-based environment to survive in, and there are various physical (anatomical) and physiological mechanisms that keep all of the trillions of living cells in the human body moist. This is one aspect of homeostasis. When a particular parameter, such as blood pressure or

blood oxygen content, moves far enough *out* of homeostasis (generally becoming too high or too low), illness or disease—and sometimes death—inevitably results.

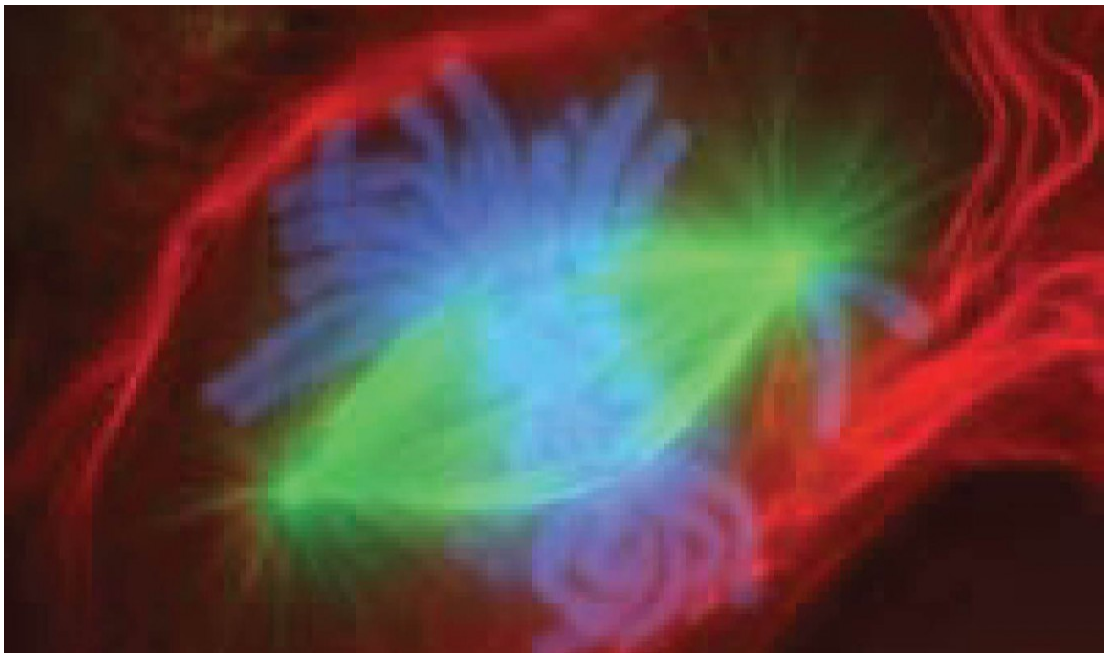


Figure 1. Flourescence-stained Cell Undergoing Mitosis. *A lung cell from a newt, commonly studied for its similarity to human lung cells, is stained with fluorescent dyes. The green stain reveals mitotic spindles, red is the cell membrane and part of the cytoplasm, and the structures that appear light blue are chromosomes. This cell is in anaphase of mitosis. (credit: "Mortadelo2005"/Wikimedia Commons)*

The concept of a cell started with microscopic observations of dead cork tissue by scientist Robert Hooke in 1665. Without realizing their function or importance, Hook coined the term "cell" based on the resemblance of the small subdivisions in the cork to the rooms that monks inhabited, called cells. About ten years later, Antonie van Leeuwenhoek became the first person to observe living and moving cells under a microscope. In the century that followed, the theory that cells represented the basic unit of life would develop. These tiny fluid-filled sacs house components responsible for the thousands of biochemical reactions necessary for an organism to grow and survive. In this chapter, you will learn about the major components and functions of a prototypical, generalized cell and discover some of the different types of cells in the human body.

THE CELL MEMBRANE

Learning Objectives

- Describe the molecular components that make up the cell membrane
- Explain the major features and properties of the cell membrane
- Differentiate between materials that can and cannot diffuse through the lipid bilayer
- Compare and contrast different types of passive transport with active transport, providing examples of each

Despite differences in structure and function, all living cells in multicellular organisms have a surrounding cell membrane. As the outer layer of your skin separates your body from its environment, the cell membrane (also known as the plasma membrane) separates the inner contents of a cell from its exterior environment. This cell membrane provides a protective barrier around the cell and regulates which materials can pass in or out.

Structure and Composition of the Cell Membrane

The **cell membrane** is an extremely pliable structure composed primarily of back-to-back phospholipids (a "bilayer"). Cholesterol is also present, which contributes to the fluidity of the membrane, and there are various proteins embedded within the membrane that have a variety of functions. A single phospholipid molecule has a phosphate group on one end, called the "head," and two side-by-side chains of fatty acids that make up the lipid tails (Figure 1). The phosphate group is negatively charged, making the head polar and hydrophilic—or "water loving."

A **hydrophilic** molecule (or region of a molecule) is one that is attracted to water. The phosphate heads are thus attracted to the water molecules of both the extracellular and intracellular environments. The lipid tails, on the other hand, are uncharged, or nonpolar, and are hydrophobic—or "water fearing."

A **hydrophobic** molecule (or region of a molecule) repels and is repelled by water. Some lipid tails consist of saturated fatty acids and some contain unsaturated fatty acids. This combination adds to the fluidity of the tails that are constantly in motion. Phospholipids are thus amphipathic molecules.

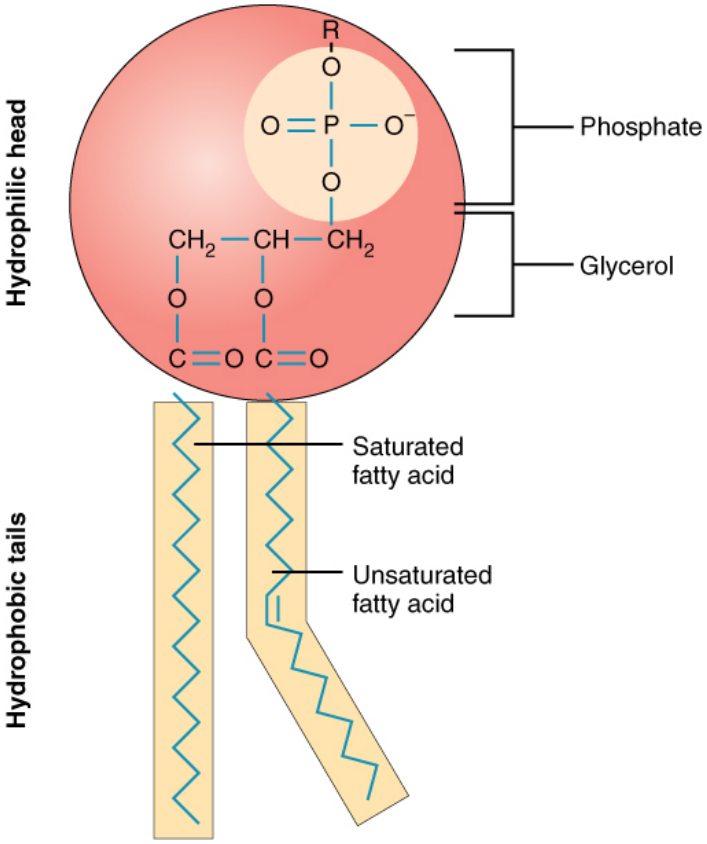


Figure 1. Phospholipid Structure. *A phospholipid molecule consists of a polar phosphate "head," which is hydrophilic and a non-polar lipid "tail," which is hydrophobic. Unsaturated fatty acids result in kinks in the hydrophobic tails.*

An **amphipathic** molecule is one that contains both a hydrophilic and a hydrophobic region. In fact, soap works to remove oil and grease stains because it has amphipathic properties. The hydrophilic portion can dissolve in water while the hydrophobic portion can trap grease in micelles that then can be washed away.

The cell membrane consists of two adjacent layers of phospholipids. The lipid tails of one layer face the lipid tails of the other layer, meeting at the interface of the two layers. The phospholipid heads face outward, one layer exposed to the interior of the cell and one layer exposed to the exterior (Figure 2).

Because the phosphate groups are polar and hydrophilic, they are attracted to water in the intracellular fluid. **Intracellular fluid (ICF)** is the fluid interior of the cell. The phosphate groups are also attracted to the extracellular fluid. **Extracellular fluid (ECF)** is the fluid environment outside the enclosure of the cell membrane. **Interstitial fluid (IF)** is the term given to extracellular fluid not contained within blood vessels. Because the lipid tails are hydrophobic, they meet in the inner region of the membrane, excluding watery intracellular and extracellular fluid from this space. The cell membrane has many proteins, as well as other lipids (such as cholesterol), that are associated with the phospholipid bilayer. An important feature of the membrane is that it remains fluid; the lipids and proteins in the cell membrane are not rigidly locked in place.

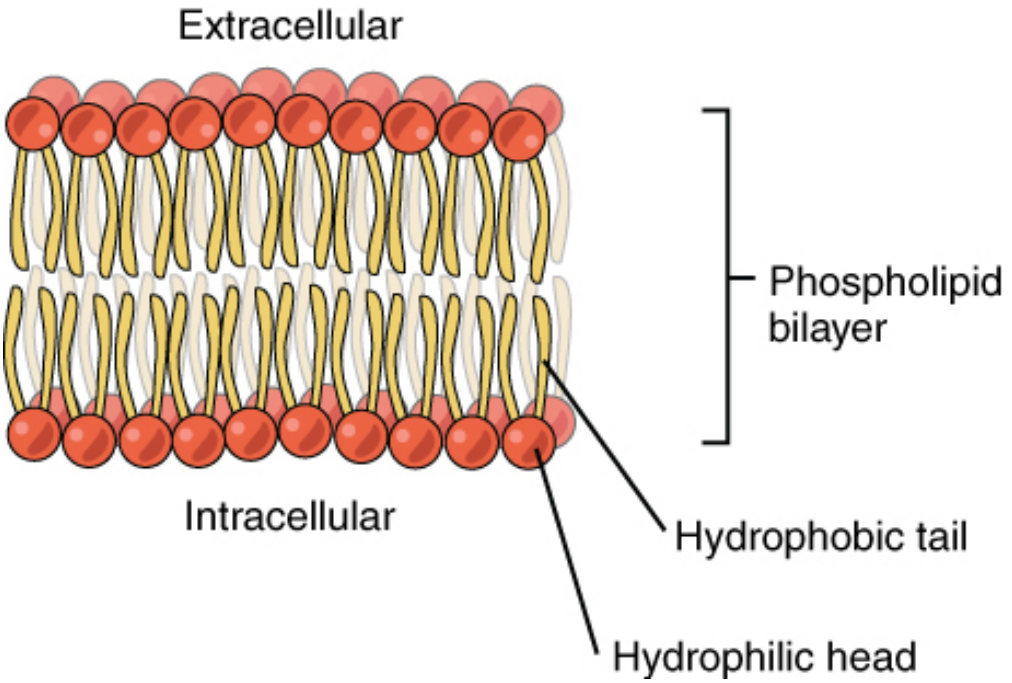


Figure 2. Phospolipid Bilayer. *The phospholipid bilayer consists of two adjacent sheets of phospholipids, arranged tail to tail. The hydrophobic tails associate with one another, forming the interior of the membrane. The polar heads contact the fluid inside and outside of the cell.*

Membrane Proteins

The lipid bilayer forms the basis of the cell membrane, but it is peppered throughout with various proteins. Two different types of proteins that are commonly associated with the cell membrane are the integral proteins and peripheral protein (Figure 3). As its name suggests, an integral protein is a protein that is embedded in the membrane. A channel protein is an example of an integral protein that selectively allows particular materials, such as certain ions, to pass into or out of the cell.

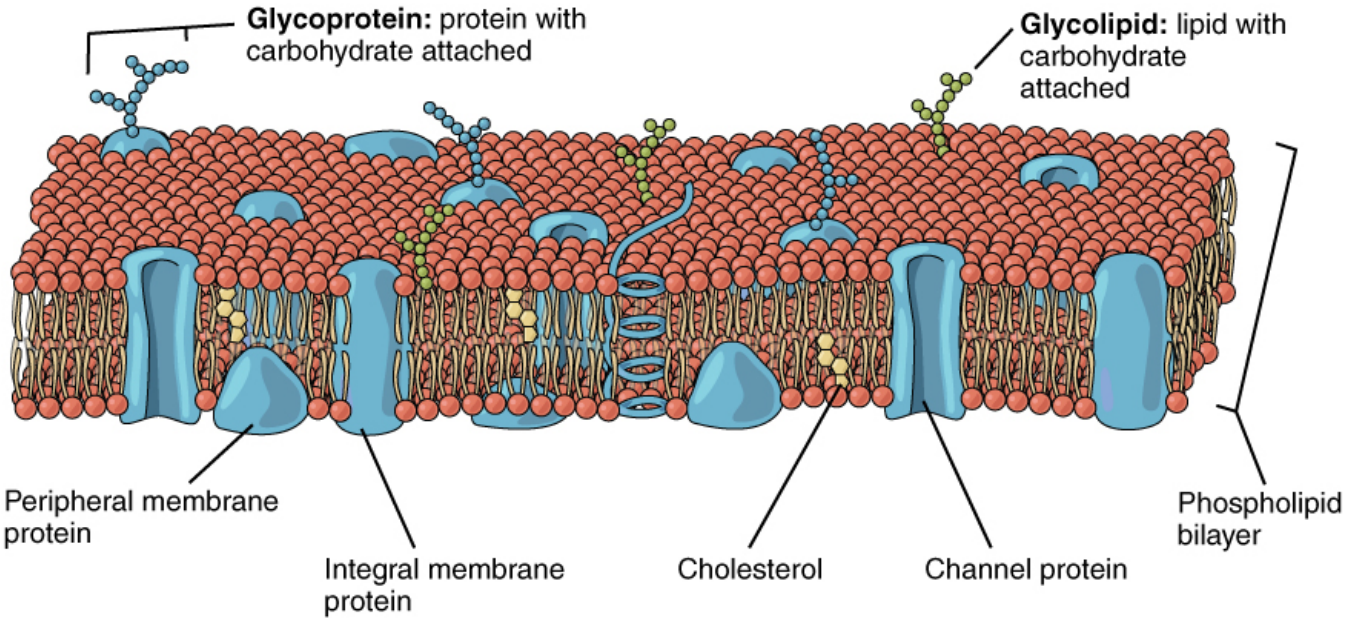


Figure 3. Cell Membrane. *The cell membrane of the cell is a phospholipid bilayer containing many different molecular components, including proteins and cholesterol, some with carbohydrate groups attached.*

Another important group of integral proteins are cell recognition proteins, which serve to mark a cell's identity so that it can be recognized by other cells. A **receptor** is a type of recognition protein that can selectively bind a specific molecule outside the cell, and this binding induces a chemical reaction within the cell. A **ligand** is the specific molecule that binds to and activates a receptor. Some integral proteins serve dual roles as both a receptor and an ion channel. One example of a receptor-ligand interaction is the receptors on nerve cells that bind neurotransmitters, such as dopamine. When a dopamine molecule binds to a dopamine receptor protein, a channel within the transmembrane protein opens to allow certain ions to flow into the cell.

Some integral membrane proteins are glycoproteins. A **glycoprotein** is a protein that has carbohydrate molecules attached, which extend into the extracellular matrix. The attached carbohydrate tags on glycoproteins aid in cell recognition. The carbohydrates that extend from membrane proteins and even from some membrane lipids collectively form the glycocalyx.

The **glycocalyx** is a fuzzy-appearing coating around the cell formed from glycoproteins and other carbohydrates attached to the cell membrane. The glycocalyx can have various roles. For example, it may have molecules that allow the cell to bind to another cell, it may contain receptors for hormones, or it might have enzymes to break down nutrients. The glycocalyces found in a person's body are products of that person's genetic makeup. They give each of the individual's trillions of cells the "identity" of belonging in the person's body. This identity is the primary way that a person's immune defense cells "know" not to attack the person's own body cells, but it also is the reason organs donated by another person might be rejected.

Peripheral proteins are typically found on the inner or outer surface of the lipid bilayer but can also be attached to the internal or external surface of an integral protein. These proteins typically perform a specific function for the cell. Some peripheral proteins on the surface of intestinal cells, for example, act as digestive enzymes to break down nutrients to sizes that can pass through the cells and into the bloodstream.

Transport across the Cell Membrane

One of the great wonders of the cell membrane is its ability to regulate the concentration of substances inside the cell. These substances include ions such as Ca^{++}, Na^{+}, K^{+}, and Cl^{-}; nutrients including sugars, fatty acids, and amino acids; and waste products, particularly carbon dioxide (CO_2), which must leave the cell. The membrane's lipid bilayer structure provides the first level of control. The phospholipids are tightly packed together, and the membrane has a hydrophobic interior. This structure causes the membrane to be selectively permeable. A membrane that has **selective permeability** allows only substances meeting certain criteria to pass through it unaided. In the case of the cell membrane, only relatively small, nonpolar materials can move through the lipid bilayer (remember, the lipid tails of the membrane are nonpolar). Some examples of these are other lipids, oxygen and carbon dioxide gases, and alcohol. However, water-soluble materials—like glucose, amino acids, and electrolytes—need some assistance to cross the membrane because they are repelled by the hydrophobic tails of the phospholipid bilayer. All substances that move through the membrane do so by one of two general methods, which are categorized based on whether or not energy is required. **Passive transport** is the movement of substances across the membrane without the expenditure of cellular energy. In contrast, **active transport** is the movement of substances across the membrane using energy from adenosine triphosphate (ATP).

Passive Transport

In order to understand *how* substances move passively across a cell membrane, it is necessary to understand concentration gradients and diffusion. A **concentration gradient** is the difference in concentration of a substance across a space. Molecules (or ions) will spread/diffuse from where they are more concentrated to where they are less concentrated until they are equally distributed in that space. (When molecules move in this way, they are said to move *down* their concentration gradient.) **Diffusion** is the movement of particles from an area of higher concentration to an area of lower concentration. A couple of common examples will help to illustrate this concept. Imagine being inside a closed bathroom. If a bottle of perfume were sprayed, the scent molecules would naturally diffuse from the spot where they left the bottle to all corners of the bathroom, and this diffusion would go on until no more concentration gradient remains. Another example is a spoonful of sugar placed in a cup of tea. Eventually the sugar will diffuse throughout the tea until no concentration gradient remains. In both cases, if the room is warmer or the tea hotter, diffusion occurs even faster as the molecules are bumping into each other and spreading out faster than at cooler temperatures. Having an internal body temperature around 98.6° F thus also aids in diffusion of particles within the body.

Visit this link to see diffusion and how it is propelled by the kinetic energy of molecules in solution. How does temperature affect diffusion rate, and why?

Whenever a substance exists in greater concentration on one side of a semipermeable membrane, such as the cell membranes, any substance that can move down its concentration gradient across the membrane will do so. Consider substances that can easily diffuse through the lipid bilayer of the cell membrane, such as the gases oxygen (O_2) and CO_2. O_2 generally diffuses into cells because it is more concentrated outside of them, and CO_2 typically diffuses out of cells because it is more concentrated inside of them. Neither of these examples requires any energy on the part of the cell, and therefore they use passive transport to move across the membrane. Before moving on, you need to review the gases that can diffuse across a cell membrane. Because cells rapidly use up oxygen during metabolism, there is typically a lower concentration of O_2 inside the cell than outside. As a result, oxygen will diffuse from the interstitial fluid directly through the lipid bilayer of the membrane and into the cytoplasm within the cell. On the other hand, because cells produce CO_2 as a byproduct of metabolism, CO_2 concentrations rise within the cytoplasm; therefore, CO_2 will move from the cell through the lipid bilayer and into the interstitial fluid, where its concentration is lower. This mechanism of molecules spreading from where they are more concentrated to where they are less concentration is a form of passive transport called simple diffusion (Figure 4).

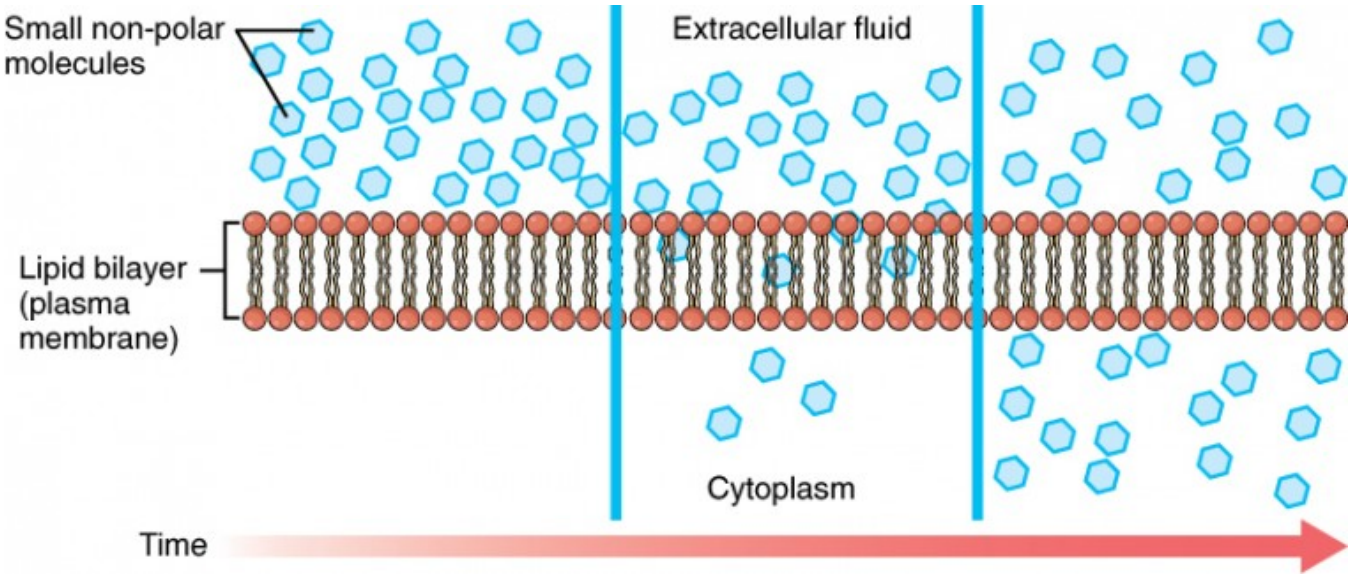


Figure 4. Simple Diffusion across the Cell (Plasma) Membrane. *The structure of the lipid bilayer allows only small, non-polar substances such as oxygen and carbon dioxide to pass through the cell membrane, down their concentration gradient, by simple diffusion.*

Solutes dissolved in water on either side of the cell membrane will tend to diffuse down their concentration gradients, but because most substances cannot pass freely through the lipid bilayer of the cell membrane, their movement is restricted to protein channels and specialized transport mechanisms in the membrane. **Facilitated diffusion** is the diffusion process used for those substances that cannot cross the lipid bilayer due to their size and/or polarity (Figure 5). A common example of facilitated diffusion is the movement of glucose into the cell, where it is used to make ATP. Although glucose can be more concentrated outside of a cell, it cannot cross the lipid bilayer via simple diffusion because it is both large and polar. To resolve this, a specialized carrier protein called the glucose transporter will transfer glucose molecules into the cell to facilitate its inward diffusion.

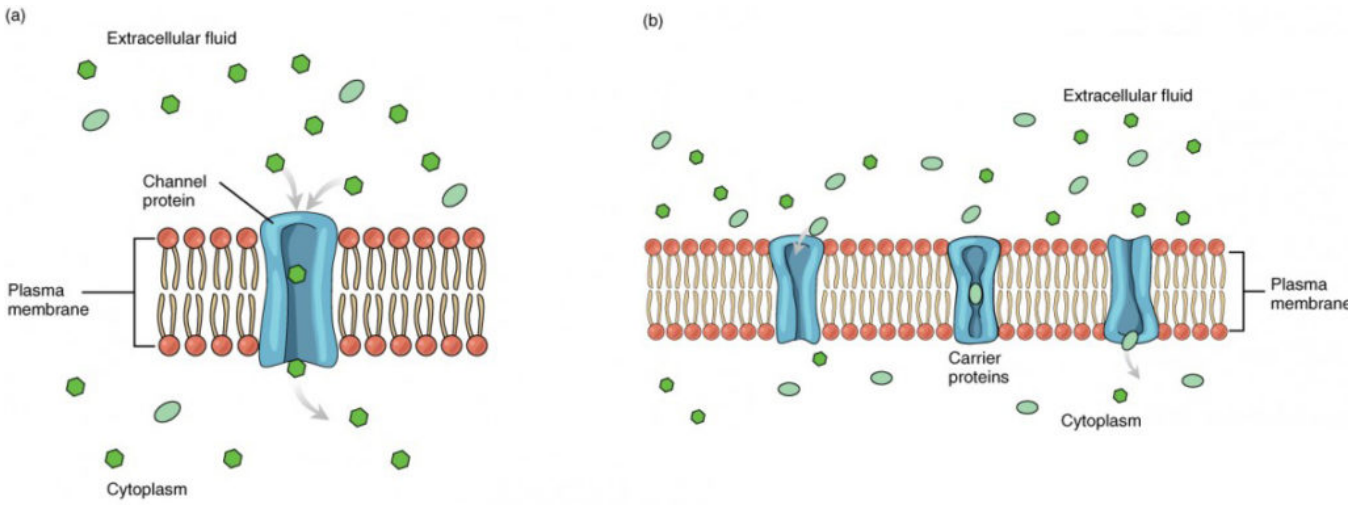


Figure 5. Facilitated Diffusion. *(a) Facilitated diffusion of substances crossing the cell (plasma) membrane takes place with the help of proteins such as channel proteins and carrier proteins. Channel proteins are less selective than carrier proteins, and usually mildly discriminate between their cargo based on size and charge. (b) Carrier proteins are more selective, often only allowing one particular type of molecule to cross.*

In some cases, facilitated diffusion might move two substances in the same direction across the membrane, called a "symport." For example, in intestinal cells, sodium ions and glucose molecules are co-transported into the cells. In other cases, the facilitated diffusion might only require a tunnel-like channel for particular solutes, such as electrolytes (small charged ions), to pass through the membrane (this is called a "uniport"). As an example, even though sodium ions (Na^+) are highly concentrated outside of cells, these electrolytes are polarized and cannot pass through the nonpolar lipid bilayer of the membrane. Their diffusion is facilitated by membrane proteins that form sodium channels (or "pores"), so that Na^+ ions can move down their concentration gradient from outside the cells to inside the cells. There are many other solutes that must undergo facilitated diffusion to move into a cell, such as amino acids, or to move out of a cell, such as wastes. Because facilitated diffusion is a passive process, it does not require energy expenditure by the cell. Water also can move freely across the cell membrane of all cells, either through protein channels or by slipping between the lipid tails of the membrane itself. *Osmosis* is the diffusion of water through a semipermeable membrane (Figure 6).

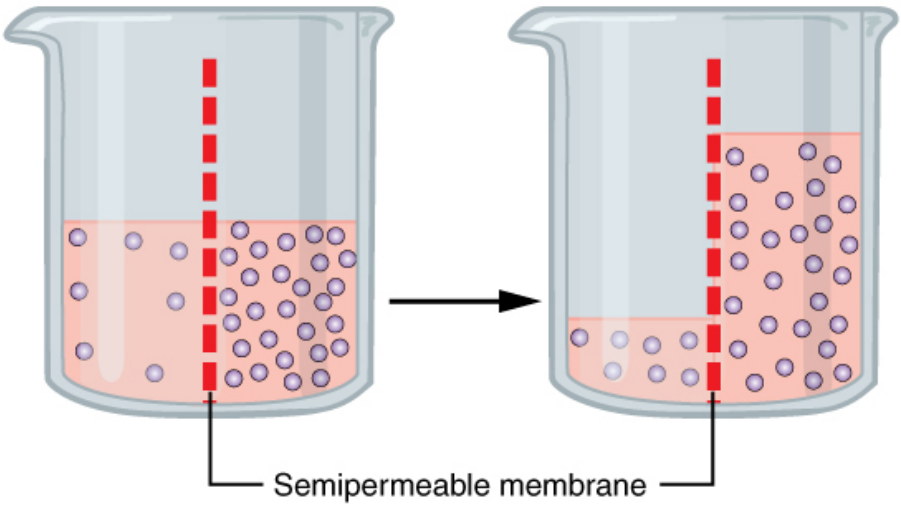


Figure 6. Osmosis. Osmosis is the diffusion of water through a semipermeable membrane down its concentration gradient. If a membrane is permeable to water, though not to a solute, water will equalize its own concentration by diffusing to the side of lower water concentration (and thus the side of higher solute concentration). In the beaker on the left, the solution on the right side of the membrane is hypertonic.

The movement of water molecules is not itself regulated by cells, so it is important that cells are exposed to an environment in which the concentration of solutes outside of the cells (in the extracellular fluid) is equal to the

concentration of solutes inside the cells (in the cytoplasm). Two solutions that have the same concentration of solutes are said to be **isotonic** (equal tension). When cells and their extracellular environments are isotonic, the concentration of water molecules is the same outside and inside the cells, and the cells maintain their normal shape (and function). Osmosis occurs when there is an imbalance of solutes outside of a cell versus inside the cell. A solution that has a higher concentration of solutes than another solution is said to be **hypertonic**, and water molecules tend to diffuse into a hypertonic solution (Figure 7). Cells in a hypertonic solution will shrivel as water leaves the cell via osmosis. In contrast, a solution that has a lower concentration of solutes than another solution is said to be **hypotonic**, and water molecules tend to diffuse out of a hypotonic solution. Cells in a hypotonic solution will take on too much water and swell, with the risk of eventually bursting. A critical aspect of homeostasis in living things is to create an internal environment in which all of the body's cells are in an isotonic solution. Various organ systems, particularly the kidneys, work to maintain this homeostasis.

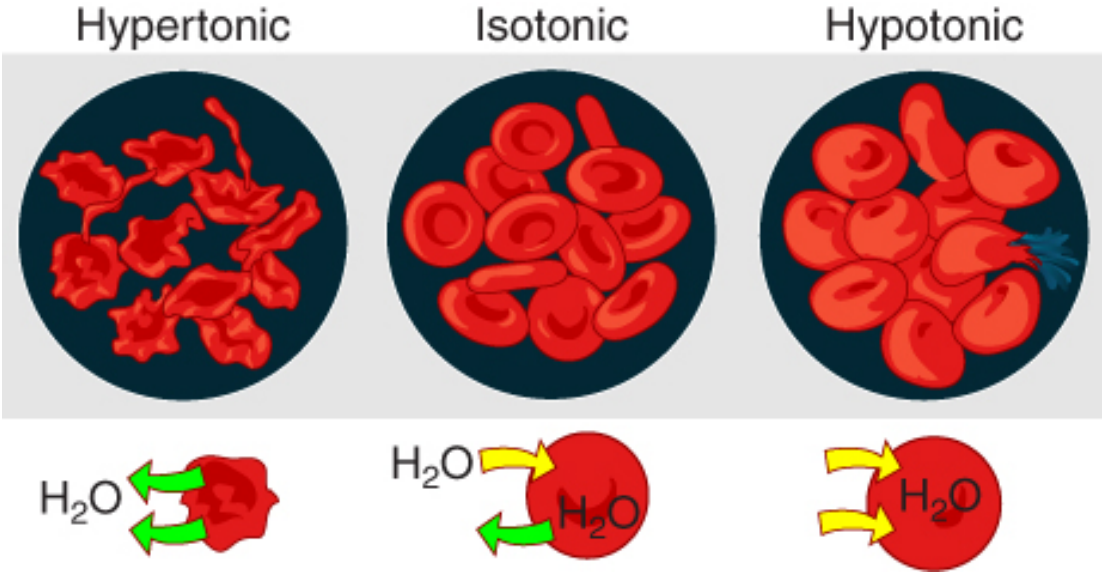


Figure 7. Concentration of Solutions. *A hypertonic solution has a solute concentration higher than another solution. An isotonic solution has a solute concentration equal to another solution. A hypotonic solution has a solute concentration lower than another solution.*

Another mechanism besides diffusion to passively transport materials between compartments is filtration. Unlike diffusion of a substance from where it is more concentrated to less concentrated, filtration uses a hydrostatic pressure gradient that pushes the fluid—and the solutes within it—from a higher pressure area to a lower pressure area. Filtration is an extremely important process in the body. For example, the circulatory system uses filtration to move plasma and substances across the endothelial lining of capillaries and into surrounding tissues, supplying cells with the nutrients. Filtration pressure in the kidneys provides the mechanism to remove wastes from the bloodstream.

Active Transport

For all of the transport methods described above, the cell expends no energy. Membrane proteins that aid in the passive transport of substances do so without the use of ATP. During active transport, ATP is required to move a substance across a membrane, often with the help of protein carriers, and usually *against* its concentration gradient. One of the most common types of active transport involves proteins that serve as pumps. The word "pump" probably conjures up thoughts of using energy to pump up the tire of a bicycle or a basketball. Similarly, energy from ATP is required for these membrane proteins to transport substances—molecules or ions—across the membrane, usually against their concentration gradients (from an area of low concentration to an area of high concentration). The **sodium-potassium pump**, which is also called N^+/K^+ ATPase, transports sodium out of a cell while moving potassium into the cell. The Na^+/K^+ pump is an important ion pump found in the membranes of many types of cells. These pumps are particularly abundant in nerve cells, which are constantly pumping out sodium ions and pulling in potassium ions to maintain an electrical gradient across their cell membranes.
An **electrical gradient** is a difference in electrical charge across a space. In the case of nerve cells, for example, the electrical gradient exists between the inside and outside of the cell, with the inside being negatively-charged

(at around -70 mV) relative to the outside. The negative electrical gradient is maintained because each Na^+/K^+ pump moves three Na^+ ions out of the cell and two K^+ ions into the cell for each ATP molecule that is used (Figure 8). This process is so important for nerve cells that it accounts for the majority of their ATP usage.

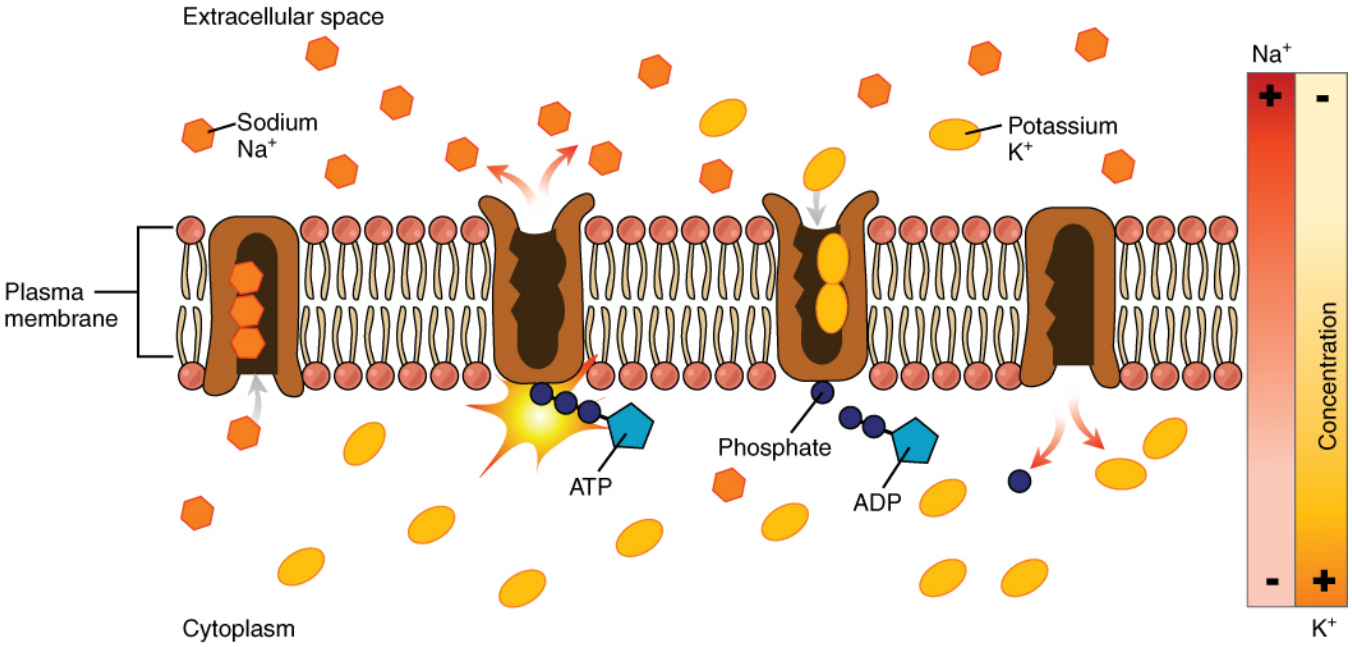


Figure 8. Sodium-Potassium Pump. *The sodium-potassium pump is found in many cell (plasma) membranes. Powered by ATP, the pump moves sodium and potassium ions in opposite directions, each against its concentration gradient. In a single cycle of the pump, three sodium ions are extruded from and two potassium ions are imported into the cell.*

Other forms of active transport do not involve membrane carriers. **Endocytosis** (bringing "into the cell") is the process of a cell ingesting material by enveloping it in a portion of its cell membrane, and then pinching off that portion of membrane (Figure 9).

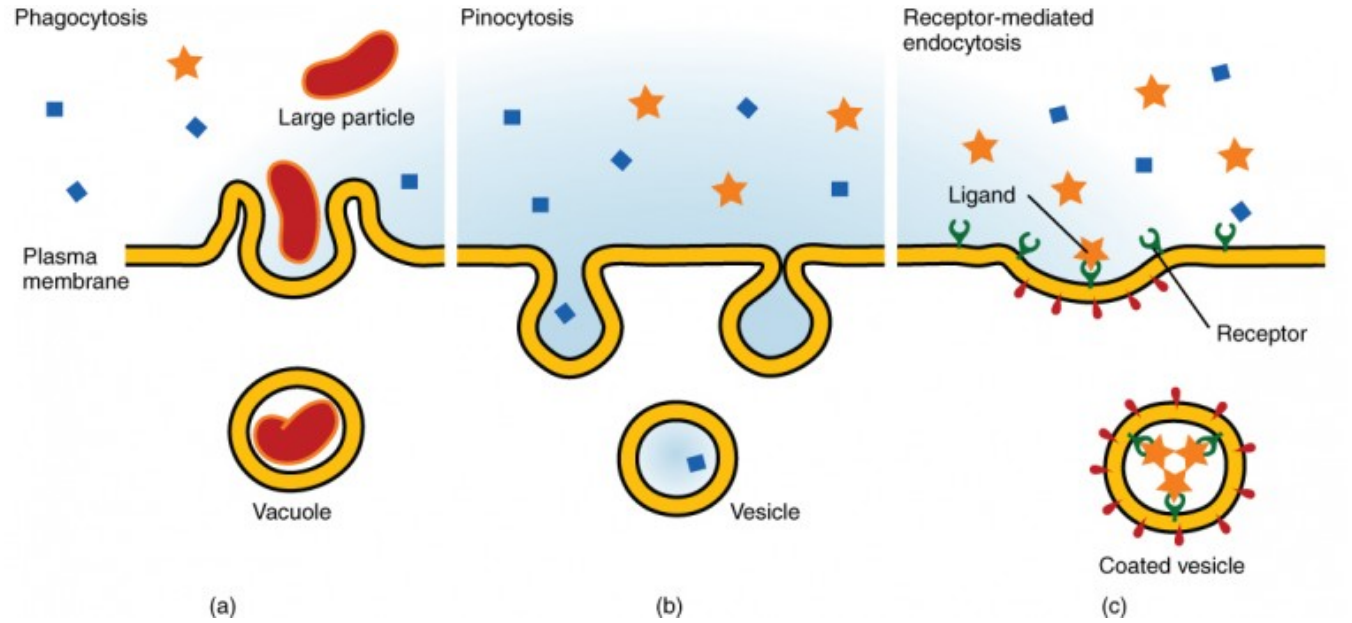


Figure 9. Three Forms of Endocytosis. *Endocytosis is a form of active transport in which a cell envelopes extracellular materials using its cell membrane. (a) In phagocytosis, which is relatively nonselective, the cell takes in a large particle. (b) In pinocytosis, the cell takes in small particles in fluid. (c) In contrast, receptor-mediated endocytosis is quite selective. When external receptors bind a specific ligand, the cell responds by endocytosing the ligand.*

Once pinched off, the portion of membrane and its contents becomes an independent, intracellular vesicle. A **vesicle** is a membranous sac—a spherical and hollow organelle bounded by a lipid bilayer membrane. Endocytosis often brings materials into the cell that must to be broken down or digested. **Phagocytosis** ("cell eating") is the endocytosis of large particles. Many immune cells engage in phagocytosis of invading pathogens. Like little Pac-men, their job is to patrol body tissues for unwanted matter, such as invading bacterial cells, phagocytize them, and digest them. In contrast to phagocytosis, **pinocytosis** ("cell drinking") brings fluid containing dissolved substances into a cell through membrane vesicles.

Phagocytosis and pinocytosis take in large portions of extracellular material, and they are typically not highly selective in the substances they bring in. Cells regulate the endocytosis of specific substances via receptor-mediated endocytosis. **Receptor-mediated endocytosis** is endocytosis by a portion of the cell membrane that contains many receptors that are specific for a certain substance. Once the surface receptors have bound sufficient amounts of the specific substance (the receptor's ligand), the cell will endocytose the part of the cell membrane containing the receptor-ligand complexes. Iron, a required component of hemoglobin, is endocytosed by red blood cells in this way. Iron is bound to a protein called transferrin in the blood. Specific transferrin receptors on red blood cell surfaces bind the iron-transferrin molecules, and the cell endocytoses the receptor-ligand complexes. In contrast with endocytosis, **exocytosis** (taking "out of the cell") is the process of a cell exporting material using vesicular transport (Figure 10).

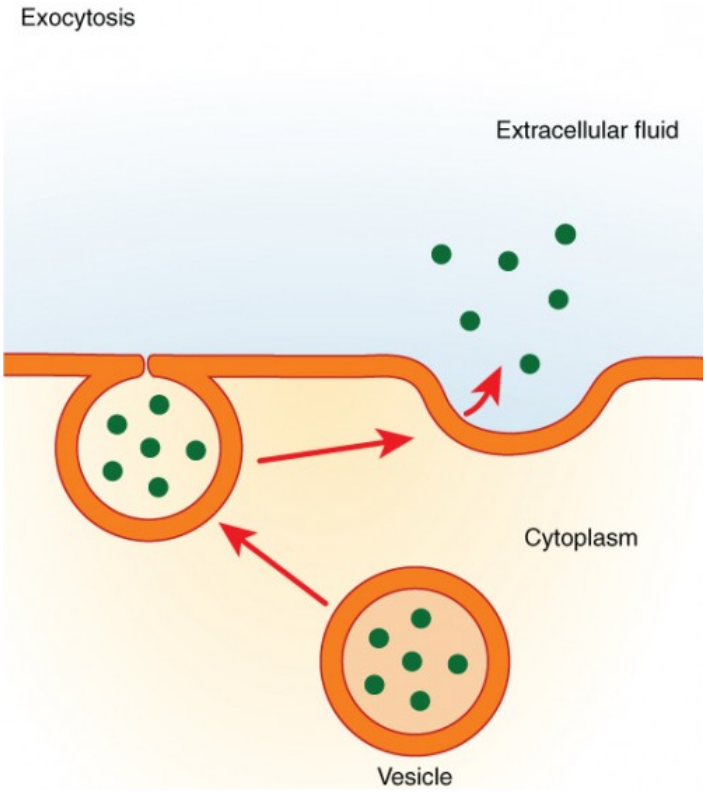


Figure 10. Exocytosis. *Exocytosis is much like endocytosis in reverse. Material destined for export is packaged into a vesicle inside the cell. The membrane of the vesicle fuses with the cell membrane, and the contents are released into the extracellular space.*

Many cells manufacture substances that must be secreted, like a factory manufacturing a product for export. These substances are typically packaged into membrane-bound vesicles within the cell. When the vesicle membrane fuses with the cell membrane, the vesicle releases it contents into the interstitial fluid. The vesicle membrane then becomes part of the cell membrane. Cells of the stomach and pancreas produce and secrete digestive enzymes through exocytosis (Figure 11). Endocrine cells produce and secrete hormones that are sent throughout the body, and certain immune cells produce and secrete large amounts of histamine, a chemical important for immune responses.

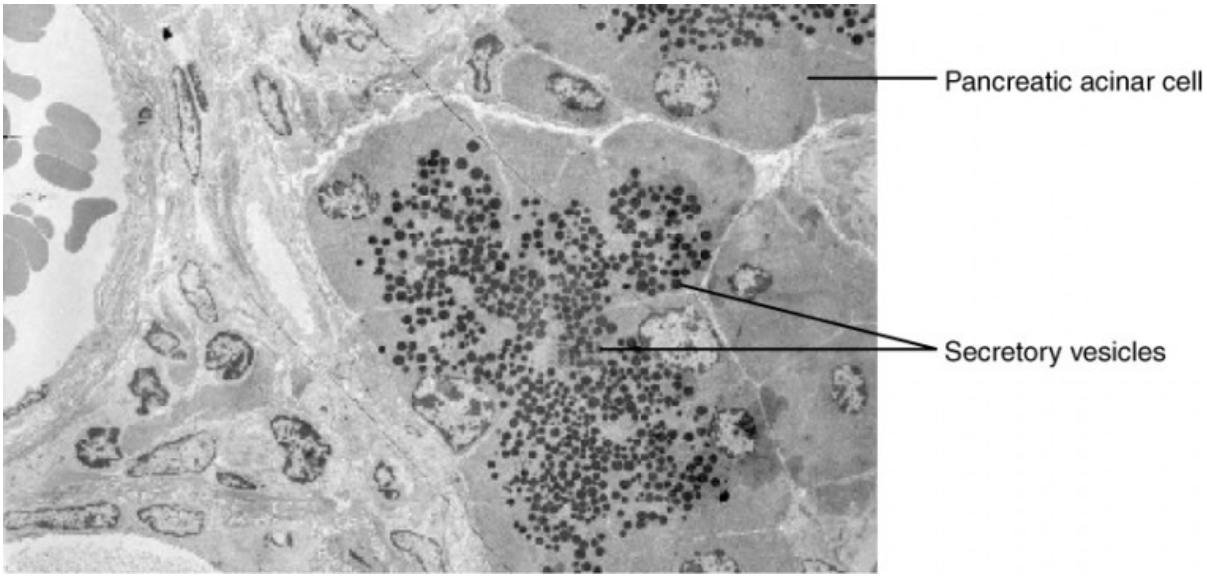


Figure 11. Pancreatic Cells' Enzyme Products. *The pancreatic acinar cells produce and secrete many enzymes that digest food. The tiny black granules in this electron micrograph are secretory vesicles filled with enzymes that will be exported from the cells via exocytosis. LM × 2900. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

View the University of Michigan WebScope to explore the tissue sample in greater detail.

Diseases of the Cell: Cystic Fibrosis

Cystic fibrosis (CF) affects approximately 30,000 people in the United States, with about 1,000 new cases reported each year. The genetic disease is most well known for its damage to the lungs, causing breathing difficulties and chronic lung infections, but it also affects the liver, pancreas, and intestines. Only about 50 years ago, the prognosis for children born with CF was very grim—a life expectancy rarely over 10 years. Today, with advances in medical treatment, many CF patients live into their 30s.

The symptoms of CF result from a malfunctioning membrane ion channel called the cystic fibrosis transmembrane conductance regulator, or CFTR. In healthy people, the CFTR protein is an integral membrane protein that transports Cl^- ions out of the cell. In a person who has CF, the gene for the CFTR is mutated, thus, the cell manufactures a defective channel protein that typically is not incorporated into the membrane, but is instead degraded by the cell. The CFTR requires ATP in order to function, making its Cl^- transport a form of active transport. This characteristic puzzled researchers for a long time because the Cl^- ions are actually flowing *down* their concentration gradient when transported out of cells. Active transport generally pumps ions *against* their concentration gradient, but the CFTR presents an exception to this rule. In normal lung tissue, the movement of Cl^- out of the cell maintains a Cl^--rich, negatively charged environment immediately outside of the cell. This is particularly important in the epithelial lining of the respiratory system.

Respiratory epithelial cells secrete mucus, which serves to trap dust, bacteria, and other debris. A cilium (plural = *cilia*) is one of the hair-like appendages found on certain cells. Cilia on the epithelial cells move the mucus and its trapped particles up the airways away from the lungs and toward the outside. In order to be effectively moved upward, the mucus cannot be too viscous; rather it must have a thin, watery consistency.

The transport of Cl^- and the maintenance of an electronegative environment outside of the cell attract positive ions such as Na^+ to the extracellular space. The accumulation of both Cl^- and Na^+ ions in the extracellular space creates solute-rich mucus, which has a low concentration of water molecules. As a result, through osmosis, water moves from cells and extracellular matrix into the mucus, "thinning" it out. This is how, in a normal respiratory system, the mucus is kept sufficiently watered-down to be propelled out of the respiratory system.

If the CFTR channel is absent, Cl^- ions are not transported out of the cell in adequate numbers, thus preventing them from drawing positive ions. The absence of ions in the secreted mucus results in the lack of a normal water concentration gradient. Thus, there is no osmotic pressure pulling water into the mucus. The resulting mucus is thick and sticky, and the ciliated epithelia cannot effectively remove it from the respiratory system. Passageways in the lungs become blocked with mucus, along with the debris it carries. Bacterial infections occur more easily because bacterial cells are not effectively carried away from the lungs.

THE CYTOPLASM AND CELLULAR ORGANELLES

Learning Objectives

- Describe the structure and function of the cellular organelles associated with the endomembrane system, including the endoplasmic reticulum, Golgi apparatus, and lysosomes
- Describe the structure and function of mitochondria and peroxisomes
- Explain the three components of the cytoskeleton, including their composition and functions

Now that you have learned that the cell membrane surrounds all cells, you can dive inside of a prototypical human cell to learn about its internal components and their functions. All living cells in multicellular organisms contain an internal cytoplasmic compartment, and a nucleus within the cytoplasm. **Cytosol**, the jelly-like substance within the cell, provides the fluid medium necessary for biochemical reactions. Eukaryotic cells, including all animal cells, also contain various cellular organelles. An **organelle** (“little organ”) is one of several different types of membrane-enclosed bodies in the cell, each performing a unique function. Just as the various bodily organs work together in harmony to perform all of a human’s functions, the many different cellular organelles work together to keep the cell healthy and performing all of its important functions. The organelles and cytosol, taken together, compose the cell’s **cytoplasm**. The **nucleus** is a cell’s central organelle, which contains the cell’s DNA (Figure 1).

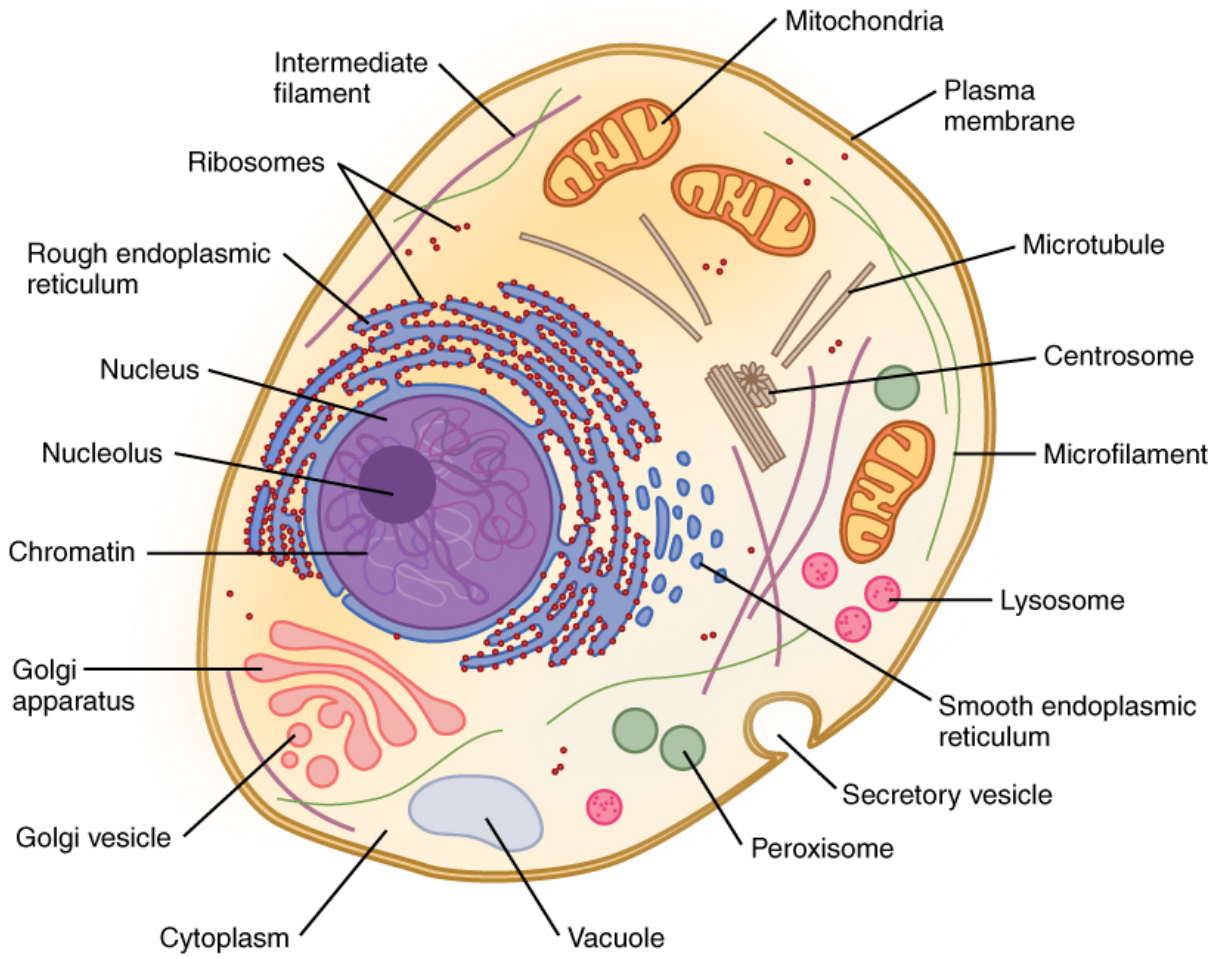


Figure 1. Prototypical Human Cell. *While this image is not indicative of any one particular human cell, it is a prototypical example of a cell containing the primary organelles and internal structures.*

Organelles of the Endomembrane System

A set of three major organelles together form a system within the cell called the endomembrane system. These organelles work together to perform various cellular jobs, including the task of producing, packaging, and exporting certain cellular products. The organelles of the endomembrane system include the endoplasmic reticulum, Golgi apparatus, and vesicles.

Endoplasmic Reticulum

The **endoplasmic reticulum (ER)** is a system of channels that is continuous with the nuclear membrane (or "envelope") covering the nucleus and composed of the same lipid bilayer material. The ER can be thought of as a series of winding thoroughfares similar to the waterway canals in Venice. The ER provides passages throughout much of the cell that function in transporting, synthesizing, and storing materials. The winding structure of the ER results in a large membranous surface area that supports its many functions (Figure 2).

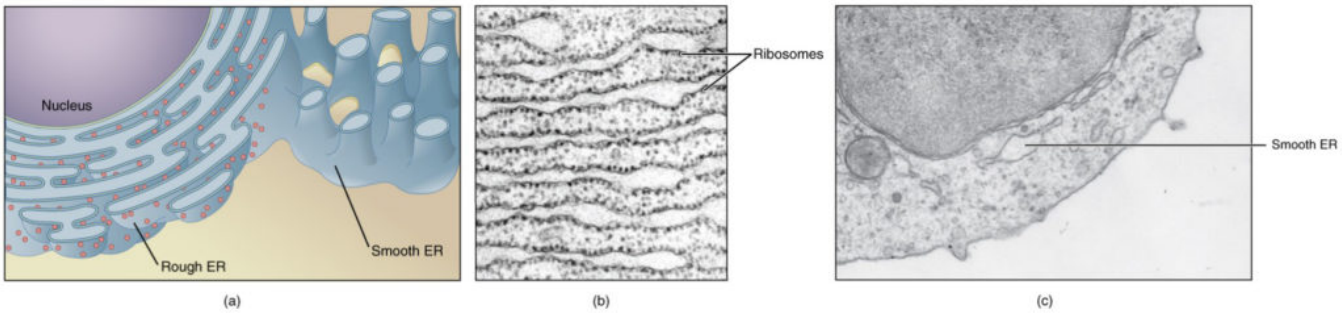


Figure 2. Endoplasmic Reticulum (ER). *Click for a larger image. (a) The ER is a winding network of thin membranous sacs found in close association with the cell nucleus. The smooth and rough endoplasmic reticula are very different in appearance and function (source: mouse tissue). (b) Rough ER is studded with numerous ribosomes, which are sites of protein synthesis (source: mouse tissue). EM × 110,000. (c) Smooth ER synthesizes phospholipids, steroid hormones, regulates the concentration of cellular* Ca^{++}*,metabolizes some carbohydrates, and breaks down certain toxins (source: mouse tissue). EM × 110,510. (Micrographs provided by the Regents of University of Michigan Medical School © 2012)*

Endoplasmic reticulum can exist in two forms: rough ER and smooth ER. These two types of ER perform some very different functions and can be found in very different amounts depending on the type of cell. Rough ER (RER) is so-called because its membrane is dotted with embedded granules—organelles called ribosomes, giving the RER a bumpy appearance. A **ribosome** is an organelle that serves as the site of protein synthesis. It is composed of two ribosomal RNA subunits that wrap around mRNA to start the process of translation, followed by protein synthesis. Smooth ER (SER) lacks these ribosomes. One of the main functions of the smooth ER is in the synthesis of lipids. The smooth ER synthesizes phospholipids, the main component of biological membranes, as well as steroid hormones. For this reason, cells that produce large quantities of such hormones, such as those of the female ovaries and male testes, contain large amounts of smooth ER. In addition to lipid synthesis, the smooth ER also sequesters (i.e., stores) and regulates the concentration of cellular Ca^{++}, a function extremely important in cells of the nervous system where Ca^{++} is the trigger for neurotransmitter release. The smooth ER additionally metabolizes some carbohydrates and performs a detoxification role, breaking down certain toxins. In contrast with the smooth ER, the primary job of the rough ER is the synthesis and modification of proteins destined for the cell membrane or for export from the cell. For this protein synthesis, many ribosomes attach to the ER (giving it the studded appearance of rough ER). Typically, a protein is synthesized within the ribosome and released inside the channel of the rough ER, where sugars can be added to it (by a process called glycosylation) before it is transported within a vesicle to the next stage in the packaging and shipping process: the Golgi apparatus.

The Golgi Apparatus

The **Golgi apparatus** is responsible for sorting, modifying, and shipping off the products that come from the rough ER, much like a post-office. The Golgi apparatus looks like stacked flattened discs, almost like stacks of oddly shaped pancakes. Like the ER, these discs are membranous. The Golgi apparatus has two distinct sides, each with a different role. One side of the apparatus receives products in vesicles. These products are sorted through the apparatus, and then they are released from the opposite side after being repackaged into new vesicles. If the product is to be exported from the cell, the vesicle migrates to the cell surface and fuses to the cell membrane, and the cargo is secreted (Figure 3).

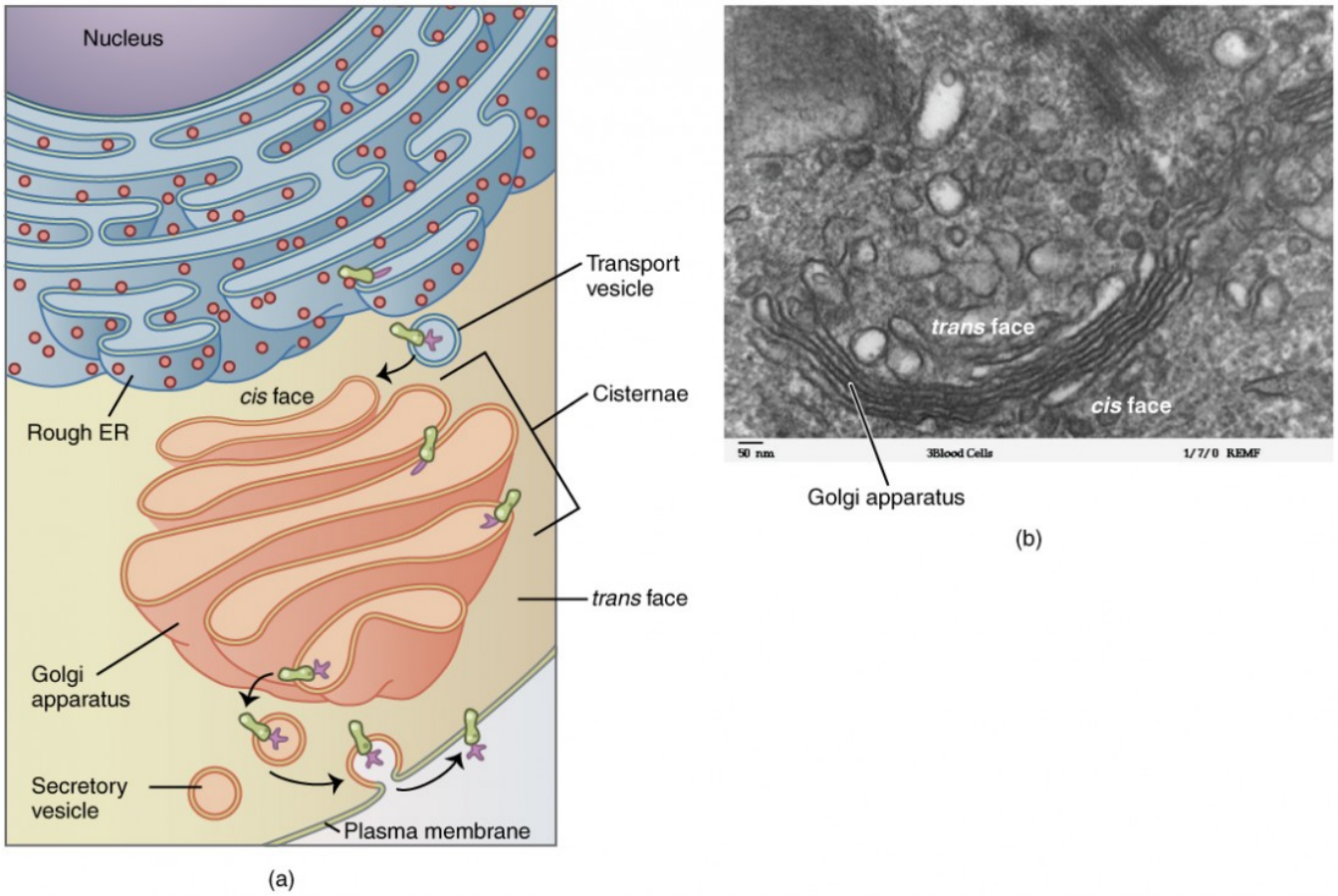


Figure 3. Golgi Apparatus. *(a) The Golgi apparatus manipulates products from the rough ER, and also produces new organelles called lysosomes. Proteins and other products of the ER are sent to the Golgi apparatus, which organizes, modifies, packages, and tags them. Some of these products are transported to other areas of the cell and some are exported from the cell through exocytosis. Enzymatic proteins are packaged as new lysosomes (or packaged and sent for fusion with existing lysosomes). (b) An electron micrograph of the Golgi apparatus.*

Lysosomes

Some of the protein products packaged by the Golgi include digestive enzymes that are meant to remain inside the cell for use in breaking down certain materials. The enzyme-containing vesicles released by the Golgi may form new lysosomes, or fuse with existing, lysosomes. A **lysosome** is an organelle that contains enzymes that break down and digest unneeded cellular components, such as a damaged organelle. (A lysosome is similar to a wrecking crew that takes down old and unsound buildings in a neighborhood.) **Autophagy** ("self-eating") is the process of a cell digesting its own structures. Lysosomes are also important for breaking down foreign material. For example, when certain immune defense cells (white blood cells) phagocytize bacteria, the bacterial cell is transported into a lysosome and digested by the enzymes inside. As one might imagine, such phagocytic defense cells contain large numbers of lysosomes. Under certain circumstances, lysosomes perform a more grand and dire function. In the case of damaged or unhealthy cells, lysosomes can be triggered to open up and release their digestive enzymes into the cytoplasm of the cell, killing the cell. This "self-destruct" mechanism is called **autolysis**, and makes the process of cell death controlled (a mechanism called "apoptosis").

Watch this video to learn about the endomembrane system, which includes the rough and smooth ER and the Golgi body as well as lysosomes and vesicles. What is the primary role of the endomembrane system?

Watch this video online: https://youtu.be/UAaTEjYmxso

Organelles for Energy Production and Detoxification

In addition to the jobs performed by the endomembrane system, the cell has many other important functions. Just as you must consume nutrients to provide yourself with energy, so must each of your cells take in nutrients, some of which convert to chemical energy that can be used to power biochemical reactions. Another important function of the cell is detoxification. Humans take in all sorts of toxins from the environment and also produce harmful chemicals as byproducts of cellular processes. Cells called hepatocytes in the liver detoxify many of these toxins.

Mitochondria

A **mitochondrion** (plural = mitochondria) is a membranous, bean-shaped organelle that is the "energy transformer" of the cell. Mitochondria consist of an outer lipid bilayer membrane as well as an additional inner lipid bilayer membrane (Figure 4). The inner membrane is highly folded into winding structures with a great deal of surface area, called cristae. It is along this inner membrane that a series of proteins, enzymes, and other molecules perform the biochemical reactions of cellular respiration. These reactions convert energy stored in nutrient molecules (such as glucose) into adenosine triphosphate (ATP), which provides usable cellular energy to the cell. Cells use ATP constantly, and so the mitochondria are constantly at work. Oxygen molecules are required during cellular respiration, which is why you must constantly breathe it in. One of the organ systems in the body that uses huge amounts of ATP is the muscular system because ATP is required to sustain muscle contraction. As a result, muscle cells are packed full of mitochondria. Nerve cells also need large quantities of ATP to run their sodium-potassium pumps. Therefore, an individual neuron will be loaded with over a thousand mitochondria. On the other hand, a bone cell, which is not nearly as metabolically-active, might only have a couple hundred mitochondria.

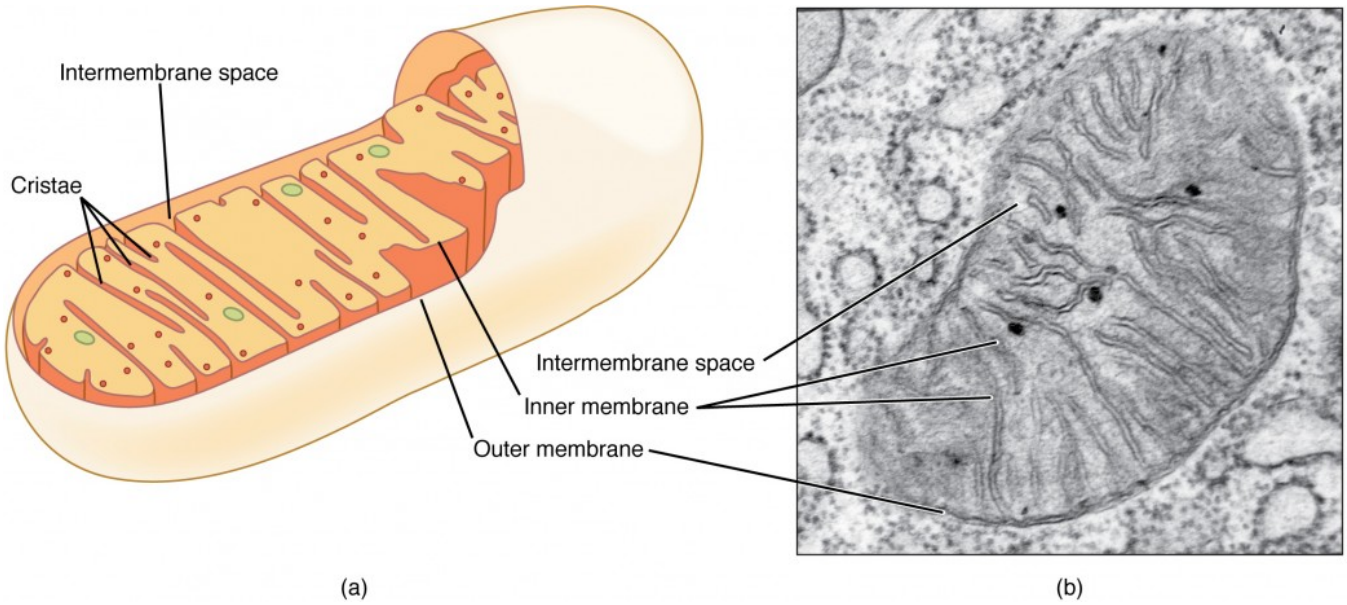


Figure 4. Mitochondrion. *The mitochondria are the energy-conversion factories of the cell. (a) A mitochondrion is composed of two separate lipid bilayer membranes. Along the inner membrane are various molecules that work together to produce ATP, the cell's major energy currency. (b) An electron micrograph of mitochondria. EM × 236,000. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

Peroxisomes

Like lysosomes, a **peroxisome** is a membrane-bound cellular organelle that contains mostly enzymes (Figure 5). Peroxisomes perform a couple of different functions, including lipid metabolism and chemical detoxification. In contrast to the digestive enzymes found in lysosomes, the enzymes within peroxisomes serve to transfer hydrogen atoms from various molecules to oxygen, producing hydrogen peroxide (H_2O_2). In this way, peroxisomes neutralize poisons such as alcohol. In order to appreciate the importance of peroxisomes, it is necessary to understand the concept of reactive oxygen species.

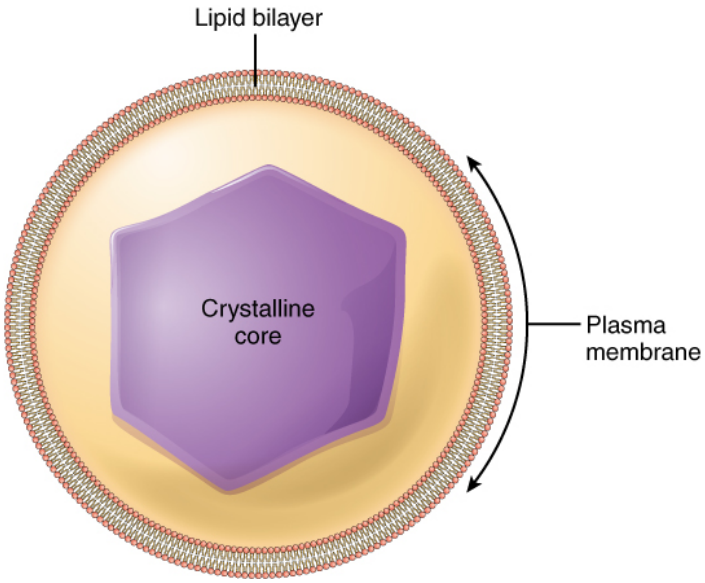


Figure 5. Peroxisome. *Peroxisomes are membrane-bound organelles that contain an abundance of enzymes for detoxifying harmful substances and lipid metabolism.*

Reactive oxygen species (ROS) such as peroxides and free radicals are the highly reactive products of many normal cellular processes, including the mitochondrial reactions that produce ATP and oxygen metabolism. Examples of ROS include the hydroxyl radical OH, H_2O_2, and superoxide (O_2^-). Some ROS are important for certain cellular functions, such as cell signaling processes and immune responses against foreign substances.

Free radicals are reactive because they contain free unpaired electrons; they can easily oxidize other molecules throughout the cell, causing cellular damage and even cell death. Free radicals are thought to play a role in many destructive processes in the body, from cancer to coronary artery disease.

Peroxisomes, on the other hand, oversee reactions that neutralize free radicals. Peroxisomes produce large amounts of the toxic H_2O_2 in the process, but peroxisomes contain enzymes that convert H_2O_2 into water and oxygen. These byproducts are safely released into the cytoplasm. Like miniature sewage treatment plants, peroxisomes neutralize harmful toxins so that they do not wreak havoc in the cells. The liver is the organ primarily responsible for detoxifying the blood before it travels throughout the body, and liver cells contain an exceptionally high number of peroxisomes. Defense mechanisms such as detoxification within the peroxisome and certain cellular antioxidants serve to neutralize many of these molecules. Some vitamins and other substances, found primarily in fruits and vegetables, have antioxidant properties. Antioxidants work by being oxidized themselves, halting the destructive reaction cascades initiated by the free radicals.

Sometimes though, ROS accumulate beyond the capacity of such defenses. **Oxidative stress** is the term used to describe damage to cellular components caused by ROS. Due to their characteristic unpaired electrons, ROS can set off chain reactions where they remove electrons from other molecules, which then become oxidized and reactive, and do the same to other molecules, causing a chain reaction. ROS can cause permanent damage to cellular lipids, proteins, carbohydrates, and nucleic acids. Damaged DNA can lead to genetic mutations and even cancer.

A **mutation** is a change in the nucleotide sequence in a gene within a cell's DNA, potentially altering the protein coded by that gene. Other diseases believed to be triggered or exacerbated by ROS include Alzheimer's disease, cardiovascular diseases, diabetes, Parkinson's disease, arthritis, Huntington's disease, and schizophrenia, among many others. It is noteworthy that these diseases are largely age-related. Many scientists believe that oxidative stress is a major contributor to the aging process.

Aging and the Cell: The Free Radical Theory

The free radical theory on aging was originally proposed in the 1950s, and still remains under debate. Generally speaking, the free radical theory of aging suggests that accumulated cellular damage from oxidative stress contributes to the physiological and anatomical effects of aging. There are two significantly different versions of this theory: one states that the aging process itself is a result of oxidative damage, and the other states that oxidative damage causes age-related disease and disorders. The latter version of the theory is more widely accepted than the former. However, many lines of evidence suggest that oxidative damage does contribute to the aging process. Research has shown that reducing oxidative damage can result in a longer lifespan in certain organisms such as yeast, worms, and fruit flies. Conversely, increasing oxidative damage can shorten the lifespan of mice and worms. Interestingly, a manipulation called calorie-restriction (moderately restricting the caloric intake) has been shown to increase life span in some laboratory animals. It is believed that this increase is at least in part due to a reduction of oxidative stress. However, a long-term study of primates with calorie-restriction showed no increase in their lifespan. A great deal of additional research will be required to better understand the link between reactive oxygen species and aging.

The Cytoskeleton

Much like the bony skeleton structurally supports the human body, the cytoskeleton helps the cells to maintain their structural integrity. The **cytoskeleton** is a group of fibrous proteins that provide structural support for cells, but this is only one of the functions of the cytoskeleton. Cytoskeletal components are also critical for cell motility, cell reproduction, and transportation of substances within the cell. The cytoskeleton forms a complex thread-like network throughout the cell consisting of three different kinds of protein-based filaments: microfilaments, intermediate filaments, and microtubules (Figure 6).

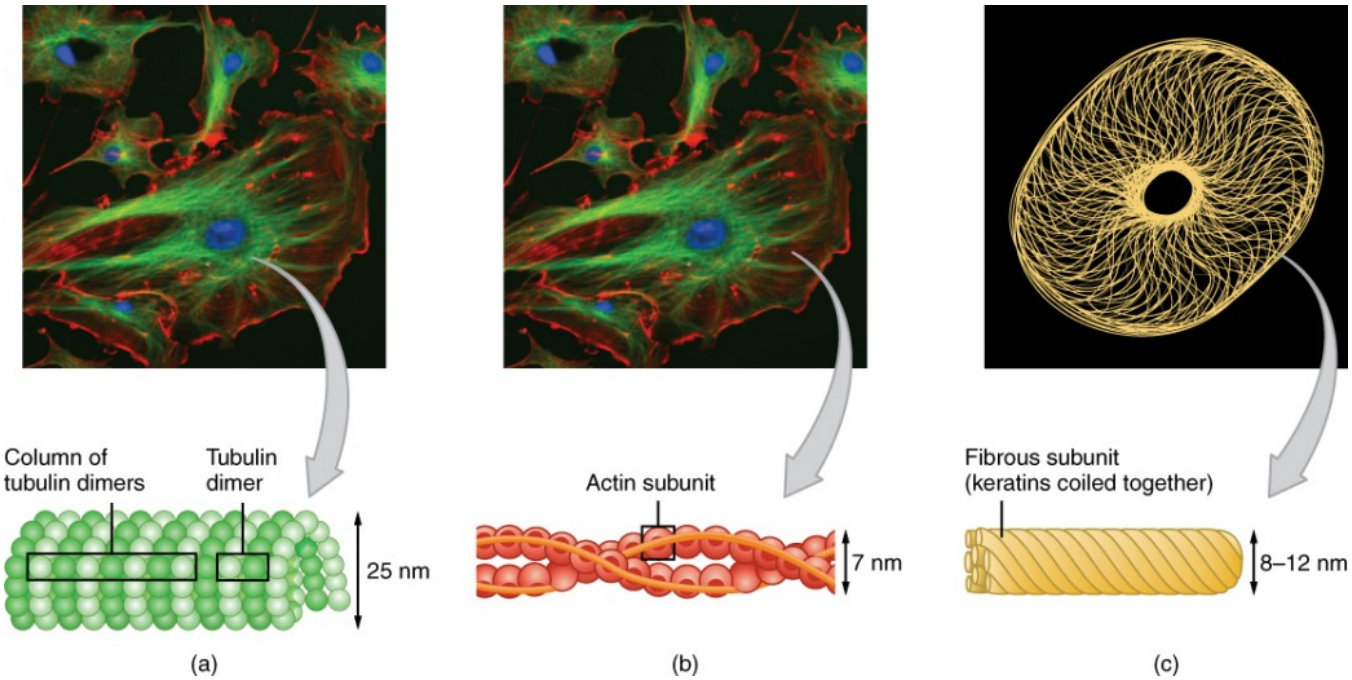


Figure 6. The Three Components of the Cytoskeleton. *The cytoskeleton consists of (a) microtubules, (b) microfilaments, and (c) intermediate filaments. The cytoskeleton plays an important role in maintaining cell shape and structure, promoting cellular movement, and aiding cell division.*

The thickest of the three components is the **microtubule**, a structural filament composed of subunits of a protein called tubulin. Microtubules maintain cell shape and structure, help resist compression of the cell, and play a role in positioning the organelles within the cell. Microtubules also make up two types of cellular appendages important for motion: cilia and flagella. **Cilia** are found on many cells of the body, including the epithelial cells that line the airways of the respiratory system. Cilia move rhythmically; they beat constantly, moving waste materials

such as dust, mucus, and bacteria upward through the airways, away from the lungs and toward the mouth. Beating cilia on cells in the female fallopian tubes move egg cells from the ovary towards the uterus.
A **flagellum** (plural = *flagella*) is an appendage larger than a cilium and specialized for cell locomotion. The only flagellated cell in humans is the sperm cell that must propel itself towards female egg cells.

A very important function of microtubules is to set the paths (somewhat like railroad tracks) along which the genetic material can be pulled (a process requiring ATP) during cell division, so that each new daughter cell receives the appropriate set of chromosomes. Two short, identical microtubule structures called centrioles are found near the nucleus of cells. A **centriole** can serve as the cellular origin point for microtubules extending outward as cilia or flagella or can assist with the separation of DNA during cell division. Microtubules grow out from the centrioles by adding more tubulin subunits, like adding additional links to a chain.

In contrast with microtubules, the **microfilament** is a thinner type of cytoskeletal filament (see Figure 6b). Actin, a protein that forms chains, is the primary component of these microfilaments. Actin fibers, twisted chains of actin filaments, constitute a large component of muscle tissue and, along with the protein myosin, are responsible for muscle contraction. Like microtubules, actin filaments are long chains of single subunits (called actin subunits). In muscle cells, these long actin strands, called thin filaments, are “pulled” by thick filaments of the myosin protein to contract the cell. Actin also has an important role during cell division. When a cell is about to split in half during cell division, actin filaments work with myosin to create a cleavage furrow that eventually splits the cell down the middle, forming two new cells from the original cell.

The final cytoskeletal filament is the intermediate filament. As its name would suggest, an **intermediate filament** is a filament intermediate in thickness between the microtubules and microfilaments (see Figure 6c). Intermediate filaments are made up of long fibrous subunits of a protein called keratin that are wound together like the threads that compose a rope. Intermediate filaments, in concert with the microtubules, are important for maintaining cell shape and structure. Unlike the microtubules, which resist compression, intermediate filaments resist tension—the forces that pull apart cells. There are many cases in which cells are prone to tension, such as when epithelial cells of the skin are compressed, tugging them in different directions. Intermediate filaments help anchor organelles together within a cell and also link cells to other cells by forming special cell-to-cell junctions.

THE NUCLEUS AND DNA REPLICATION

Learning Objectives

- Describe the structure and features of the nuclear membrane
- List the contents of the nucleus
- Explain the organization of the DNA molecule within the nucleus
- Describe the process of DNA replication

The nucleus is the largest and most prominent of a cell’s organelles (Figure 1a). The nucleus is generally considered the control center of the cell because it stores all of the genetic instructions for manufacturing proteins. Interestingly, some cells in the body, such as muscle cells, contain more than one nucleus (Figure 1b), which is known as multinucleated. Other cells, such as mammalian red blood cells (RBCs), do not contain nuclei at all. RBCs eject their nuclei as they mature, making space for the large numbers of hemoglobin molecules that carry oxygen throughout the body (Figure 2). Without nuclei, the life span of RBCs is short, and so the body must produce new ones constantly.

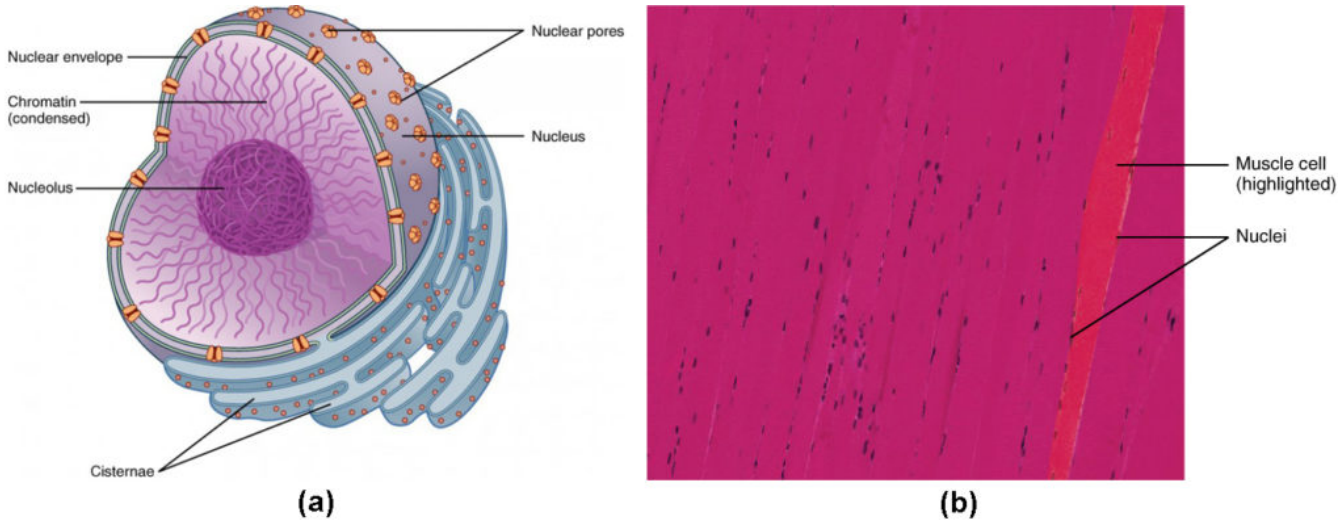


Figure 1. The Nucleus in Muscle Cells. (a) The nucleus is the control center of the cell. The nucleus of living cells contains the genetic material that determines the entire structure and function of that cell. (b) Unlike cardiac muscle cells and smooth muscle cells, which have a single nucleus, a skeletal muscle cell contains many nuclei, and is referred to as "multinucleated." These muscle cells are long and fibrous (often referred to as muscle fibers). During development, many smaller cells fuse to form a mature muscle fiber. The nuclei of the fused cells are conserved in the mature cell, thus imparting a multinucleate characteristic to mature muscle cells. LM × 104.3. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

View the University of Michigan WebScope to explore the tissue sample in greater detail.

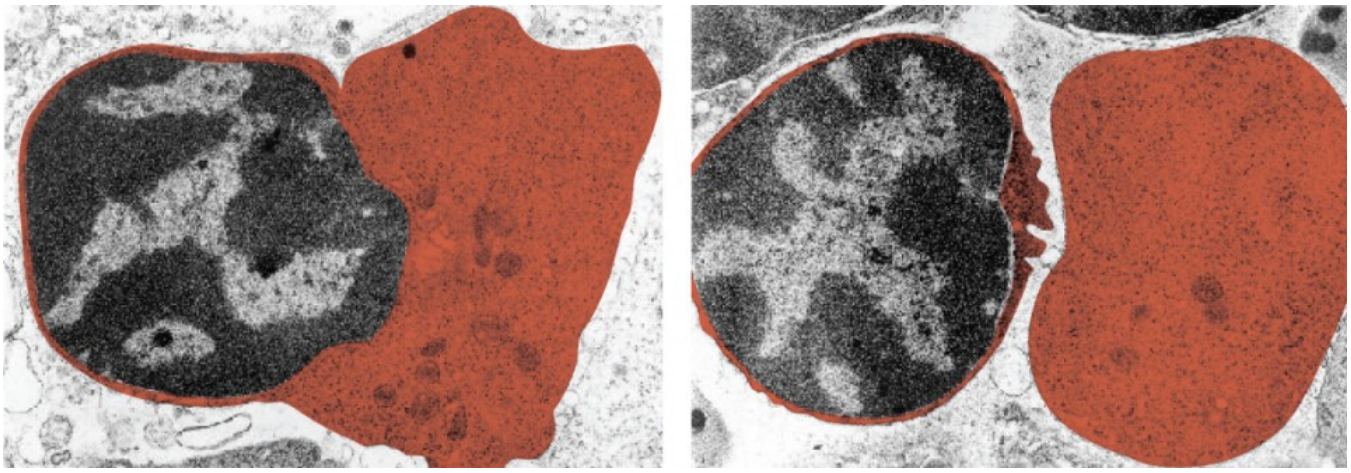


Figure 2. Red Blood Cell Extruding Its Nucleus. *Mature red blood cells lack a nucleus. As they mature, erythroblasts extrude their nucleus, making room for more hemoglobin. The two panels here show an erythroblast before and after ejecting its nucleus, respectively. (credit: modification of micrograph provided by the Regents of University of Michigan Medical School © 2012)*

View the University of Michigan WebScope to explore the tissue sample in greater detail.

Inside the nucleus lies the blueprint that dictates everything a cell will do and all of the products it will make. This information is stored within DNA. The nucleus sends "commands" to the cell via molecular messengers that translate the information from DNA. Each cell in your body (with the exception of germ cells) contains the complete set of your DNA. When a cell divides, the DNA must be duplicated so that the each new cell receives a full complement of DNA. The following section will explore the structure of the nucleus and its contents, as well as the process of DNA replication.

Organization of the Nucleus and Its DNA

Like most other cellular organelles, the nucleus is surrounded by a membrane called the **nuclear envelope**. This membranous covering consists of two adjacent lipid bilayers with a thin fluid space in between them. Spanning these two bilayers are nuclear pores. A **nuclear pore** is a tiny passageway for the passage of proteins, RNA, and solutes between the nucleus and the cytoplasm. Proteins called pore complexes lining the nuclear pores regulate the passage of materials into and out of the nucleus.

Inside the nuclear envelope is a gel-like nucleoplasm with solutes that include the building blocks of nucleic acids. There also can be a dark-staining mass often visible under a simple light microscope, called a **nucleolus** (plural = *nucleoli*). The nucleolus is a region of the nucleus that is responsible for manufacturing the RNA necessary for construction of ribosomes.

Once synthesized, newly made ribosomal subunits exit the cell's nucleus through the nuclear pores. The genetic instructions that are used to build and maintain an organism are arranged in an orderly manner in strands of DNA. Within the nucleus are threads of **chromatin** composed of DNA and associated proteins (Figure 3).

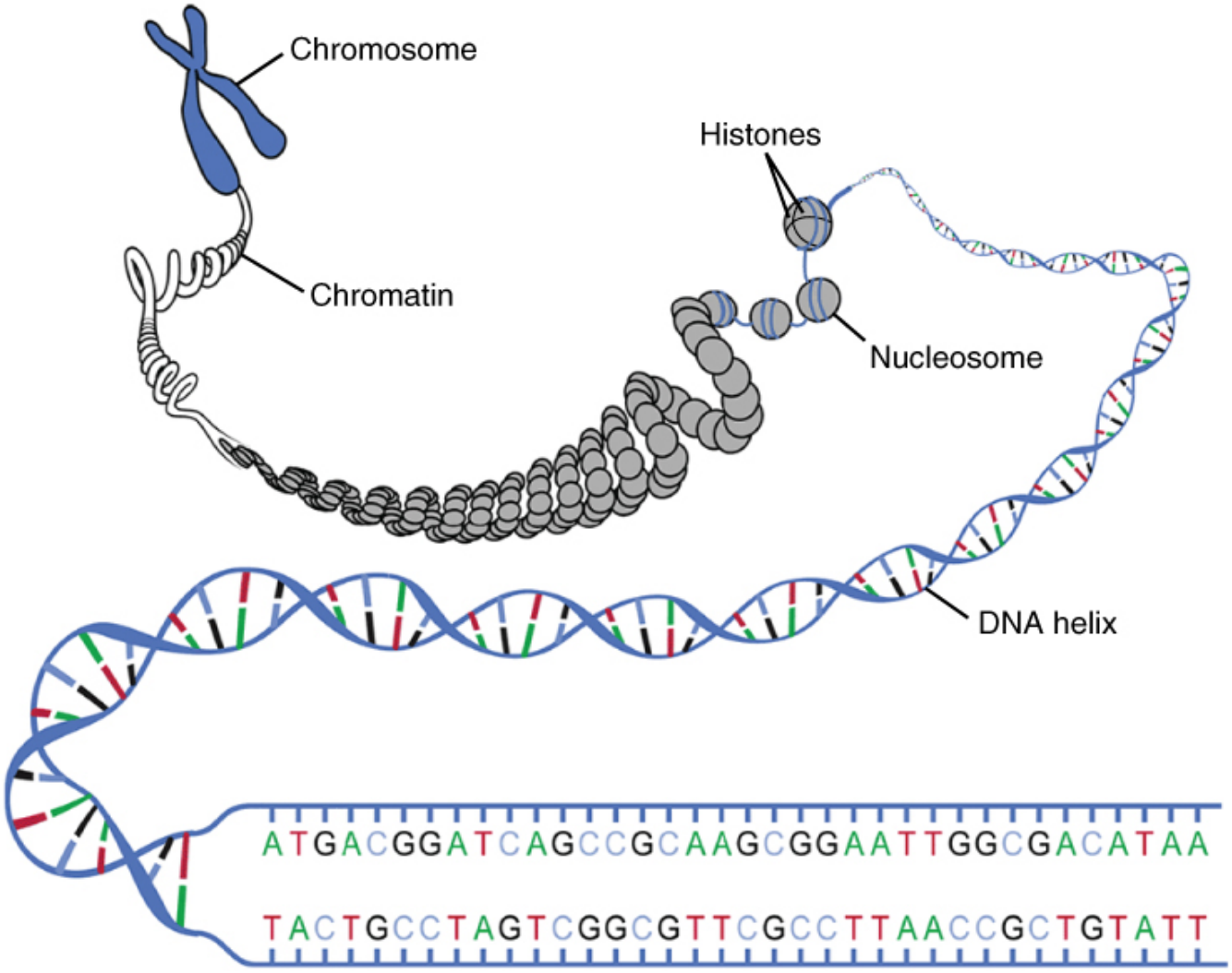


Figure 3. DNA Macrostructure. *Strands of DNA are wrapped around supporting histones. These proteins are increasingly bundled and condensed into chromatin, which is packed tightly into chromosomes when the cell is ready to divide.*

Along the chromatin threads, the DNA is wrapped around a set of **histone** proteins. A **nucleosome** is a single, wrapped DNA-histone complex. Multiple nucleosomes along the entire molecule of DNA appear like a beaded necklace, in which the string is the DNA and the beads are the associated histones. When a cell is in the process

of division, the chromatin condenses into chromosomes, so that the DNA can be safely transported to the "daughter cells."

The **chromosome** is composed of DNA and proteins; it is the condensed form of chromatin. It is estimated that humans have almost 22,000 genes distributed on 46 chromosomes.

DNA Replication

In order for an organism to grow, develop, and maintain its health, cells must replicated themselves by dividing to produce two new daughter cells, each with the full complement of DNA as found in the original cell. Billions of new cells are produced in an adult human every day. There are a few cell types in the body do not divide, including nerve cells, skeletal muscle fibers, and cardiac muscle cells. The division time of different cell types varies. Epithelial cells of the skin and gastrointestinal lining, for instance, divide very frequently to replace those that are constantly being rubbed off of the surface by friction.

A DNA molecule is made of two strands that "complement" each other: the molecules that compose the strands fit together and bind to each other, creating a double-stranded molecule that looks much like a long, twisted ladder. Each side rail of the DNA ladder is composed of alternating sugar and phosphate groups (Figure 4).

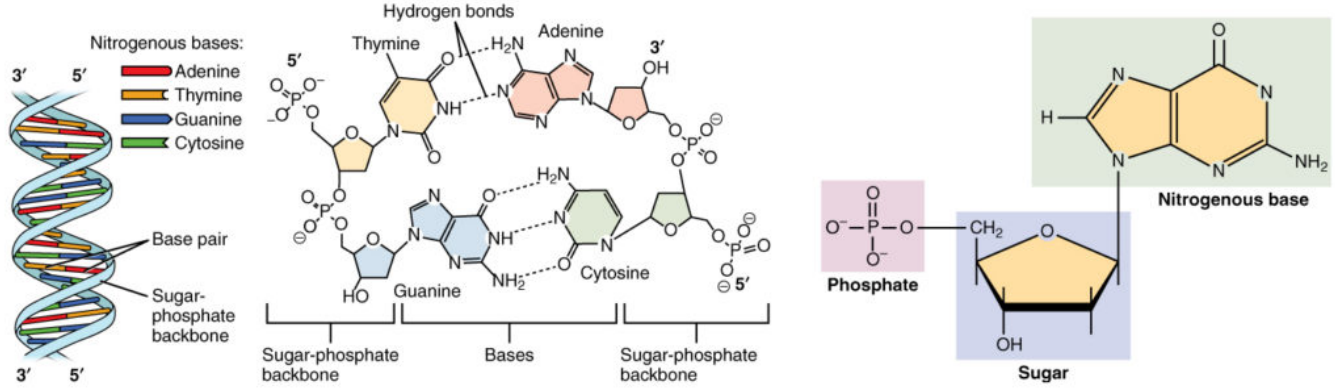


Figure 4. Molecular Structure of DNA. *The DNA double helix is composed of two complementary strands. The strands are bonded together via their nitrogenous base pairs using hydrogen bonds.*

The two sides of the ladder are not identical, but are complementary. These two backbones are bonded to each other across pairs of protruding bases, each bonded pair forming one "rung," or cross member. The four DNA bases are adenine (A), thymine (T), cytosine (C), and guanine (G). Because of their shape and charge, the two bases that compose a pair always bond together. Adenine always binds with thymine, and cytosine always binds with guanine. The particular sequence of bases along the DNA molecule determines the genetic code. Therefore, if the two complementary strands of DNA were pulled apart, you could infer the order of the bases in one strand from the bases in the other, complementary strand. For example, if one strand has a region with the sequence AGTGCCT, then the sequence of the complementary strand would be TCACGGA.

DNA replication is the copying of DNA that occurs before cell division can take place. After a great deal of debate and experimentation, the general method of DNA replication was deduced in 1958 by two scientists in California, Matthew Meselson and Franklin Stahl. This method is illustrated in Figure 5 and described below.

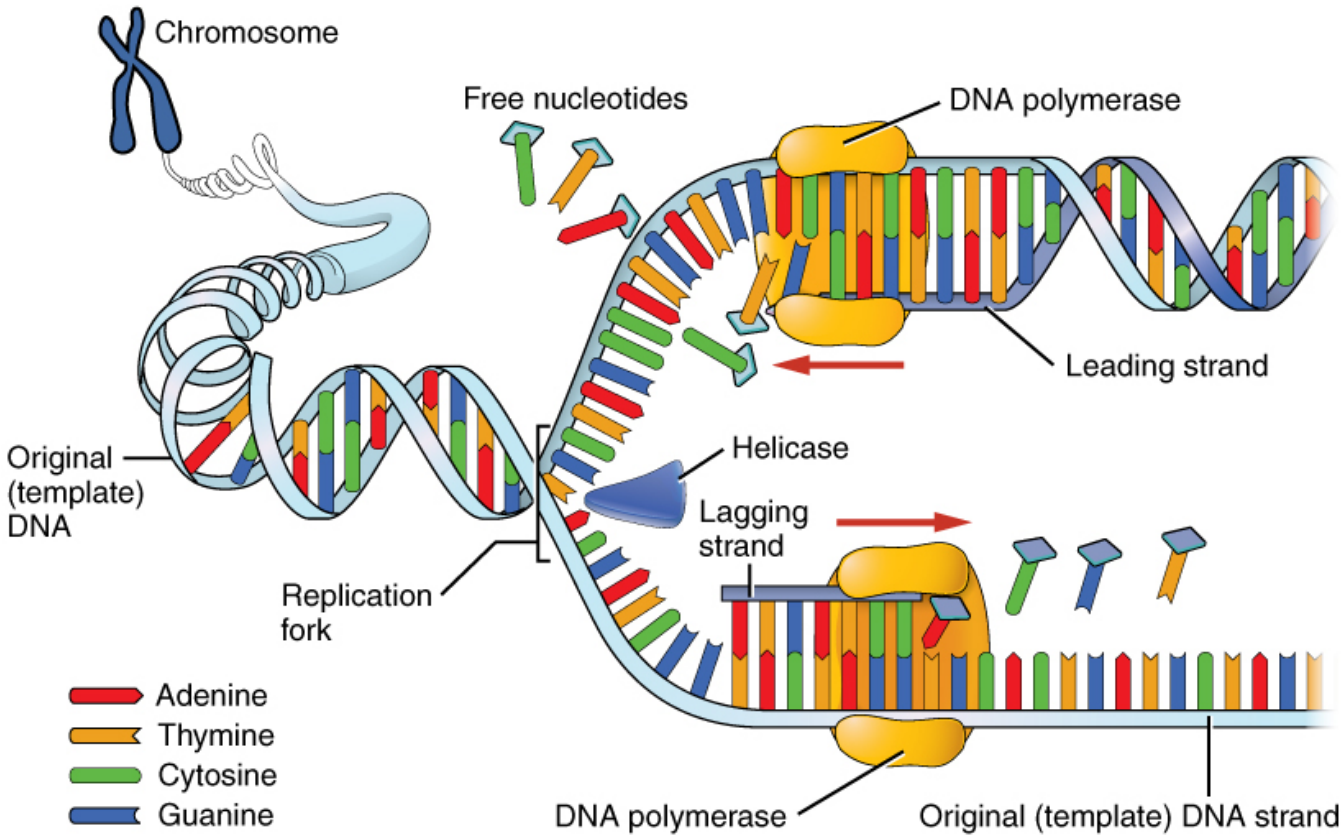


Figure 5. DNA Replication. *DNA replication faithfully duplicates the entire genome of the cell. During DNA replication, a number of different enzymes work together to pull apart the two strands so each strand can be used as a template to synthesize new complementary strands. The two new daughter DNA molecules each contain one pre-existing strand and one newly synthesized strand. Thus, DNA replication is said to be "semiconservative."*

Stage 1: Initiation

The two complementary strands are separated, much like unzipping a zipper. Special enzymes, including **helicase**, untwist and separate the two strands of DNA.

Stage 2: Elongation

Each strand becomes a template along which a new complementary strand is built. **DNA polymerase** brings in the correct bases to complement the template strand, synthesizing a new strand base by base. A DNA polymerase is an enzyme that adds free nucleotides to the end of a chain of DNA, making a new double strand. This growing strand continues to be built until it has fully complemented the template strand.

Stage 3: Termination

Once the two original strands are bound to their own, finished, complementary strands, DNA replication is stopped and the two new identical DNA molecules are complete. Each new DNA molecule contains one strand from the original molecule and one newly synthesized strand. The term for this mode of replication is "semiconservative," because half of the original DNA molecule is conserved in each new DNA molecule. This process continues until the cell's entire **genome**, the entire complement of an organism's DNA, is replicated. As you might imagine, it is very important that DNA replication take place precisely so that new cells in the body contain the exact same genetic material as their parent cells. Mistakes made during DNA replication, such as the accidental addition of an inappropriate nucleotide, have the potential to render a gene dysfunctional or useless. Fortunately, there are mechanisms in place to minimize such mistakes. A DNA proofreading process enlists the help of special enzymes that scan the newly synthesized molecule for mistakes and corrects them. Once the

process of DNA replication is complete, the cell is ready to divide. You will explore the process of cell division later in the chapter.

Watch this video to learn about DNA replication. DNA replication proceeds simultaneously at several sites on the same molecule. What separates the base pair at the start of DNA replication?

Watch this video online: https://youtu.be/FBmO_rmXxIw

PROTEIN SYNTHESIS

Learning Objectives

- Explain how the genetic code stored within DNA determines the protein that will form
- Describe the process of transcription
- Describe the process of translation
- Discuss the function of ribosomes

It was mentioned earlier that DNA provides a “blueprint” for the cell structure and physiology. This refers to the fact that DNA contains the information necessary for the cell to build one very important type of molecule: the protein. Most structural components of the cell are made up, at least in part, by proteins and virtually all the functions that a cell carries out are completed with the help of proteins. One of the most important classes of proteins is enzymes, which help speed up necessary biochemical reactions that take place inside the cell. Some of these critical biochemical reactions include building larger molecules from smaller components (such as occurs during DNA replication or synthesis of microtubules) and breaking down larger molecules into smaller components (such as when harvesting chemical energy from nutrient molecules). Whatever the cellular process may be, it is almost sure to involve proteins. Just as the cell’s genome describes its full complement of DNA, a cell’s **proteome** is its full complement of proteins.

Protein synthesis begins with genes. A **gene** is a functional segment of DNA that provides the genetic information necessary to build a protein. Each particular gene provides the code necessary to construct a particular protein. **Gene expression**, which transforms the information coded in a gene to a final gene product, ultimately dictates the structure and function of a cell by determining which proteins are made. The interpretation of genes works in the following way. Recall that proteins are polymers, or chains, of many amino acid building blocks. The sequence of bases in a gene (that is, its sequence of A, T, C, G nucleotides) translates to an amino acid sequence. A **triplet** is a section of three DNA bases in a row that codes for a specific amino acid. Similar to the way in which the three-letter code *d-o-g* signals the image of a dog, the three-letter DNA base code signals the use of a particular amino acid.

For example, the DNA triplet CAC (cytosine, adenine, and cytosine) specifies the amino acid valine. Therefore, a gene, which is composed of multiple triplets in a unique sequence, provides the code to build an entire protein, with multiple amino acids in the proper sequence (Figure 1). The mechanism by which cells turn the DNA code into a protein product is a two-step process, with an RNA molecule as the intermediate.

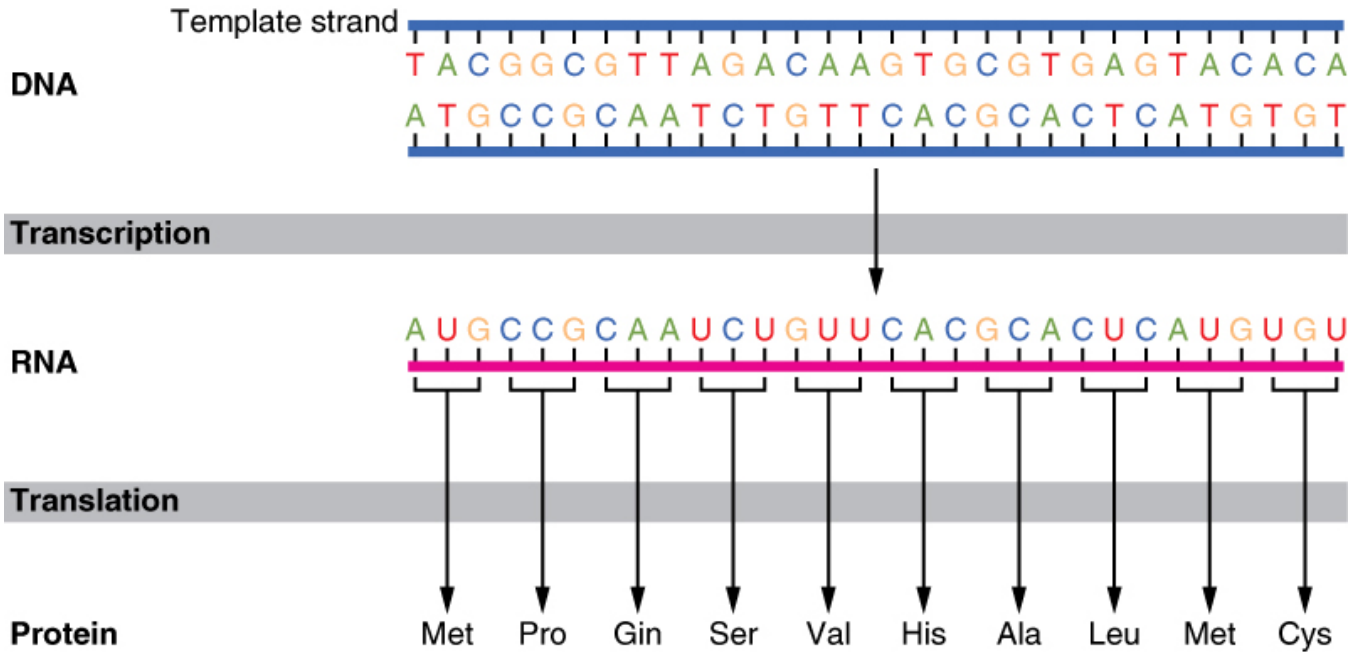


Figure 1. The Genetic Code. *DNA holds all of the genetic information necessary to build a cell's proteins. The nucleotide sequence of a gene is ultimately translated into an amino acid sequence of the gene's corresponding protein.*

From DNA to RNA: Transcription

DNA is housed within the nucleus, and protein synthesis takes place in the cytoplasm, thus there must be some sort of intermediate messenger that leaves the nucleus and manages protein synthesis. This intermediate messenger is **messenger RNA (mRNA)**, a single-stranded nucleic acid that carries a copy of the genetic code for a single gene out of the nucleus and into the cytoplasm where it is used to produce proteins.

There are several different types of RNA, each having different functions in the cell. The structure of RNA is similar to DNA with a few small exceptions. For one thing, unlike DNA, most types of RNA, including mRNA, are single-stranded and contain no complementary strand. Second, the ribose sugar in RNA contains an additional oxygen atom compared with DNA. Finally, instead of the base thymine, RNA contains the base uracil. This means that adenine will always pair up with uracil during the protein synthesis process.

Gene expression begins with the process called **transcription**, which is the synthesis of a strand of mRNA that is complementary to the gene of interest. This process is called transcription because the mRNA is like a transcript, or copy, of the gene's DNA code. Transcription begins in a fashion somewhat like DNA replication, in that a region of DNA unwinds and the two strands separate, however, only that small portion of the DNA will be split apart. The triplets within the gene on this section of the DNA molecule are used as the template to transcribe the complementary strand of RNA (Figure 2). A **codon** is a three-base sequence of mRNA, so-called because they directly encode amino acids. Like DNA replication, there are three stages to transcription: initiation, elongation, and termination.

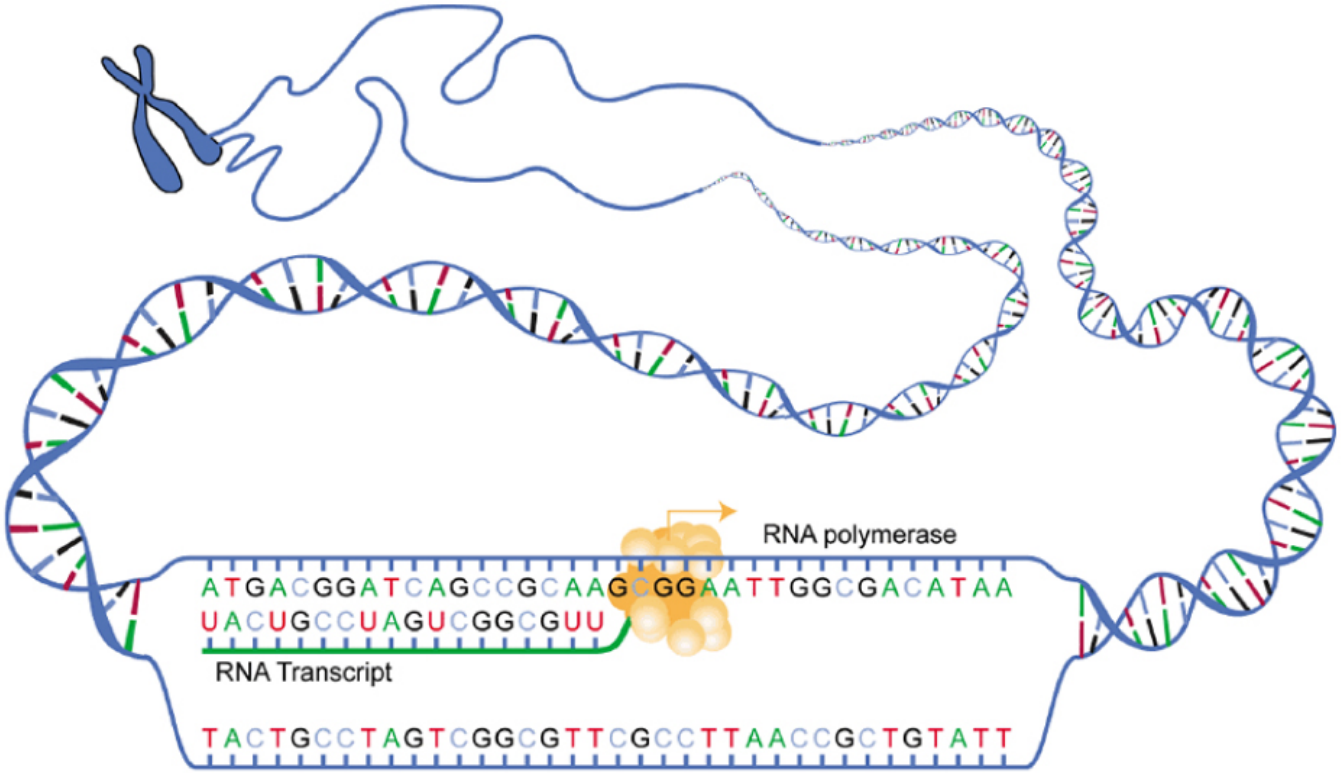


Figure 2. Transcription: from DNA to mRNA. *In the first of the two stages of making protein from DNA, a gene on the DNA molecule is transcribed into a complementary mRNA molecule.*

Stage 1: Initiation

A region at the beginning of the gene called a **promoter**—a particular sequence of nucleotides—triggers the start of transcription.

Stage 2: Elongation

Transcription starts when RNA polymerase unwinds the DNA segment. One strand, referred to as the coding strand, becomes the template with the genes to be coded. The polymerase then aligns the correct nucleic acid (A, C, G, or U) with its complementary base on the coding strand of DNA. **RNA polymerase** is an enzyme that adds new nucleotides to a growing strand of RNA. This process builds a strand of mRNA.

Stage 3: Termination

When the polymerase has reached the end of the gene, one of three specific triplets (UAA, UAG, or UGA) codes a “stop” signal, which triggers the enzymes to terminate transcription and release the mRNA transcript. Before the mRNA molecule leaves the nucleus and proceeds to protein synthesis, it is modified in a number of ways. For this reason, it is often called a pre-mRNA at this stage. For example, your DNA, and thus complementary mRNA, contains long regions called non-coding regions that do not code for amino acids. Their function is still a mystery, but the process called **splicing** removes these non-coding regions from the pre-mRNA transcript (Figure 3).

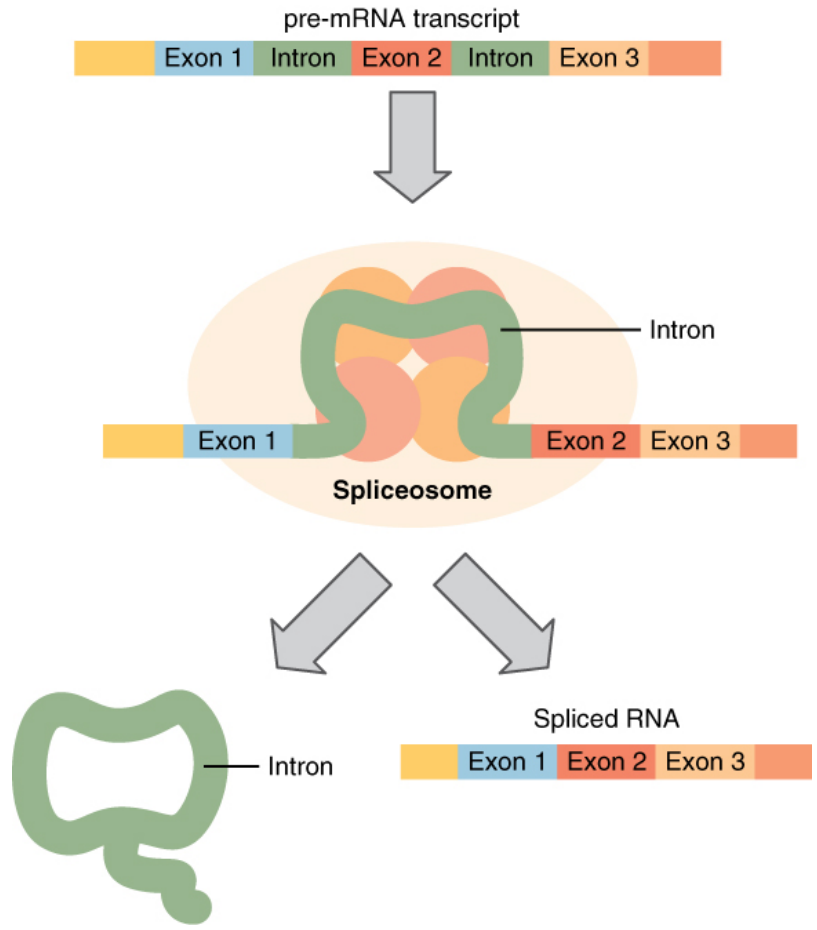


Figure 3. Splicing DNA. *In the nucleus, a structure called a spliceosome cuts out introns (noncoding regions) within a pre-mRNA transcript and reconnects the exons.*

A **spliceosome**—a structure composed of various proteins and other molecules—attaches to the mRNA and "splices" or cuts out the non-coding regions. The removed segment of the transcript is called an **intron**. The remaining exons are pasted together. An **exon** is a segment of RNA that remains after splicing. Interestingly, some introns that are removed from mRNA are not always non-coding. When different coding regions of mRNA are spliced out, different variations of the protein will eventually result, with differences in structure and function. This process results in a much larger variety of possible proteins and protein functions. When the mRNA transcript is ready, it travels out of the nucleus and into the cytoplasm.

From RNA to Protein: Translation

Like translating a book from one language into another, the codons on a strand of mRNA must be translated into the amino acid alphabet of proteins. **Translation** is the process of synthesizing a chain of amino acids called a **polypeptide**. Translation requires two major aids: first, a "translator," the molecule that will conduct the translation, and second, a substrate on which the mRNA strand is translated into a new protein, like the translator's "desk." Both of these requirements are fulfilled by other types of RNA. The substrate on which translation takes place is the ribosome. Remember that many of a cell's ribosomes are found associated with the rough ER, and carry out the synthesis of proteins destined for the Golgi apparatus.

Ribosomal RNA (rRNA) is a type of RNA that, together with proteins, composes the structure of the ribosome. Ribosomes exist in the cytoplasm as two distinct components, a small and a large subunit. When an mRNA molecule is ready to be translated, the two subunits come together and attach to the mRNA. The ribosome provides a substrate for translation, bringing together and aligning the mRNA molecule with the molecular "translators" that must decipher its code. The other major requirement for protein synthesis is the translator molecules that physically "read" the mRNA codons.

Transfer RNA (tRNA) is a type of RNA that ferries the appropriate corresponding amino acids to the ribosome, and attaches each new amino acid to the last, building the polypeptide chain one-by-one. Thus tRNA transfers specific amino acids from the cytoplasm to a growing polypeptide. The tRNA molecules must be able to recognize the codons on mRNA and match them with the correct amino acid. The tRNA is modified for this function. On one end of its structure is a binding site for a specific amino acid. On the other end is a base sequence that matches the codon specifying its particular amino acid. This sequence of three bases on the tRNA molecule is called an anticodon. For example, a tRNA responsible for shuttling the amino acid glycine contains a binding site for glycine on one end. On the other end it contains an anticodon that complements the glycine codon (GGA is a codon for glycine, and so the tRNAs anticodon would read CCU). Equipped with its particular cargo and matching anticodon, a tRNA molecule can read its recognized mRNA codon and bring the corresponding amino acid to the growing chain (Figure 4).

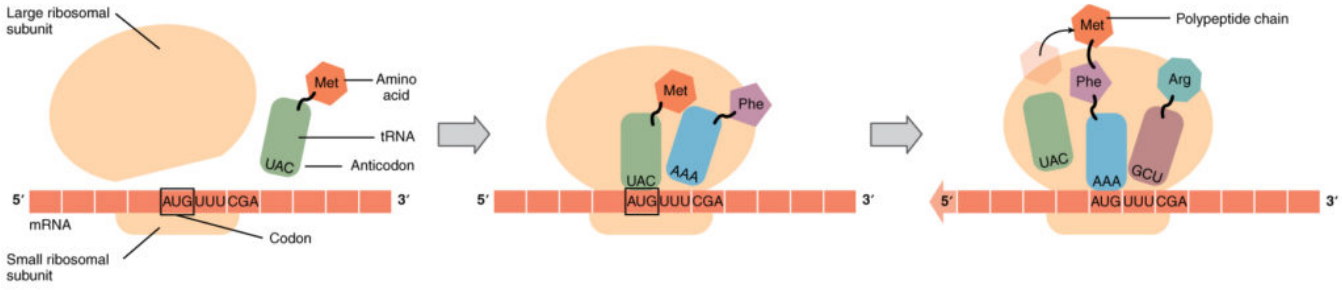


Figure 4. Translation from RNA to Protein. *Click for a larger image. During translation, the mRNA transcript is "read" by a functional complex consisting of the ribosome and tRNA molecules. tRNAs bring the appropriate amino acids in sequence to the growing polypeptide chain by matching their anti-codons with codons on the mRNA strand.*

Much like the processes of DNA replication and transcription, translation consists of three main stages: initiation, elongation, and termination. Initiation takes place with the binding of a ribosome to an mRNA transcript. The elongation stage involves the recognition of a tRNA anticodon with the next mRNA codon in the sequence. Once the anticodon and codon sequences are bound (remember, they are complementary base pairs), the tRNA presents its amino acid cargo and the growing polypeptide strand is attached to this next amino acid. This attachment takes place with the assistance of various enzymes and requires energy. The tRNA molecule then releases the mRNA strand, the mRNA strand shifts one codon over in the ribosome, and the next appropriate tRNA arrives with its matching anticodon. This process continues until the final codon on the mRNA is reached which provides a "stop" message that signals termination of translation and triggers the release of the complete, newly synthesized protein. Thus, a gene within the DNA molecule is transcribed into mRNA, which is then translated into a protein product (Figure 5).

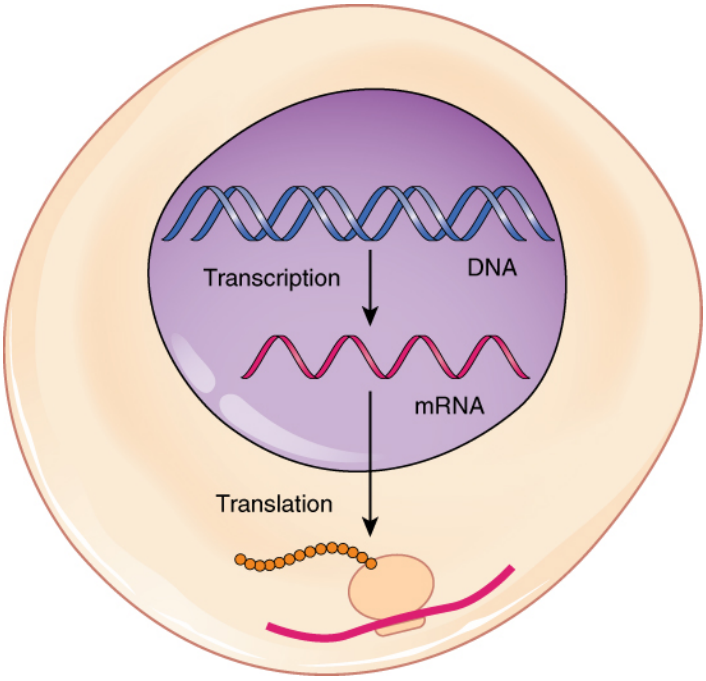


Figure 5. From DNA to Protein: Transcription through Translation. *Transcription within the cell nucleus produces an mRNA molecule, which is modified and then sent into the cytoplasm for translation. The transcript is decoded into a protein with the help of a ribosome and tRNA molecules.*

Commonly, an mRNA transcription will be translated simultaneously by several adjacent ribosomes. This increases the efficiency of protein synthesis. A single ribosome might translate an mRNA molecule in approximately one minute; so multiple ribosomes aboard a single transcript could produce multiple times the number of the same protein in the same minute. A *polyribosome* is a string of ribosomes translating a single mRNA strand.

Watch this video to learn about ribosomes. The ribosome binds to the mRNA molecule to start translation of its code into a protein. What happens to the small and large ribosomal subunits at the end of translation?

Watch this video online: https://youtu.be/MiVqjxi0DfQ

CELL GROWTH AND DIVISION

Learning Objectives

- Describe the stages of the cell cycle
- Discuss how the cell cycle is regulated
- Describe the implications of losing control over the cell cycle
- Describe the stages of mitosis and cytokinesis, in order

So far in this chapter, you have read numerous times of the importance and prevalence of cell division. While there are a few cells in the body that do not undergo cell division (such as gametes, red blood cells, most neurons, and some muscle cells), most somatic cells divide regularly. A **somatic cell** is a general term for a body cell, and all human cells, except for the cells that produce eggs and sperm (which are referred to as germ cells), are somatic cells. Somatic cells contain **two** copies of each of their chromosomes (one copy received from each parent).

A **homologous** pair of chromosomes is the two copies of a single chromosome found in each somatic cell. The human is a **diploid** organism, having 23 homologous pairs of chromosomes in each of the somatic cells. The condition of having pairs of chromosomes is known as diploidy. Cells in the body replace themselves over the lifetime of a person. For example, the cells lining the gastrointestinal tract must be frequently replaced when constantly "worn off" by the movement of food through the gut. But what triggers a cell to divide, and how does it prepare for and complete cell division? The **cell cycle** is the sequence of events in the life of the cell from the moment it is created at the end of a previous cycle of cell division until it then divides itself, generating two new cells.

The Cell Cycle

One "turn" or cycle of the cell cycle consists of two general phases: interphase, followed by mitosis and cytokinesis. **Interphase** is the period of the cell cycle during which the cell is not dividing. The majority of cells are in interphase most of the time. **Mitosis** is the division of genetic material, during which the cell nucleus breaks down and two new, fully functional, nuclei are formed. **Cytokinesis** divides the cytoplasm into two distinctive cells.

Interphase

A cell grows and carries out all normal metabolic functions and processes in a period called G_1 (Figure 1). **G_1 phase** (gap 1 phase) is the first gap, or growth phase in the cell cycle. For cells that will divide again, G_1 is followed by replication of the DNA, during the S phase. The **S phase** (synthesis phase) is period during which a cell replicates its DNA.

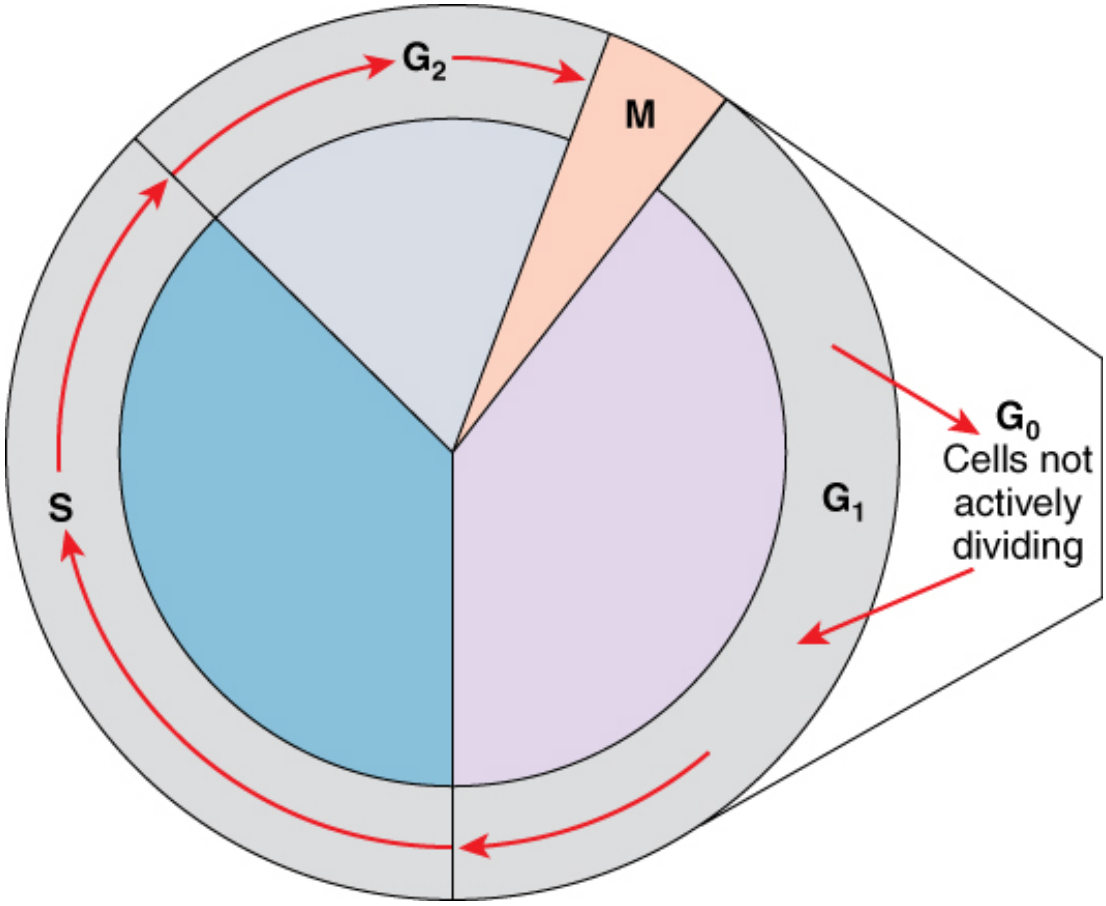


Figure 1. Cell Cycle. *The two major phases of the cell cycle include mitosis (cell division), and interphase, when the cell grows and performs all of its normal functions. Interphase is further subdivided into G_1, S, and G_2 phases.*

After the synthesis phase, the cell proceeds through the G_2 phase. The **G_2 phase** is a second gap phase, during which the cell continues to grow and makes the necessary preparations for mitosis. Between G_1, S, and G_2 phases, cells will vary the most in their duration of the G1 phase. It is here that a cell might spend a couple of hours, or many days. The S phase typically lasts between 8-10 hours and the G_2 phase approximately 5 hours. In contrast to these phases, the **G_0 phase** is a resting phase of the cell cycle. Cells that have temporarily stopped dividing and are resting (a common condition) and cells that have permanently ceased dividing (like nerve cells) are said to be in G_0.

The Structure of Chromosomes

Billions of cells in the human body divide every day. During the synthesis phase (S, for DNA synthesis) of interphase, the amount of DNA within the cell precisely doubles. Therefore, after DNA replication but before cell division, each cell actually contains **two** copies of each chromosome. Each copy of the chromosome is referred to as a **sister chromatid** and is physically bound to the other copy. The **centromere** is the structure that attaches one sister chromatid to another. Because a human cell has 46 chromosomes, during this phase, there are 92 chromatids (46 × 2) in the cell. Make sure not to confuse the concept of a pair of chromatids (one chromosome and its exact copy attached during mitosis) and a homologous pair of chromosomes (two paired chromosomes which were inherited separately, one from each parent) (Figure 2).

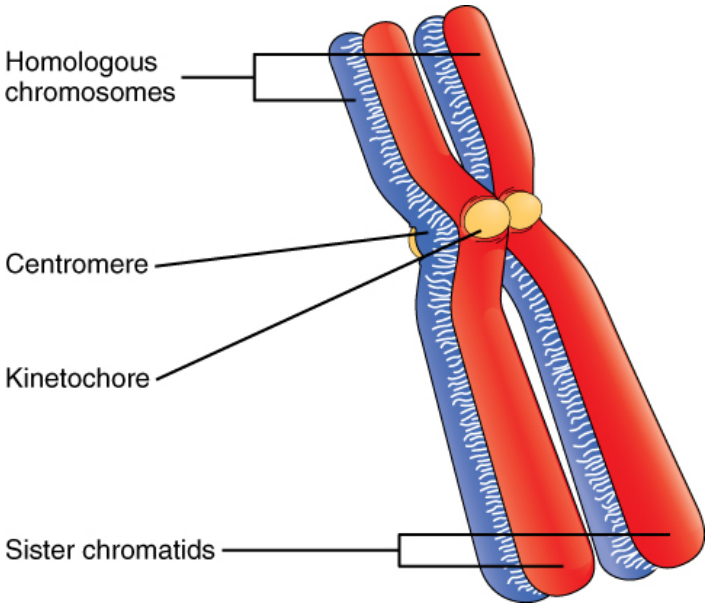
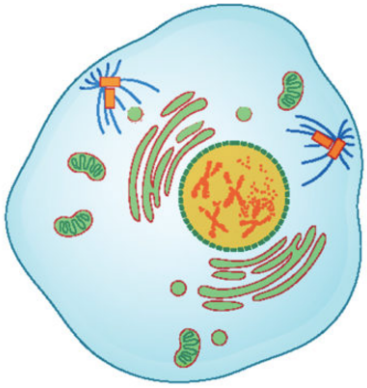
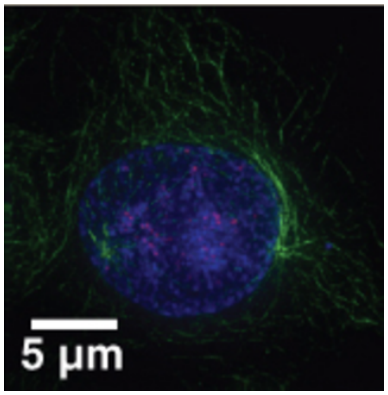


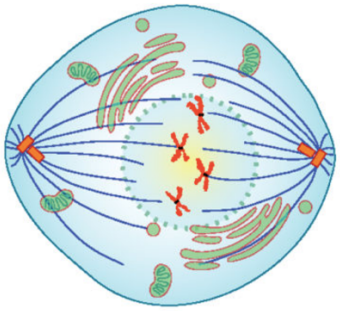
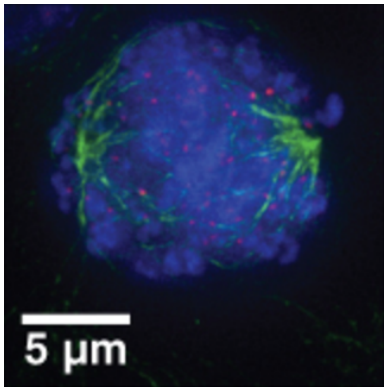
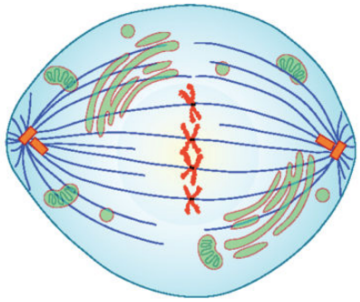
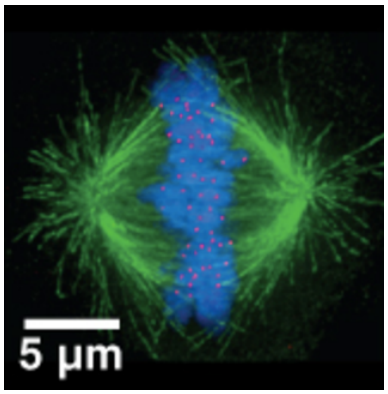
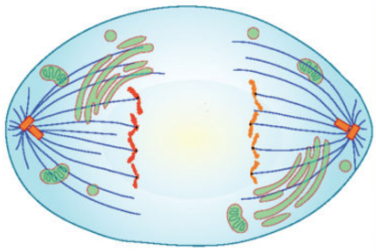
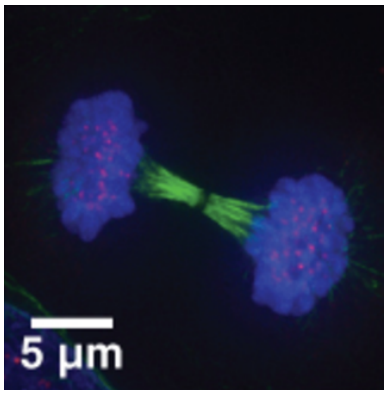
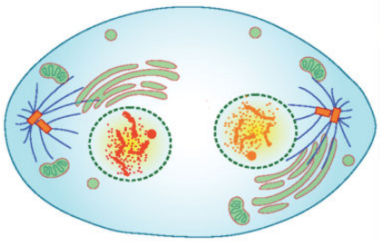
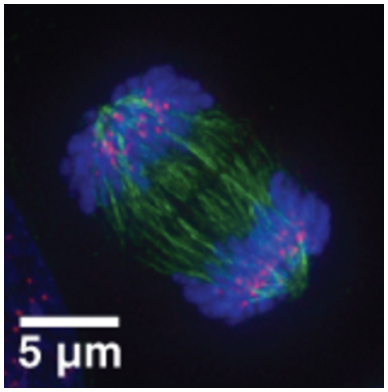
Figure 2. A Homologous Pair of Chromosomes with their Attached Sister Chromatids. *The red and blue colors correspond to a homologous pair of chromosomes. Each member of the pair was separately inherited from one parent. Each chromosome in the homologous pair is also bound to an identical sister chromatid, which is produced by DNA replication, and results in the familiar "X" shape.*

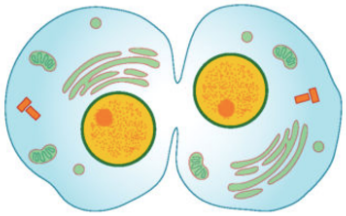
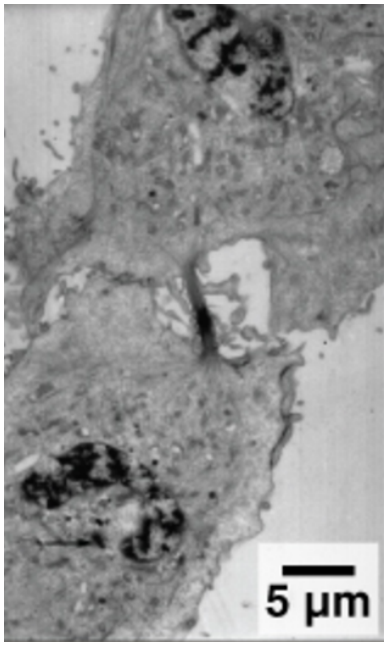
Mitosis

The **mitotic phase** of the cell typically takes between 1 and 2 hours. During this phase, a cell undergoes two major processes. First, it completes mitosis, during which the contents of the nucleus are equitably pulled apart and distributed between its two halves. Cytokinesis then occurs, dividing the cytoplasm and cell body into two new cells. Mitosis is divided into four major stages that take place after interphase (Table 1) and in the following order: prophase, metaphase, anaphase, and telophase. The process is then followed by cytokinesis.

Table 1. Cell Division: Mitosis Followed by Cytokinesis

Phase	Illustration	Key Events	Micrograph
Prophase		Chromosomes condense and become visible Spindle fibers emerge from the centrosomes Nuclear envelope breaks down Centrosomes move toward opposite poles	

Prometaphase		Chromosomes continue to condense Kinetochores appear at the centromeres Mitotic spindle microtubules attach to kinetochores	
Metaphase		Chromosomes are lined up at the metaphase plate Each sister chromatid is attached to a spindle fiber originating from opposite poles	
Anaphase		Centromeres split in two Sister chromatids (now called chromosomes) are pulled toward opposite poles Certain spindle fibers begin to elongate the cell	
Telophase		Chromosomes arrive at opposite poles and begin to decondense Nuclear envelope surrounds each set of chromosomes The mitotic spindle breaks down Spindle fibers continue to push poles apart	

Cytokinesis		Animal cells: a cleavage furrow separates the daughter cells Plant cells: a cell plate, the precursor to a new cell wall, separates the daughter cells	

Prophase is the first phase of mitosis, during which the loosely packed chromatin coils and condenses into visible chromosomes. During prophase, each chromosome becomes visible with its identical partner attached, forming the familiar X-shape of sister chromatids. The nucleolus disappears early during this phase, and the nuclear envelope also disintegrates. A major occurrence during prophase concerns a very important structure that contains the origin site for microtubule growth. Recall the cellular structures called centrioles that serve as origin points from which microtubules extend. These tiny structures also play a very important role during mitosis.
A **centrosome** is a pair of centrioles together. The cell contains two centrosomes side-by-side, which begin to move apart during prophase. As the centrosomes migrate to two different sides of the cell, microtubules begin to extend from each like long fingers from two hands extending toward each other. The **mitotic spindle** is the structure composed of the centrosomes and their emerging microtubules. Near the end of prophase there is an invasion of the nuclear area by microtubules from the mitotic spindle. The nuclear membrane has disintegrated, and the microtubules attach themselves to the centromeres that adjoin pairs of sister chromatids.
The **kinetochore** is a protein structure on the centromere that is the point of attachment between the mitotic spindle and the sister chromatids. This stage is referred to as late prophase or “prometaphase” to indicate the transition between prophase and metaphase.

Metaphase is the second stage of mitosis. During this stage, the sister chromatids, with their attached microtubules, line up along a linear plane in the middle of the cell. A metaphase plate forms between the centrosomes that are now located at either end of the cell. The **metaphase plate** is the name for the plane through the center of the spindle on which the sister chromatids are positioned. The microtubules are now poised to pull apart the sister chromatids and bring one from each pair to each side of the cell.

Anaphase is the third stage of mitosis. Anaphase takes place over a few minutes, when the pairs of sister chromatids are separated from one another, forming individual chromosomes once again. These chromosomes are pulled to opposite ends of the cell by their kinetochores, as the microtubules shorten. Each end of the cell receives one partner from each pair of sister chromatids, ensuring that the two new daughter cells will contain identical genetic material.

Telophase is the final stage of mitosis. Telophase is characterized by the formation of two new daughter nuclei at either end of the dividing cell. These newly formed nuclei surround the genetic material, which uncoils such that the chromosomes return to loosely packed chromatin. Nucleoli also reappear within the new nuclei, and the mitotic spindle breaks apart, each new cell receiving its own complement of DNA, organelles, membranes, and centrioles. At this point, the cell is already beginning to split in half as cytokinesis begins.

Cytokinesis

The **cleavage furrow** is a contractile band made up of microfilaments that forms around the midline of the cell during cytokinesis. (Recall that microfilaments consist of actin.) This contractile band squeezes the two cells apart until they finally separate. Two new cells are now formed. One of these cells (the “stem cell”) enters its own cell cycle; able to grow and divide again at some future time. The other cell transforms into the functional cell of the tissue, typically replacing an “old” cell there. Imagine a cell that completed mitosis but never underwent cytokinesis. In some cases, a cell may divide its genetic material and grow in size, but fail to undergo cytokinesis. This results in larger cells with more than one nucleus. Usually this is an unwanted aberration and can be a sign of cancerous cells.

Cell Cycle Control

A very elaborate and precise system of regulation controls direct the way cells proceed from one phase to the next in the cell cycle and begin mitosis. The control system involves molecules within the cell as well as external triggers. These internal and external control triggers provide “stop” and “advance” signals for the cell. Precise regulation of the cell cycle is critical for maintaining the health of an organism, and loss of cell cycle control can lead to cancer.

Mechanisms of Cell Cycle Control

As the cell proceeds through its cycle, each phase involves certain processes that must be completed before the cell should advance to the next phase. A **checkpoint** is a point in the cell cycle at which the cycle can be signaled to move forward or stopped. At each of these checkpoints, different varieties of molecules provide the stop or go signals, depending on certain conditions within the cell. A **cyclin** is one of the primary classes of cell cycle control molecules (Figure 3). A **cyclin-dependent kinase (CDK)** is one of a group of molecules that work together with cyclins to determine progression past cell checkpoints. By interacting with many additional molecules, these triggers push the cell cycle forward unless prevented from doing so by “stop” signals, if for some reason the cell is not ready. At the G_1 checkpoint, the cell must be ready for DNA synthesis to occur. At the G_2 checkpoint the cell must be fully prepared for mitosis. Even during mitosis, a crucial stop and go checkpoint in metaphase ensures that the cell is fully prepared to complete cell division. The metaphase checkpoint ensures that all sister chromatids are properly attached to their respective microtubules and lined up at the metaphase plate before the signal is given to separate them during anaphase.

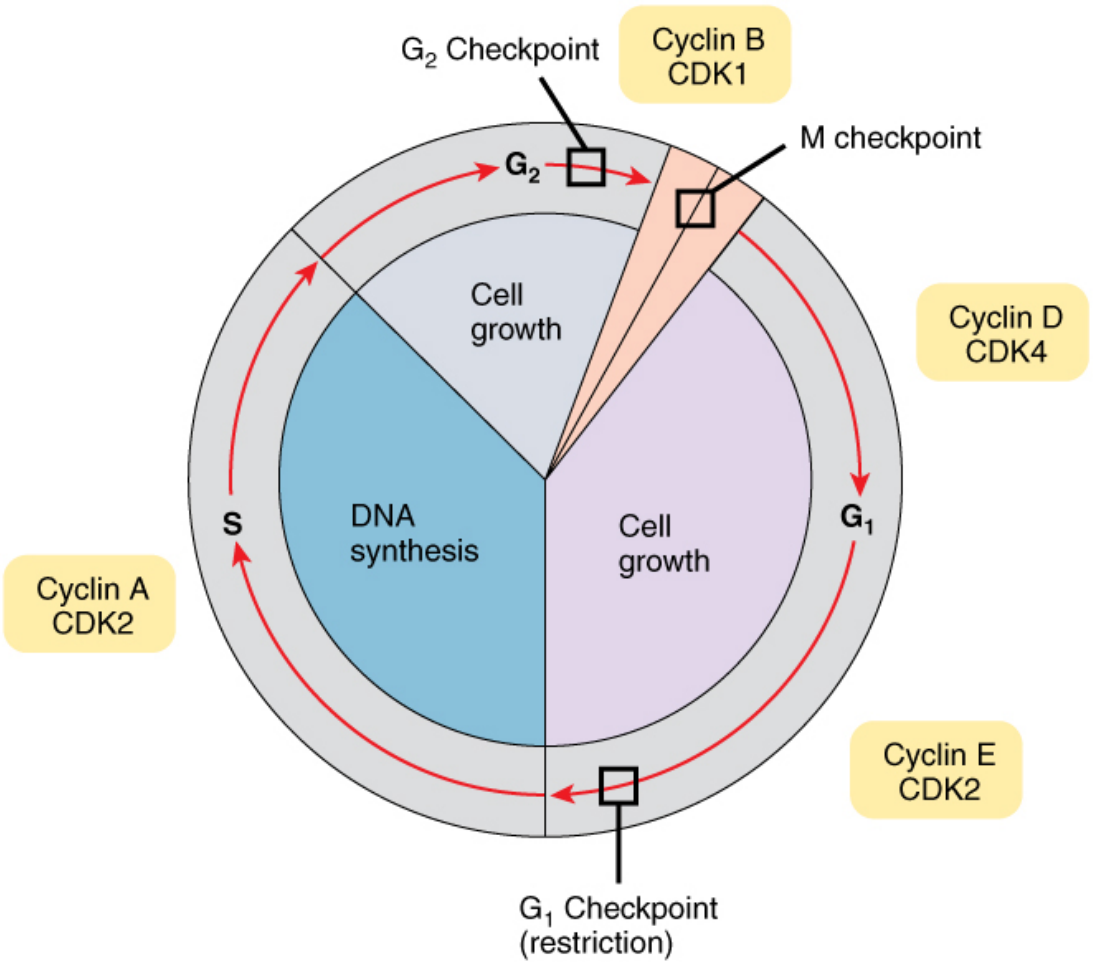


Figure 3. Control of the Cell Cycle. *Cells proceed through the cell cycle under the control of a variety of molecules, such as cyclins and cyclin-dependent kinases. These control molecules determine whether or not the cell is prepared to move into the following stage.*

The Cell Cycle Out of Control: Implications

Most people understand that cancer or tumors are caused by abnormal cells that multiply continuously. If the abnormal cells continue to divide unstopped, they can damage the tissues around them, spread to other parts of the body, and eventually result in death. In healthy cells, the tight regulation mechanisms of the cell cycle prevent this from happening, while failures of cell cycle control can cause unwanted and excessive cell division. Failures of control may be caused by inherited genetic abnormalities that compromise the function of certain “stop” and “go” signals. Environmental insult that damages DNA can also cause dysfunction in those signals. Often, a combination of both genetic predisposition and environmental factors lead to cancer. The process of a cell escaping its normal control system and becoming cancerous may actually happen throughout the body quite frequently. Fortunately, certain cells of the immune system are capable of recognizing cells that have become cancerous and destroying them. However, in certain cases the cancerous cells remain undetected and continue to proliferate. If the resulting tumor does not pose a threat to surrounding tissues, it is said to be benign and can usually be easily removed. If capable of damage, the tumor is considered malignant and the patient is diagnosed with cancer.

Homeostatic Imbalances: Cancer Arises from Homeostatic Imbalances

Cancer is an extremely complex condition, capable of arising from a wide variety of genetic and environmental causes. Typically, mutations or aberrations in a cell’s DNA that compromise normal cell cycle control systems

lead to cancerous tumors. Cell cycle control is an example of a homeostatic mechanism that maintains proper cell function and health. While progressing through the phases of the cell cycle, a large variety of intracellular molecules provide stop and go signals to regulate movement forward to the next phase. These signals are maintained in an intricate balance so that the cell only proceeds to the next phase when it is ready.

The homeostatic control of the cell cycle can be thought of like a car's cruise control. Cruise control will continually apply just the right amount of acceleration to maintain a desired speed, unless the driver hits the brakes, in which case the car will slow down. Similarly, the cell includes molecular messengers, such as cyclins, that push the cell forward in its cycle. In addition to cyclins, a class of proteins that are encoded by genes called proto-oncogenes provide important signals that regulate the cell cycle and move it forward. Examples of proto-oncogene products include cell-surface receptors for growth factors, or cell-signaling molecules, two classes of molecules that can promote DNA replication and cell division.

In contrast, a second class of genes known as tumor suppressor genes sends stop signals during a cell cycle. For example, certain protein products of tumor suppressor genes signal potential problems with the DNA and thus stop the cell from dividing, while other proteins signal the cell to die if it is damaged beyond repair. Some tumor suppressor proteins also signal a sufficient surrounding cellular density, which indicates that the cell need not presently divide. The latter function is uniquely important in preventing tumor growth: normal cells exhibit a phenomenon called "contact inhibition;" thus, extensive cellular contact with neighboring cells causes a signal that stops further cell division.

These two contrasting classes of genes, proto-oncogenes and tumor suppressor genes, are like the accelerator and brake pedal of the cell's own "cruise control system," respectively. Under normal conditions, these stop and go signals are maintained in a homeostatic balance. Generally speaking, there are two ways that the cell's cruise control can lose control: a malfunctioning (overactive) accelerator, or a malfunctioning (underactive) brake. When compromised through a mutation, or otherwise altered, proto-oncogenes can be converted to oncogenes, which produce oncoproteins that push a cell forward in its cycle and stimulate cell division even when it is undesirable to do so.

For example, a cell that should be programmed to self-destruct (a process called apoptosis) due to extensive DNA damage might instead be triggered to proliferate by an oncoprotein. On the other hand, a dysfunctional tumor suppressor gene may fail to provide the cell with a necessary stop signal, also resulting in unwanted cell division and proliferation. A delicate homeostatic balance between the many proto-oncogenes and tumor suppressor genes delicately controls the cell cycle and ensures that only healthy cells replicate. Therefore, a disruption of this homeostatic balance can cause aberrant cell division and cancerous growths.

CELLULAR DIFFERENTIATION

Learning Objectives

By the end of this section, you will be able to:

- Discuss how the generalized cells of a developing embryo or the stem cells of an adult organism become differentiated into specialized cells
- Distinguish between the categories of stem cells

How does a complex organism such as a human develop from a single cell—a fertilized egg—into the vast array of cell types such as nerve cells, muscle cells, and epithelial cells that characterize the adult? Throughout development and adulthood, the process of cellular differentiation leads cells to assume their final morphology

and physiology. Differentiation is the process by which unspecialized cells become specialized to carry out distinct functions.

Stem Cells

A **stem cell** is an unspecialized cell that can divide without limit as needed and can, under specific conditions, differentiate into specialized cells. Stem cells are divided into several categories according to their potential to differentiate. The first embryonic cells that arise from the division of the zygote are the ultimate stem cells; these stems cells are described as **totipotent** because they have the potential to differentiate into any of the cells needed to enable an organism to grow and develop.

The embryonic cells that develop from totipotent stem cells and are precursors to the fundamental tissue layers of the embryo are classified as pluripotent. A **pluripotent** stem cell is one that has the potential to differentiate into any type of human tissue but cannot support the full development of an organism.

These cells then become slightly more specialized, and are referred to as multipotent cells. A **multipotent** stem cell has the potential to differentiate into different types of cells within a given cell lineage or small number of lineages, such as a red blood cell or white blood cell.

Finally, multipotent cells can become further specialized oligopotent cells. An **oligopotent** stem cell is limited to becoming one of a few different cell types. In contrast, a **unipotent** cell is fully specialized and can only reproduce to generate more of its own specific cell type.

Stem cells are unique in that they can also continually divide and regenerate new stem cells instead of further specializing. There are different stem cells present at different stages of a human's life. They include the embryonic stem cells of the embryo, fetal stem cells of the fetus, and adult stem cells in the adult. One type of adult stem cell is the epithelial stem cell, which gives rise to the keratinocytes in the multiple layers of epithelial cells in the epidermis of skin. Adult bone marrow has three distinct types of stem cells: hematopoietic stem cells, which give rise to red blood cells, white blood cells, and platelets (Figure 1); endothelial stem cells, which give rise to the endothelial cell types that line blood and lymph vessels; and mesenchymal stem cells, which give rise to the different types of muscle cells.

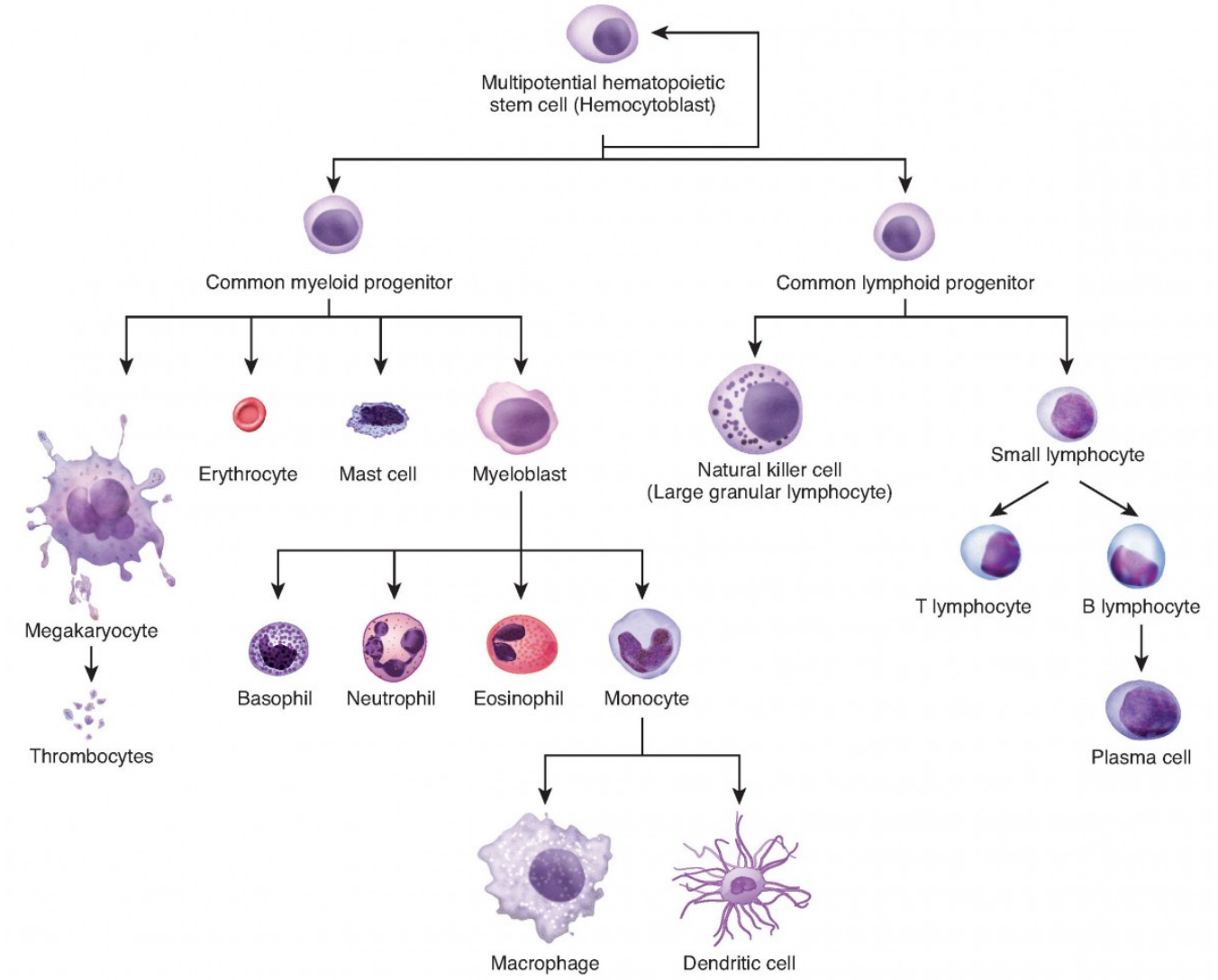


Figure 1. Hematopoiesis. *The process of hematopoiesis involves the differentiation of multipotent cells into blood and immune cells. The multipotent hematopoietic stem cells give rise to many different cell types, including the cells of the immune system and red blood cells.*

Differentiation

When a cell differentiates (becomes more specialized), it may undertake major changes in its size, shape, metabolic activity, and overall function. Because all cells in the body, beginning with the fertilized egg, contain the same DNA, how do the different cell types come to be so different? The answer is analogous to a movie script. The different actors in a movie all read from the same script, however, they are each only reading their own part of the script. Similarly, all cells contain the same full complement of DNA, but each type of cell only "reads" the portions of DNA that are relevant to its own function. In biology, this is referred to as the unique genetic expression of each cell.

In order for a cell to differentiate into its specialized form and function, it need only manipulate those genes (and thus those proteins) that will be expressed, and not those that will remain silent. The primary mechanism by which genes are turned "on" or "off" is through transcription factors. A **transcription factor** is one of a class of proteins that bind to specific genes on the DNA molecule and either promote or inhibit their transcription (Figure 2).

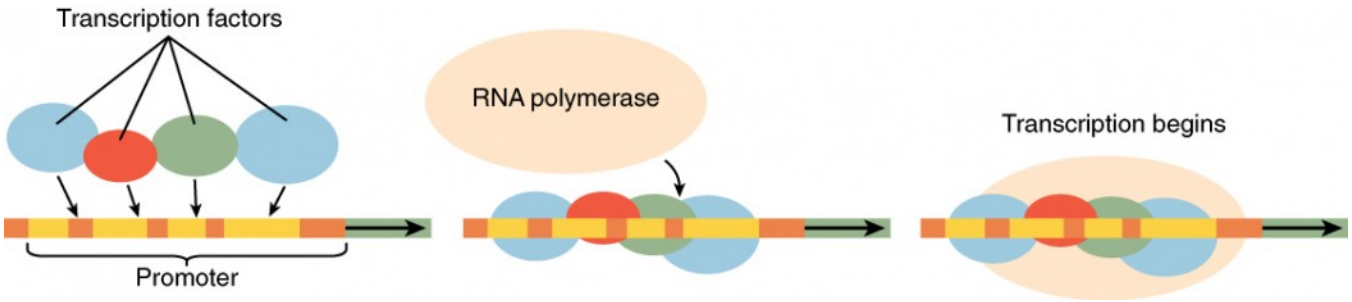


Figure 2. Transcription Factors Regulate Gene Expression. *While each body cell contains the organism's entire genome, different cells regulate gene expression with the use of various transcription factors. Transcription factors are proteins that affect the binding of RNA polymerase to a particular gene on the DNA molecule.*

Everyday Connection: Stem Cell Research

Stem cell research aims to find ways to use stem cells to regenerate and repair cellular damage. Over time, most adult cells undergo the wear and tear of aging and lose their ability to divide and repair themselves. Stem cells do not display a particular morphology or function. Adult stem cells, which exist as a small subset of cells in most tissues, keep dividing and can differentiate into a number of specialized cells generally formed by that tissue. These cells enable the body to renew and repair body tissues.

The mechanisms that induce a non-differentiated cell to become a specialized cell are poorly understood. In a laboratory setting, it is possible to induce stem cells to differentiate into specialized cells by changing the physical and chemical conditions of growth. Several sources of stem cells are used experimentally and are classified according to their origin and potential for differentiation. Human embryonic stem cells (hESCs) are extracted from embryos and are pluripotent. The adult stem cells that are present in many organs and differentiated tissues, such as bone marrow and skin, are multipotent, being limited in differentiation to the types of cells found in those tissues. The stem cells isolated from umbilical cord blood are also multipotent, as are cells from deciduous teeth (baby teeth).

Researchers have recently developed induced pluripotent stem cells (iPSCs) from mouse and human adult stem cells. These cells are genetically reprogrammed multipotent adult cells that function like embryonic stem cells; they are capable of generating cells characteristic of all three germ layers. Because of their capacity to divide and differentiate into specialized cells, stem cells offer a potential treatment for diseases such as diabetes and heart disease (Figure 3). Cell-based therapy refers to treatment in which stem cells induced to differentiate in a growth dish are injected into a patient to repair damaged or destroyed cells or tissues. Many obstacles must be overcome for the application of cell-based therapy. Although embryonic stem cells have a nearly unlimited range of differentiation potential, they are seen as foreign by the patient's immune system and may trigger rejection. Also, the destruction of embryos to isolate embryonic stem cells raises considerable ethical and legal questions.

In contrast, adult stem cells isolated from a patient are not seen as foreign by the body, but they have a limited range of differentiation. Some individuals bank the cord blood or deciduous teeth of their child, storing away those sources of stem cells for future use, should their child need it. Induced pluripotent stem cells are considered a promising advance in the field because using them avoids the legal, ethical, and immunological pitfalls of embryonic stem cells.

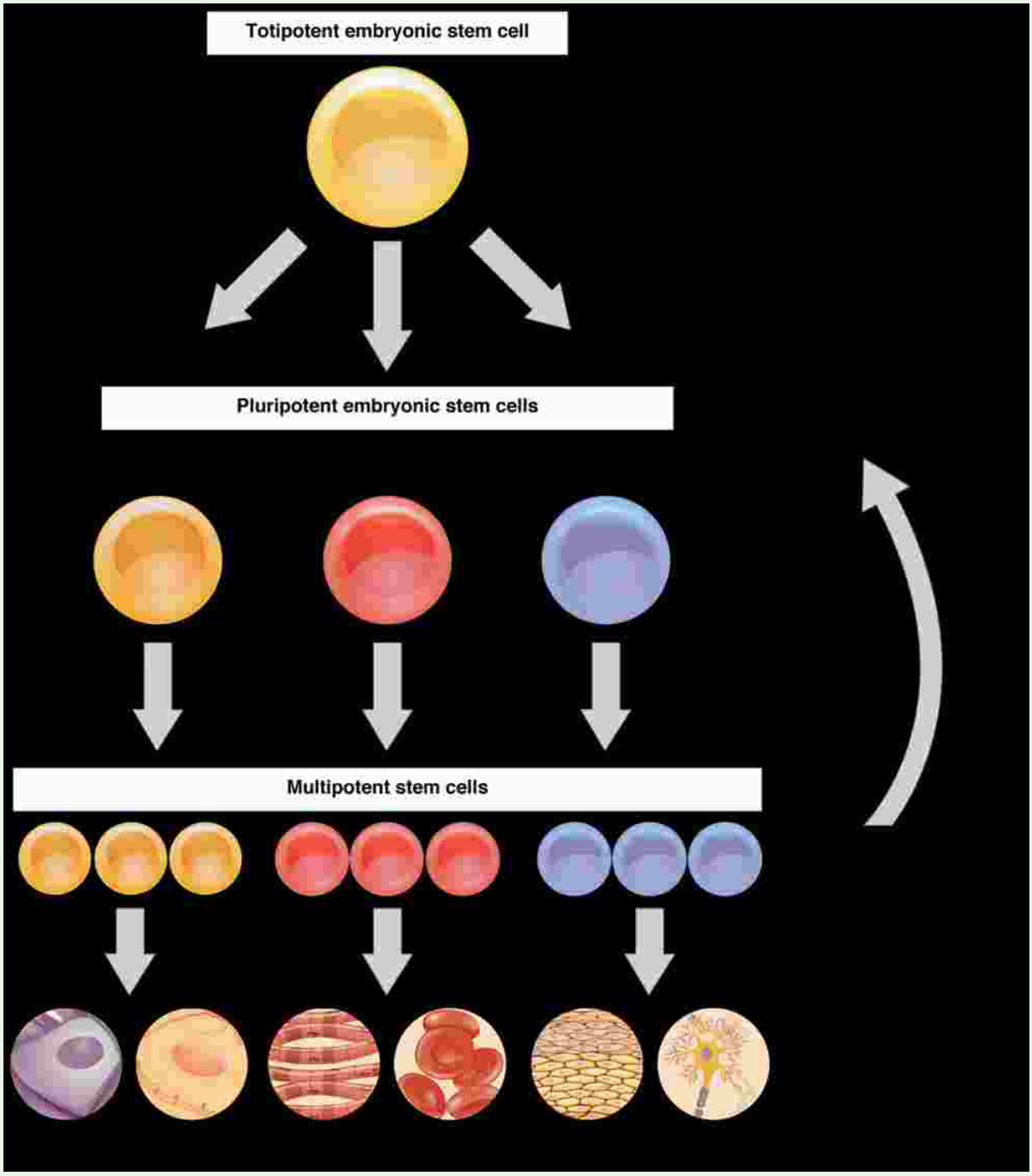


Figure 3. Stem Cells. *The capacity of stem cells to differentiate into specialized cells make them potentially valuable in therapeutic applications designed to replace damaged cells of different body tissues.*

PRACTICE: ICELL

To practice and better visualize the material this week, click on this link to download the free Hudson Alpha iCell App.

GLOSSARY: THE CELLULAR LEVEL OF ORGANIZATION

active transport: form of transport across the cell membrane that requires input of cellular energy

amphipathic: describes a molecule that exhibits a difference in polarity between its two ends, resulting in a difference in water solubility

anaphase: third stage of mitosis (and meiosis), during which sister chromatids separate into two new nuclear regions of a dividing cell

anticodon: consecutive sequence of three nucleotides on a tRNA molecule that is complementary to a specific codon on an mRNA molecule

autolysis: breakdown of cells by their own enzymatic action

autophagy: lysosomal breakdown of a cell's own components

cell cycle: life cycle of a single cell, from its birth until its division into two new daughter cells

cell membrane: membrane surrounding all animal cells, composed of a lipid bilayer interspersed with various molecules; also known as plasma membrane

centriole: small, self-replicating organelle that provides the origin for microtubule growth and moves DNA during cell division

centromere: region of attachment for two sister chromatids

centrosome: cellular structure that organizes microtubules during cell division

channel protein: membrane-spanning protein that has an inner pore which allows the passage of one or more substances

checkpoint: progress point in the cell cycle during which certain conditions must be met in order for the cell to proceed to a subsequence phase

chromatin: substance consisting of DNA and associated proteins

chromosome: condensed version of chromatin

cilia: small appendage on certain cells formed by microtubules and modified for movement of materials across the cellular surface

cleavage furrow: contractile ring that forms around a cell during cytokinesis that pinches the cell into two halves

codon: consecutive sequence of three nucleotides on an mRNA molecule that corresponds to a specific amino acid

concentration gradient: difference in the concentration of a substance between two regions

cyclin-dependent kinase (CDK): one of a group of enzymes associated with cyclins that help them perform their functions

cyclin: one of a group of proteins that function in the progression of the cell cycle

cytokinesis: final stage in cell division, where the cytoplasm divides to form two separate daughter cells

cytoplasm: internal material between the cell membrane and nucleus of a cell, mainly consisting of a water-based fluid called cytosol, within which are all the other organelles and cellular solute and suspended materials

cytoskeleton: "skeleton" of a cell; formed by rod-like proteins that support the cell's shape and provide, among other functions, locomotive abilities

cytosol: clear, semi-fluid medium of the cytoplasm, made up mostly of water

DNA polymerase: enzyme that functions in adding new nucleotides to a growing strand of DNA during DNA replication

DNA replication: process of duplicating a molecule of DNA

diffusion: movement of a substance from an area of higher concentration to one of lower concentration

diploid: condition marked by the presence of a double complement of genetic material (two sets of chromosomes, one set inherited from each of two parents)

electrical gradient: difference in the electrical charge (potential) between two regions

endocytosis: import of material into the cell by formation of a membrane-bound vesicle

endoplasmic reticulum (ER): cellular organelle that consists of interconnected membrane-bound tubules, which may or may not be associated with ribosomes (rough type or smooth type, respectively)

exocytosis: export of a substance out of a cell by formation of a membrane-bound vesicle

exon: one of the coding regions of an mRNA molecule that remain after splicing

extracellular fluid (ECF): fluid exterior to cells; includes the interstitial fluid, blood plasma, and fluid found in other reservoirs in the body

facilitated diffusion: diffusion of a substance with the aid of a membrane protein

flagellum: appendage on certain cells formed by microtubules and modified for movement

G_0 phase: phase of the cell cycle, usually entered from the G_1 phase; characterized by long or permanent periods where the cell does not move forward into the DNA synthesis phase

G_1 phase: first phase of the cell cycle, after a new cell is born

G_2 phase: third phase of the cell cycle, after the DNA synthesis phase

Golgi apparatus: cellular organelle formed by a series of flattened, membrane-bound sacs that functions in protein modification, tagging, packaging, and transport

gene expression: active interpretation of the information coded in a gene to produce a functional gene product

gene: functional length of DNA that provides the genetic information necessary to build a protein

genome: entire complement of an organism's DNA; found within virtually every cell

glycocalyx: coating of sugar molecules that surrounds the cell membrane

glycoprotein: protein that has one or more carbohydrates attached

helicase: enzyme that functions to separate the two DNA strands of a double helix during DNA replication

histone: family of proteins that associate with DNA in the nucleus to form chromatin

homologous: describes two copies of the same chromosome (not identical), one inherited from each parent

hydrophilic: describes a substance or structure attracted to water

hydrophobic: describes a substance or structure repelled by water

hypertonic: describes a solution concentration that is higher than a reference concentration

hypotonic: describes a solution concentration that is lower than a reference concentration

integral protein: membrane-associated protein that spans the entire width of the lipid bilayer

intermediate filament: type of cytoskeletal filament made of keratin, characterized by an intermediate thickness, and playing a role in resisting cellular tension

interphase: entire life cycle of a cell, excluding mitosis

interstitial fluid (IF): fluid in the small spaces between cells not contained within blood vessels

intracellular fluid (ICF): fluid in the cytosol of cells

intron: non-coding regions of a pre-mRNA transcript that may be removed during splicing

isotonic: describes a solution concentration that is the same as a reference concentration

kinetochore: region of a centromere where microtubules attach to a pair of sister chromatids

ligand: molecule that binds with specificity to a specific receptor molecule

lysosome: membrane-bound cellular organelle originating from the Golgi apparatus and containing digestive enzymes

messenger RNA (mRNA): nucleotide molecule that serves as an intermediate in the genetic code between DNA and protein

metaphase plate: linear alignment of sister chromatids in the center of the cell, which takes place during metaphase

metaphase: second stage of mitosis (and meiosis), characterized by the linear alignment of sister chromatids in the center of the cell

microfilament: the thinnest of the cytoskeletal filaments; composed of actin subunits that function in muscle contraction and cellular structural support

microtubule: the thickest of the cytoskeletal filaments, composed of tubulin subunits that function in cellular movement and structural support

mitochondrion: one of the cellular organelles bound by a double lipid bilayer that function primarily in the production of cellular energy (ATP)

mitosis: division of genetic material, during which the cell nucleus breaks down and two new, fully functional, nuclei are formed

mitotic phase: phase of the cell cycle in which a cell undergoes mitosis

mitotic spindle: network of microtubules, originating from centrioles, that arranges and pulls apart chromosomes during mitosis

multipotent: describes the condition of being able to differentiate into different types of cells within a given cell lineage or small number of lineages, such as a red blood cell or white blood cell

mutation: change in the nucleotide sequence in a gene within a cell's DNA

nuclear envelope: membrane that surrounds the nucleus; consisting of a double lipid-bilayer

nuclear pore: one of the small, protein-lined openings found scattered throughout the nuclear envelope

nucleolus: small region of the nucleus that functions in ribosome synthesis

nucleosome: unit of chromatin consisting of a DNA strand wrapped around histone proteins

nucleus: cell's central organelle; contains the cell's DNA

oligopotent: describes the condition of being more specialized than multipotency; the condition of being able to differentiate into one of a few possible cell types

organelle: any of several different types of membrane-enclosed specialized structures in the cell that perform specific functions for the cell

osmosis: diffusion of molecules down their concentration across a selectively permeable membrane

passive transport: form of transport across the cell membrane that does not require input of cellular energy

peripheral protein: membrane-associated protein that does not span the width of the lipid bilayer, but is attached peripherally to integral proteins, membrane lipids, or other components of the membrane

peroxisome: membrane-bound organelle that contains enzymes primarily responsible for detoxifying harmful substances

phagocytosis: endocytosis of large particles

pinocytosis: endocytosis of fluid

pluripotent: describes the condition of being able to differentiate into a large variety of cell types

polypeptide: chain of amino acids linked by peptide bonds

polyribosome: simultaneous translation of a single mRNA transcript by multiple ribosomes

promoter: region of DNA that signals transcription to begin at that site within the gene

prophase: first stage of mitosis (and meiosis), characterized by breakdown of the nuclear envelope and condensing of the chromatin to form chromosomes

proteome: full complement of proteins produced by a cell (determined by the cell's specific gene expression)

RNA polymerase: enzyme that unwinds DNA and then adds new nucleotides to a growing strand of RNA for the transcription phase of protein synthesis

reactive oxygen species (ROS): a group of extremely reactive peroxides and oxygen-containing radicals that may contribute to cellular damage

receptor-mediated endocytosis: endocytosis of ligands attached to membrane-bound receptors

receptor: protein molecule that contains a binding site for another specific molecule (called a ligand)

ribosomal RNA (rRNA): RNA that makes up the subunits of a ribosome

ribosome: cellular organelle that functions in protein synthesis

S phase: stage of the cell cycle during which DNA replication occurs

selective permeability: feature of any barrier that allows certain substances to cross but excludes others

sister chromatid: one of a pair of identical chromosomes, formed during DNA replication

sodium-potassium pump: (also, Na^+/K^+ ATP-ase) membrane-embedded protein pump that uses ATP to move Na^+ out of a cell and K^+ into the cell

somatic cell: all cells of the body excluding gamete cells

spliceosome: complex of enzymes that serves to splice out the introns of a pre-mRNA transcript

splicing: the process of modifying a pre-mRNA transcript by removing certain, typically non-coding, regions

stem cell: cell that is oligo-, multi-, or pleuripotent that has the ability to produce additional stem cells rather than becoming further specialized

telophase: final stage of mitosis (and meiosis), preceding cytokinesis, characterized by the formation of two new daughter nuclei

totipotent: embryonic cells that have the ability to differentiate into any type of cell and organ in the body

transcription factor: one of the proteins that regulate the transcription of genes

transcription: process of producing an mRNA molecule that is complementary to a particular gene of DNA

transfer RNA (tRNA): molecules of RNA that serve to bring amino acids to a growing polypeptide strand and properly place them into the sequence

translation: process of producing a protein from the nucleotide sequence code of an mRNA transcript

triplet: consecutive sequence of three nucleotides on a DNA molecule that, when transcribed into an mRNA codon, corresponds to a particular amino acid

unipotent: describes the condition of being committed to a single specialized cell type

vesicle: membrane-bound structure that contains materials within or outside of the cell

PRACTICE TEST: THE CELLULAR LEVEL OF ORGANIZATION

Review the material from this module by completing the practice in course online.

MODULE 5: THE TISSUE LEVEL OF ORGANIZATION

INTRODUCTION TO THE TISSUE LEVEL OF ORGANIZATION

Learning Objectives

- Identify the main tissue types and discuss their roles in the human body
- Identify the four types of tissue membranes and the characteristics of each that make them functional
- Explain the functions of various epithelial tissues and how their forms enable their functions
- Explain the functions of various connective tissues and how their forms enable their functions
- Describe the characteristics of muscle tissue and how these enable function
- Discuss the characteristics of nervous tissue and how these enable information processing and control of muscular and glandular activities

The body contains at least 200 distinct cell types. These cells contain essentially the same internal structures yet they vary enormously in shape and function. The different types of cells are not randomly distributed throughout the body; rather they occur in organized layers, a level of organization referred to as tissue. The micrograph that opens this chapter shows the high degree of organization among different types of cells in the tissue of the cervix. You can also see how that organization breaks down when cancer takes over the regular mitotic functioning of a cell.

The variety in shape reflects the many different roles that cells fulfill in your body. The human body starts as a single cell at fertilization. As this fertilized egg divides, it gives rise to trillions of cells, each built from the same blueprint, but organizing into tissues and becoming irreversibly committed to a developmental pathway.

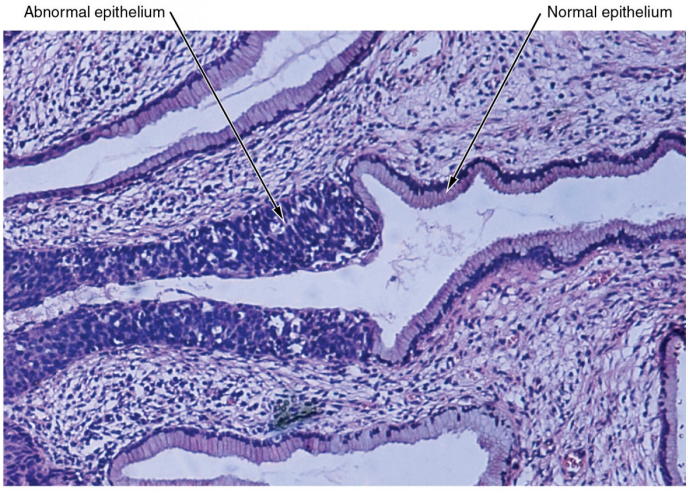


Figure 1. Micrograph of Cervical Tissue. *This figure is a view of the regular architecture of normal tissue contrasted with the irregular arrangement of cancerous cells. (credit: "Haymanj"/Wikimedia Commons)*

TYPES OF TISSUES

Learning Objectives

- Identify the four main tissue types
- Discuss the functions of each tissue type
- Relate the structure of each tissue type to their function
- Discuss the embryonic origin of tissue
- Identify the three major germ layers
- Identify the main types of tissue membranes

The term **tissue** is used to describe a group of cells found together in the body. The cells within a tissue share a common embryonic origin. Microscopic observation reveals that the cells in a tissue share morphological features and are arranged in an orderly pattern that achieves the tissue's functions. From the evolutionary perspective, tissues appear in more complex organisms. For example, multicellular protists, ancient eukaryotes, do not have cells organized into tissues.

Although there are many types of cells in the human body, they are organized into four broad categories of tissues: epithelial, connective, muscle, and nervous. Each of these categories is characterized by specific functions that contribute to the overall health and maintenance of the body. A disruption of the structure is a sign of injury or disease. Such changes can be detected through **histology**, the microscopic study of tissue appearance, organization, and function.

The Four Types of Tissues

Epithelial tissue, also referred to as epithelium, refers to the sheets of cells that cover exterior surfaces of the body, lines internal cavities and passageways, and forms certain glands. **Connective tissue**, as its name implies, binds the cells and organs of the body together and functions in the protection, support, and integration of all parts of the body. **Muscle tissue** is excitable, responding to stimulation and contracting to provide movement, and occurs as three major types: skeletal (voluntary) muscle, smooth muscle, and cardiac muscle in the heart. **Nervous tissue** is also excitable, allowing the propagation of electrochemical signals in the form of nerve impulses that communicate between different regions of the body (Figure 1).

The next level of organization is the organ, where several types of tissues come together to form a working unit. Just as knowing the structure and function of cells helps you in your study of tissues, knowledge of tissues will help you understand how organs function. The epithelial and connective tissues are discussed in detail in this chapter. Muscle and nervous tissues will be discussed only briefly in this chapter.

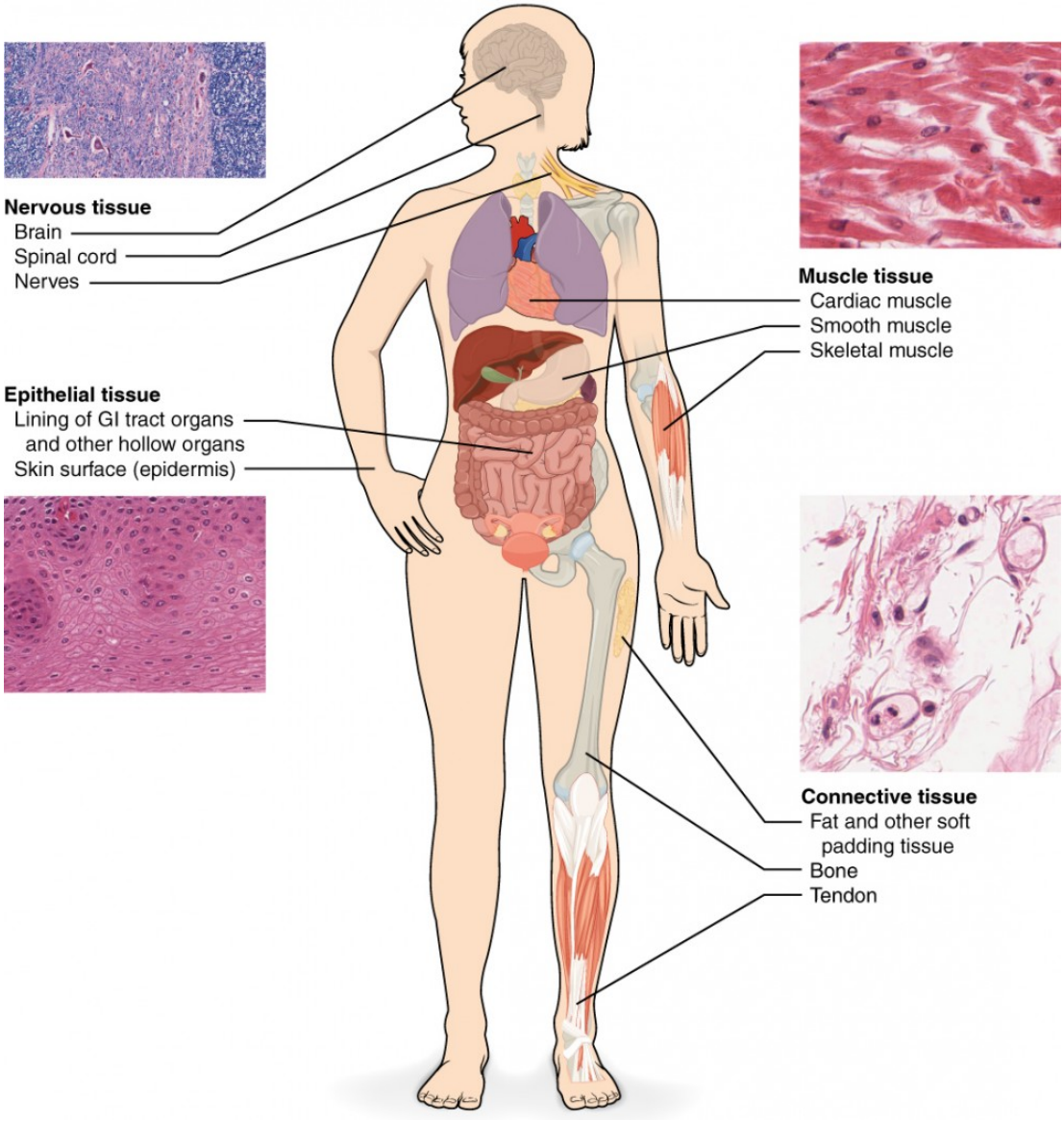


Figure 1. Four Types of Tissue: Body. *The four types of tissues are exemplified in nervous tissue, stratified squamous epithelial tissue, cardiac muscle tissue, and connective tissue in small intestine. Clockwise from nervous tissue, LM × 872, LM × 282, LM × 460, LM × 800. (Micrographs provided by the Regents of University of Michigan Medical School © 2012)*

Embryonic Origin of Tissues

The zygote, or fertilized egg, is a single cell formed by the fusion of an egg and sperm. After fertilization the zygote gives rise to rapid mitotic cycles, generating many cells to form the embryo. The first embryonic cells generated have the ability to differentiate into any type of cell in the body and, as such, are called **totipotent**, meaning each has the capacity to divide, differentiate, and develop into a new organism. As cell proliferation progresses, three major cell lineages are established within the embryo. Each of these lineages of embryonic cells forms the distinct germ layers from which all the tissues and organs of the human body eventually form. Each germ layer is identified by its relative position: **ectoderm** (*ecto–* = "outer"), **mesoderm** (*meso–* = "middle"), and **endoderm** (*endo–* = "inner"). Figure 2 shows the types of tissues and organs associated with the each of the three germ layers. Note that epithelial tissue originates in all three layers, whereas nervous tissue derives primarily from the ectoderm and muscle tissue from mesoderm.

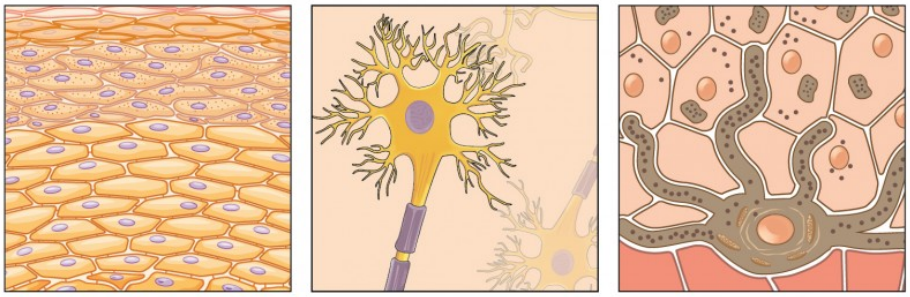
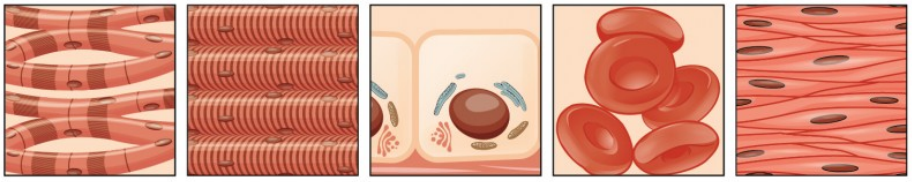
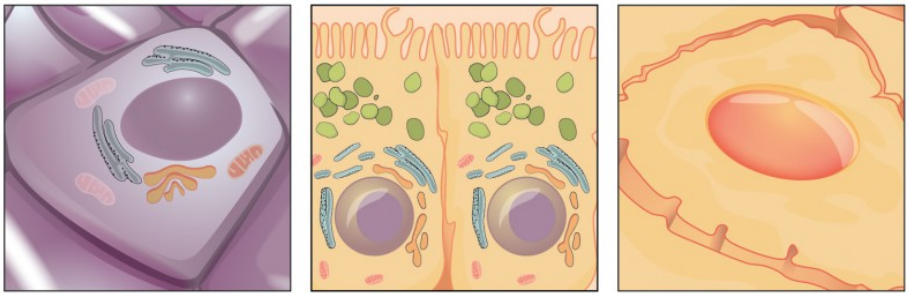
Germ Layer	Gives rise to:
Ectoderm	Epidermis, glands on skin, some cranial bones, pituitary and adrenal medulla, the nervous system, the mouth between cheek and gums, the anus  Skin cells Neurons Pigment cell
Mesoderm	Connective tissues proper, bone, cartilage, blood, endothelium of blood vessels, muscle, synovial membranes, serous membranes lining body cavities, kidneys, lining of gonads  Cardiac muscle Skeletal muscle Tubule cell of kidney Red blood cells Smooth muscle
Endoderm	Lining of airways and digestive system except the mouth and distal part of digestive system (rectum and anal canal); glands (digestive glands, endocrine glands, adrenal cortex)  Lung cell Thyroid cell Pancreatic cell

Figure 2. Embryonic Origin of Tissues and Major Organs

View this slideshow to learn more about stem cells. How do somatic stem cells differ from embryonic stem cells?

Tissue Membranes

A **tissue membrane** is a thin layer or sheet of cells that covers the outside of the body (for example, skin), the organs (for example, pericardium), internal passageways that lead to the exterior of the body (for example, abdominal mesenteries), and the lining of the moveable joint cavities. There are two basic types of tissue membranes: connective tissue and epithelial membranes (Figure 3).

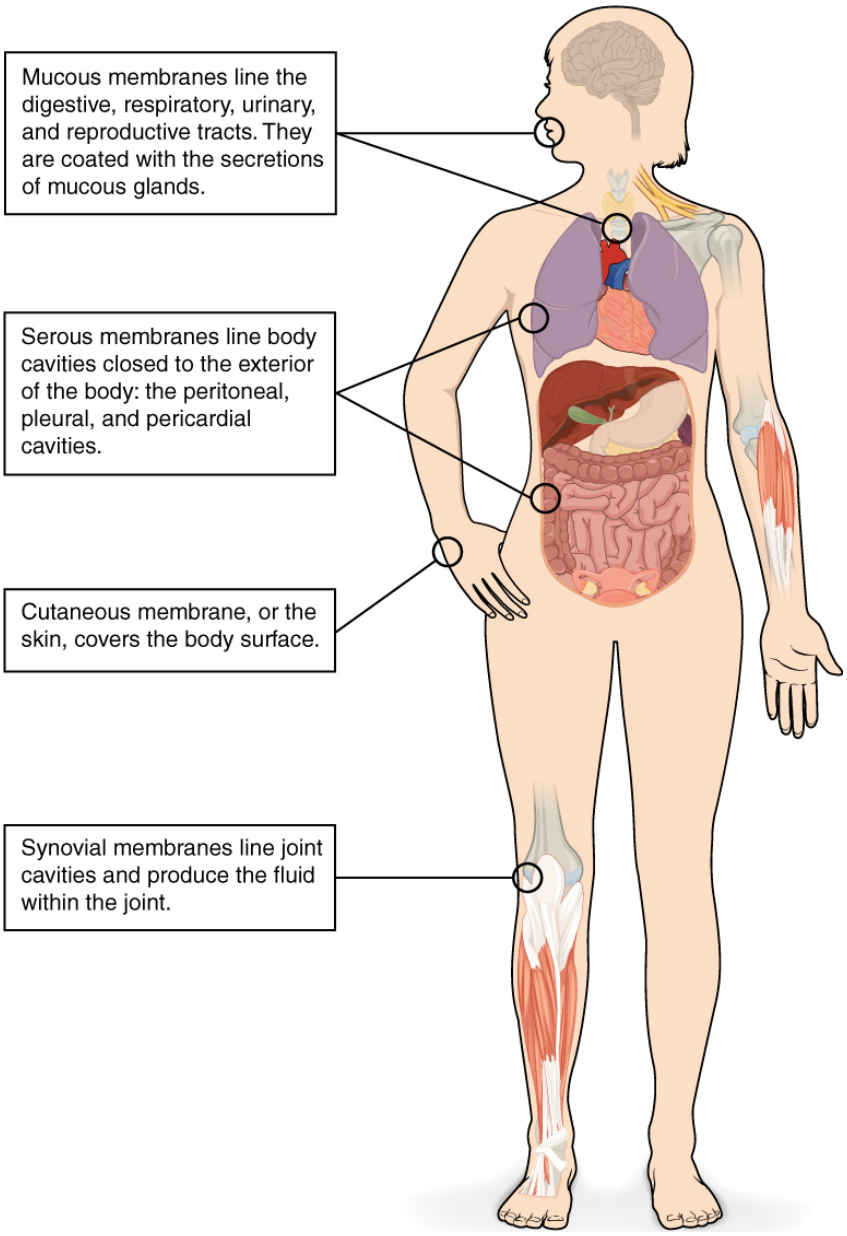


Figure 3. Tissue Membranes. *The two broad categories of tissue membranes in the body are (1) connective tissue membranes, which include synovial membranes, and (2) epithelial membranes, which include mucous membranes, serous membranes, and the cutaneous membrane, in other words, the skin.*

Connective Tissue Membranes

The **connective tissue membrane** is formed solely from connective tissue. These membranes encapsulate organs, such as the kidneys, and line our movable joints. A **synovial membrane** is a type of connective tissue membrane that lines the cavity of a freely movable joint. For example, synovial membranes surround the joints of the shoulder, elbow, and knee. Fibroblasts in the inner layer of the synovial membrane release hyaluronan into the joint cavity. The hyaluronan effectively traps available water to form the synovial fluid, a natural lubricant that enables the bones of a joint to move freely against one another without much friction. This synovial fluid readily exchanges water and nutrients with blood, as do all body fluids.

Epithelial Membranes

The **epithelial membrane** is composed of epithelium attached to a layer of connective tissue, for example, your skin. The **mucous membrane** is also a composite of connective and epithelial tissues. Sometimes called mucosae, these epithelial membranes line the body cavities and hollow passageways that open to the external environment, and include the digestive, respiratory, excretory, and reproductive tracts. Mucous, produced by the epithelial exocrine glands, covers the epithelial layer. The underlying connective tissue, called the **lamina propria** (literally "own layer"), help support the fragile epithelial layer.

A **serous membrane** is an epithelial membrane composed of mesodermally derived epithelium called the mesothelium that is supported by connective tissue. These membranes line the coelomic cavities of the body, that is, those cavities that do not open to the outside, and they cover the organs located within those cavities. They are essentially membranous bags, with mesothelium lining the inside and connective tissue on the outside. Serous fluid secreted by the cells of the thin squamous mesothelium lubricates the membrane and reduces abrasion and friction between organs. Serous membranes are identified according locations. Three serous membranes line the thoracic cavity; the two pleura that cover the lungs and the pericardium that covers the heart. A fourth, the peritoneum, is the serous membrane in the abdominal cavity that covers abdominal organs and forms double sheets of mesenteries that suspend many of the digestive organs.

The skin is an epithelial membrane also called the **cutaneous membrane**. It is a stratified squamous epithelial membrane resting on top of connective tissue. The apical surface of this membrane is exposed to the external environment and is covered with dead, keratinized cells that help protect the body from desiccation and pathogens.

Self-Check Questions

Visit your course online to take a quiz to check your understanding of Types of Tissue:

EPITHELIAL TISSUE

Learning Objectives

- Explain the structure and function of epithelial tissue
- Distinguish between tight junctions, anchoring junctions, and gap junctions
- Distinguish between simple epithelia and stratified epithelia, as well as between squamous, cuboidal, and columnar epithelia
- Describe the structure and function of endocrine and exocrine glands and their respective secretions

Most epithelial tissues are essentially large sheets of cells covering all the surfaces of the body exposed to the outside world and lining the outside of organs. Epithelium also forms much of the glandular tissue of the body. Skin is not the only area of the body exposed to the outside. Other areas include the airways, the digestive tract, as well as the urinary and reproductive systems, all of which are lined by an epithelium. Hollow organs and body cavities that do not connect to the exterior of the body, which includes, blood vessels and serous membranes, are lined by endothelium (plural = endothelia), which is a type of epithelium.

Epithelial cells derive from all three major embryonic layers. The epithelia lining the skin, parts of the mouth and nose, and the anus develop from the ectoderm. Cells lining the airways and most of the digestive system originate in the endoderm. The epithelium that lines vessels in the lymphatic and cardiovascular system derives from the mesoderm and is called an endothelium.

All epithelia share some important structural and functional features. This tissue is highly cellular, with little or no extracellular material present between cells. Adjoining cells form a specialized intercellular connection between their cell membranes called a **cell junction**. The epithelial cells exhibit polarity with differences in structure and function between the exposed or **apical** facing surface of the cell and the basal surface close to the underlying body structures. The **basal lamina**, a mixture of glycoproteins and collagen, provides an attachment site for the epithelium, separating it from underlying connective tissue. The basal lamina attaches to a **reticular lamina**, which is secreted by the underlying connective tissue, forming a **basement membrane** that helps hold it all together.

Epithelial tissues are nearly completely avascular. For instance, no blood vessels cross the basement membrane to enter the tissue, and nutrients must come by diffusion or absorption from underlying tissues or the surface. Many epithelial tissues are capable of rapidly replacing damaged and dead cells. Sloughing off of damaged or dead cells is a characteristic of surface epithelium and allows our airways and digestive tracts to rapidly replace damaged cells with new cells.

Generalized Functions of Epithelial Tissue

Epithelial tissues provide the body's first line of protection from physical, chemical, and biological wear and tear. The cells of an epithelium act as gatekeepers of the body controlling permeability and allowing selective transfer of materials across a physical barrier. All substances that enter the body must cross an epithelium. Some epithelia often include structural features that allow the selective transport of molecules and ions across their cell membranes.

Many epithelial cells are capable of secretion and release mucous and specific chemical compounds onto their apical surfaces. The epithelium of the small intestine releases digestive enzymes, for example. Cells lining the respiratory tract secrete mucous that traps incoming microorganisms and particles. A glandular epithelium contains many secretory cells.

The Epithelial Cell

Epithelial cells are typically characterized by the polarized distribution of organelles and membrane-bound proteins between their basal and apical surfaces. Particular structures found in some epithelial cells are an adaptation to specific functions. Certain organelles are segregated to the basal sides, whereas other organelles and extensions, such as cilia, when present, are on the apical surface.

Cilia are microscopic extensions of the apical cell membrane that are supported by microtubules. They beat in unison and move fluids as well as trapped particles. Ciliated epithelium lines the ventricles of the brain where it helps circulate the cerebrospinal fluid. The ciliated epithelium of your airway forms a mucociliary escalator that sweeps particles of dust and pathogens trapped in the secreted mucous toward the throat. It is called an escalator because it continuously pushes mucous with trapped particles upward. In contrast, nasal cilia sweep the mucous blanket down towards your throat. In both cases, the transported materials are usually swallowed, and end up in the acidic environment of your stomach.

Cell to Cell Junctions

Cells of epithelia are closely connected and are not separated by intracellular material. Three basic types of connections allow varying degrees of interaction between the cells: tight junctions, anchoring junctions, and gap junctions (Figure 1).

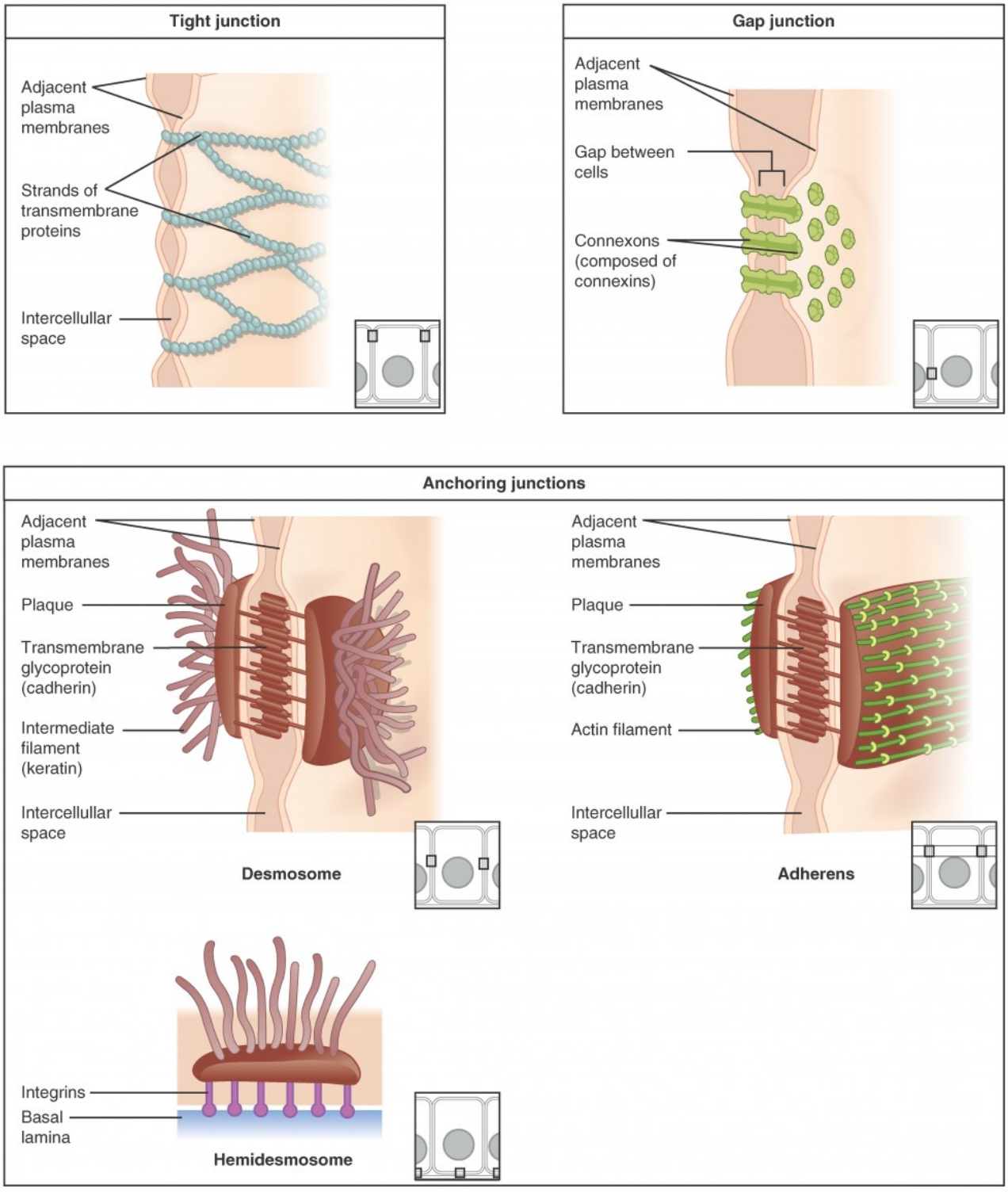


Figure 1. Types of Cell Junctions. *The three basic types of cell-to-cell junctions are tight junctions, gap junctions, and anchoring junctions.*

At one end of the spectrum is the tight junction, which separates the cells into apical and basal compartments. An anchoring junction includes several types of cell junctions that help stabilize epithelial tissues. Anchoring junctions are common on the lateral and basal surfaces of cells where they provide strong and flexible connections. There are three types of anchoring junctions: desmosomes, hemidesmosomes, and adherens. Desmosomes occur in patches on the membranes of cells. The patches are structural proteins on the inner surface of the cell's membrane. The adhesion molecule, cadherin, is embedded in these patches and projects

through the cell membrane to link with the cadherin molecules of adjacent cells. These connections are especially important in holding cells together. Hemidesmosomes, which look like half a desmosome, link cells to the extracellular matrix, for example, the basal lamina. While similar in appearance to desmosomes, they include the adhesion proteins called integrins rather than cadherins. Adherens junctions use either cadherins or integrins depending on whether they are linking to other cells or matrix. The junctions are characterized by the presence of the contractile protein actin located on the cytoplasmic surface of the cell membrane. The actin can connect isolated patches or form a belt-like structure inside the cell. These junctions influence the shape and folding of the epithelial tissue.

In contrast with the tight and anchoring junctions, a **gap junction** forms an intercellular passageway between the membranes of adjacent cells to facilitate the movement of small molecules and ions between the cytoplasm of adjacent cells. These junctions allow electrical and metabolic coupling of adjacent cells, which coordinates function in large groups of cells.

Classification of Epithelial Tissues

Epithelial tissues are classified according to the shape of the cells and number of the cell layers formed (Figure 2). Cell shapes can be squamous (flattened and thin), cuboidal (boxy, as wide as it is tall), or columnar (rectangular, taller than it is wide). Similarly, the number of cell layers in the tissue can be one—where every cell rests on the basal lamina—which is a simple epithelium, or more than one, which is a stratified epithelium and only the basal layer of cells rests on the basal lamina. Pseudostratified (pseudo- = “false”) describes tissue with a single layer of irregularly shaped cells that give the appearance of more than one layer. Transitional describes a form of specialized stratified epithelium in which the shape of the cells can vary.

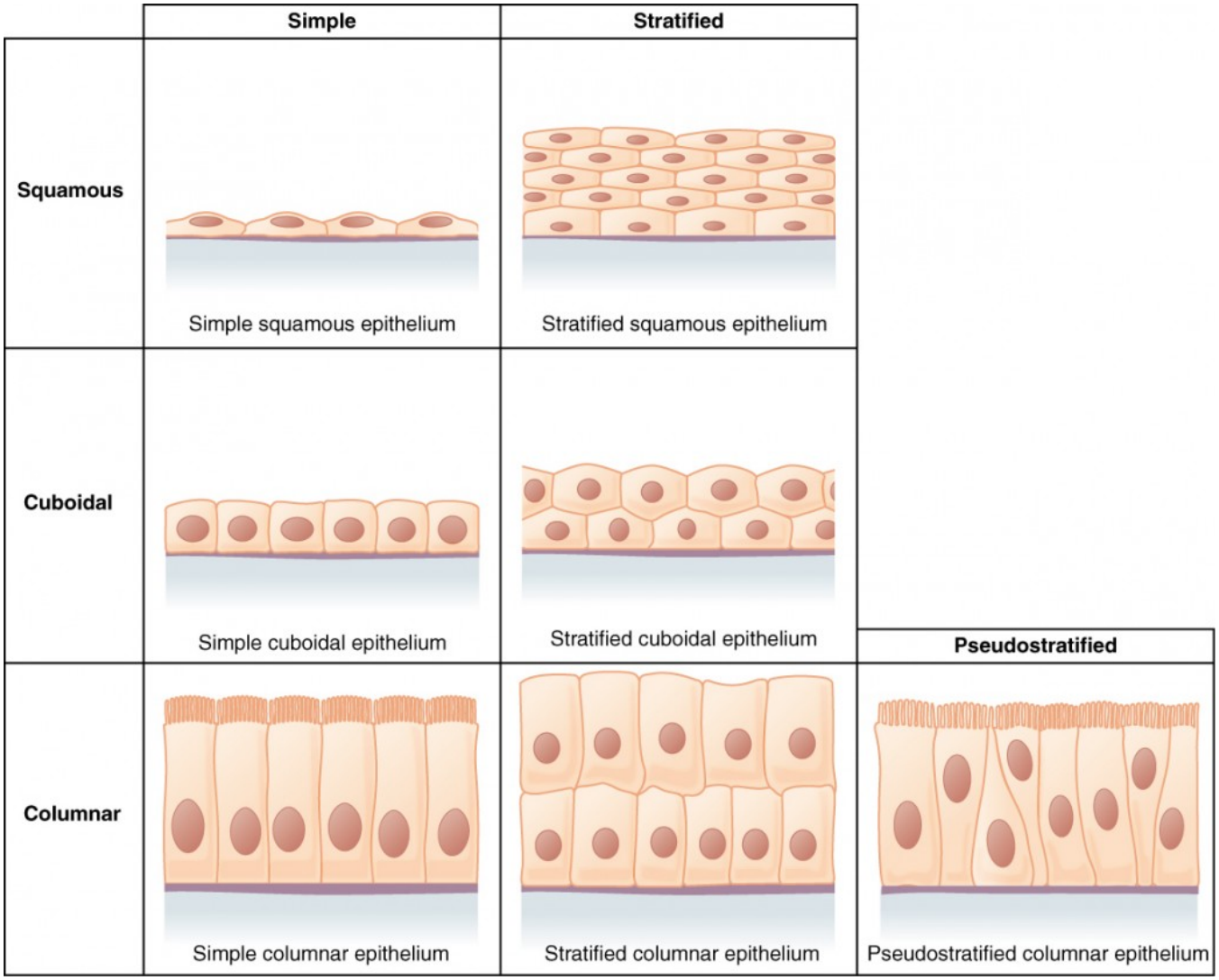


Figure 2. Cells of Epithelial Tissue. *Simple epithelial tissue is organized as a single layer of cells and stratified epithelial tissue is formed by several layers of cells.*

Simple Epithelium

The shape of the cells in the single cell layer of simple epithelium reflects the functioning of those cells. The cells in **simple squamous epithelium** have the appearance of thin scales. Squamous cell nuclei tend to be flat, horizontal, and elliptical, mirroring the form of the cell. The **endothelium** is the epithelial tissue that lines vessels of the lymphatic and cardiovascular system, and it is made up of a single layer of squamous cells. Simple squamous epithelium, because of the thinness of the cell, is present where rapid passage of chemical compounds is observed. The alveoli of lungs where gases diffuse, segments of kidney tubules, and the lining of capillaries are also made of simple squamous epithelial tissue. The **mesothelium** is a simple squamous epithelium that forms the surface layer of the serous membrane that lines body cavities and internal organs. Its primary function is to provide a smooth and protective surface. Mesothelial cells are squamous epithelial cells that secrete a fluid that lubricates the mesothelium.

In **simple cuboidal epithelium**, the nucleus of the box-like cells appears round and is generally located near the center of the cell. These epithelia are active in the secretion and absorptions of molecules. Simple cuboidal epithelia are observed in the lining of the kidney tubules and in the ducts of glands.

In **simple columnar epithelium**, the nucleus of the tall column-like cells tends to be elongated and located in the basal end of the cells. Like the cuboidal epithelia, this epithelium is active in the absorption and secretion of molecules. Simple columnar epithelium forms the lining of some sections of the digestive system and parts of the

female reproductive tract. Ciliated columnar epithelium is composed of simple columnar epithelial cells with cilia on their apical surfaces. These epithelial cells are found in the lining of the fallopian tubes and parts of the respiratory system, where the beating of the cilia helps remove particulate matter.

Pseudostratified columnar epithelium is a type of epithelium that appears to be stratified but instead consists of a single layer of irregularly shaped and differently sized columnar cells. In pseudostratified epithelium, nuclei of neighboring cells appear at different levels rather than clustered in the basal end. The arrangement gives the appearance of stratification; but in fact all the cells are in contact with the basal lamina, although some do not reach the apical surface. Pseudostratified columnar epithelium is found in the respiratory tract, where some of these cells have cilia.

Both simple and pseudostratified columnar epithelia are heterogeneous epithelia because they include additional types of cells interspersed among the epithelial cells. For example, a **goblet cell** is a mucous-secreting unicellular "gland" interspersed between the columnar epithelial cells of mucous membranes (Figure 3).

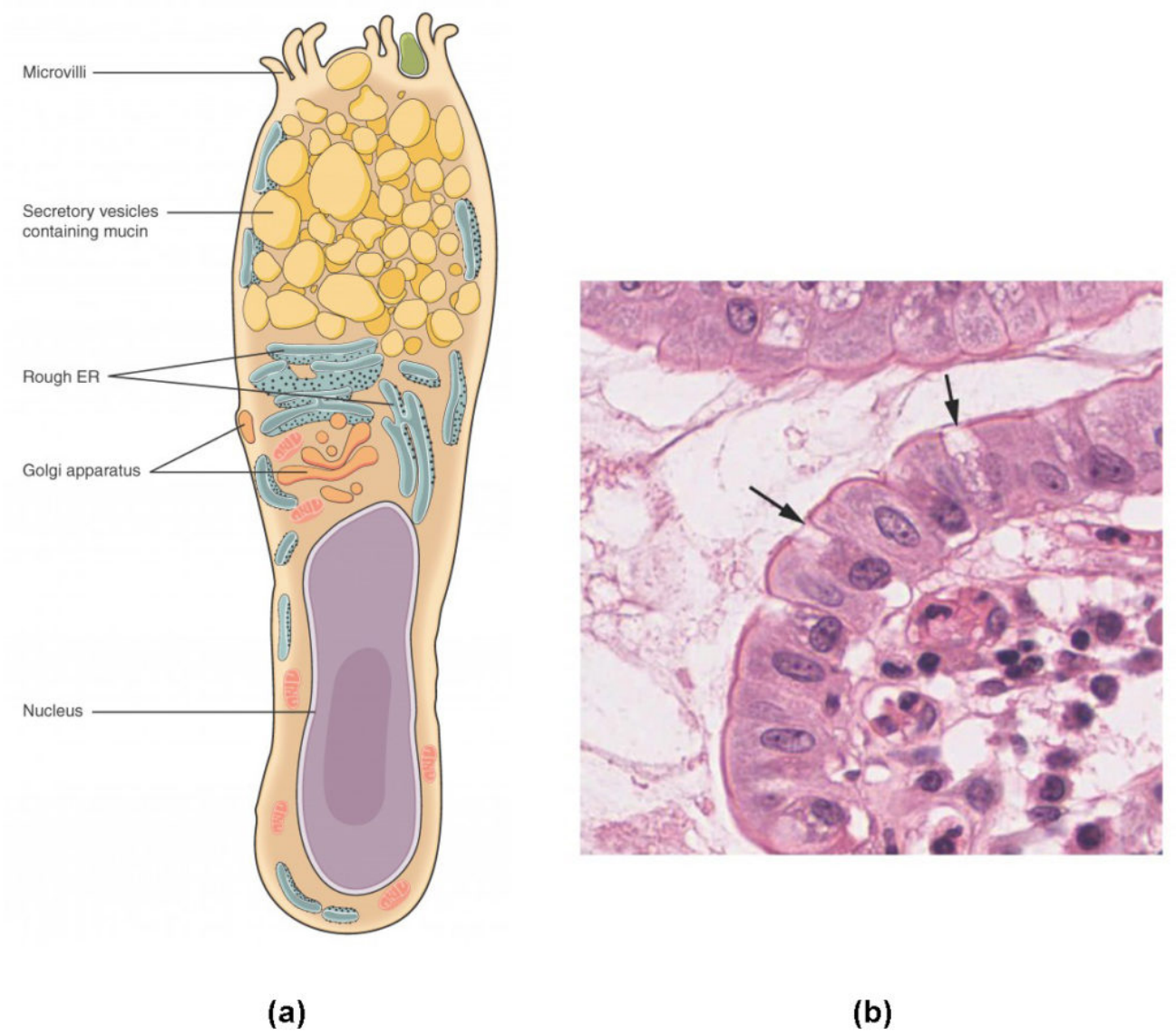


Figure 3. Goblet Cell. *(a) In the lining of the small intestine, columnar epithelium cells are interspersed with goblet cells. (b) The arrows in this micrograph point to the mucous-secreting goblet cells. LM × 1600. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

View the University of Michigan WebScope to explore the tissue sample in greater detail.

Stratified Epithelium

A stratified epithelium consists of several stacked layers of cells. This epithelium protects against physical and chemical wear and tear. The stratified epithelium is named by the shape of the most apical layer of cells, closest to the free space. **Stratified squamous epithelium** is the most common type of stratified epithelium in the human body. The apical cells are squamous, whereas the basal layer contains either columnar or cuboidal cells. The top layer may be covered with dead cells filled with keratin. Mammalian skin is an example of this dry, keratinized, stratified squamous epithelium. The lining of the mouth cavity is an example of an unkeratinized, stratified squamous epithelium. **Stratified cuboidal epithelium** and **stratified columnar epithelium** can also be found in certain glands and ducts, but are uncommon in the human body.

Another kind of stratified epithelium is **transitional epithelium**, so-called because of the gradual changes in the shapes of the apical cells as the bladder fills with urine. It is found only in the urinary system, specifically the ureters and urinary bladder. When the bladder is empty, this epithelium is convoluted and has cuboidal apical cells with convex, umbrella shaped, apical surfaces. As the bladder fills with urine, this epithelium loses its convolutions and the apical cells transition from cuboidal to squamous. It appears thicker and more multi-layered when the bladder is empty, and more stretched out and less stratified when the bladder is full and distended. Table 1 summarizes the different categories of epithelial cell tissue cells.

Table 1. Epithelial Tissue Cells

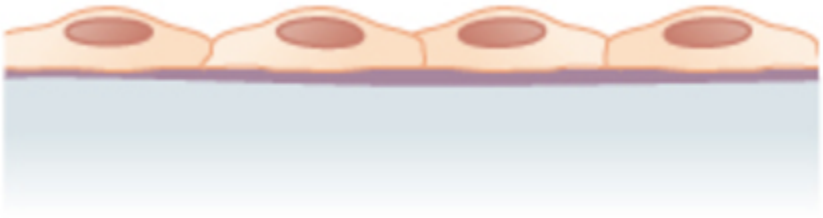
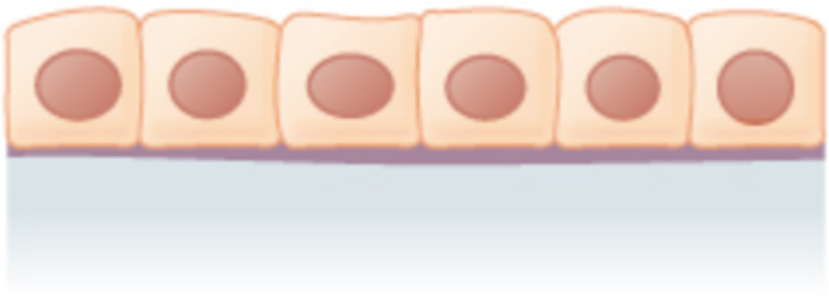
Cells	Locations	Function
Simple squamous epithelium 	Air sacs of the lungs and the lining of the heart, blood vessels and lymphatic vessels	Allows materials to pass through by diffusion and filtration, and secretes lubricating substances
Simple cuboidal epithelium 	In ducts and secretory portions of small glands and in kidney tubules	Secretes and absorbs
Simple columnar epithelium	Ciliated tissues including the bronchi, uterine tubes, and uterus; smooth (nonciliated tissues) are	Absorbs; it also secretes mucous and enzymes.

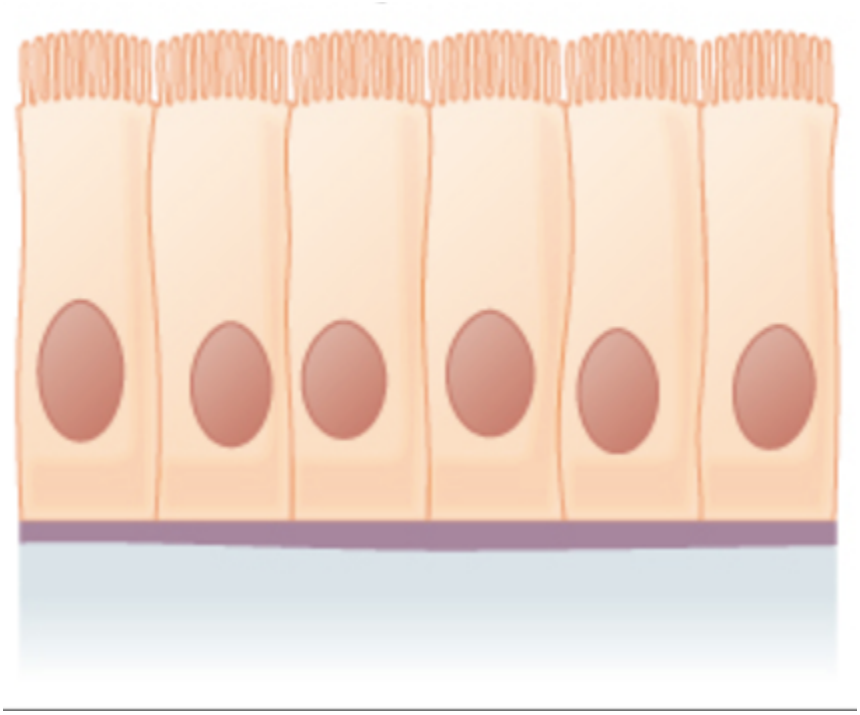
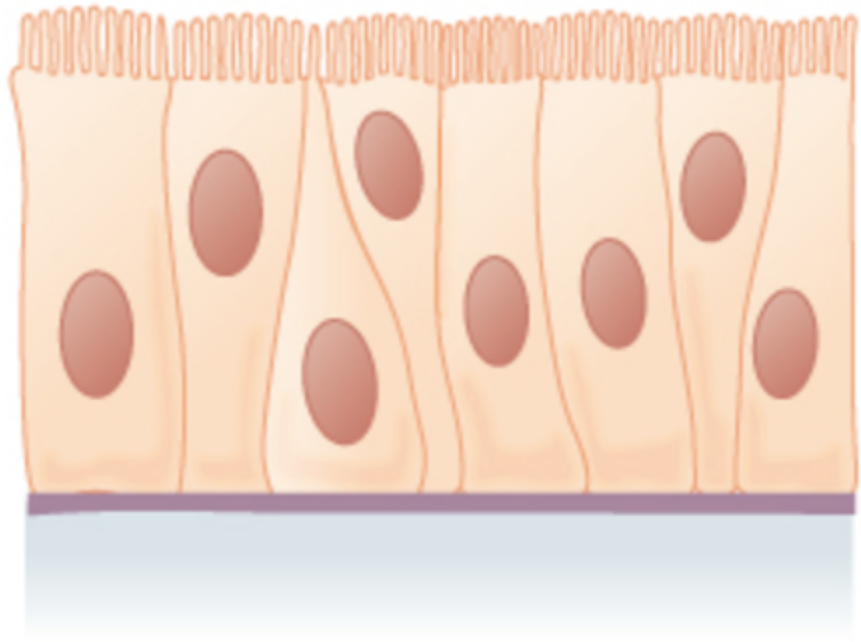
Table 1. Epithelial Tissue Cells		
Cells	Locations	Function
	in the digestive tract bladder	
Pseudostratified columnar epithelium 	Ciliated tissue lines the trachea and much of the upper respiratory tract	Secrete mucous; ciliated tissue moves mucous
Stratified squamous epithelium	Lines the esophagus, mouth, and vagina	Protects against abrasion

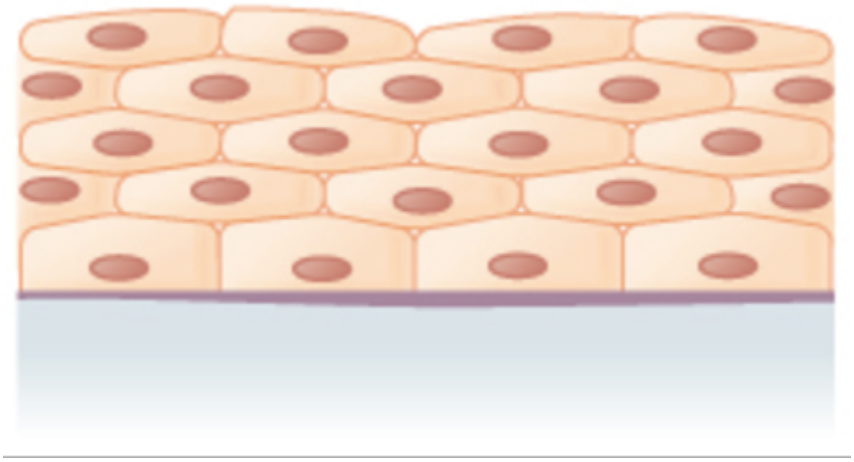
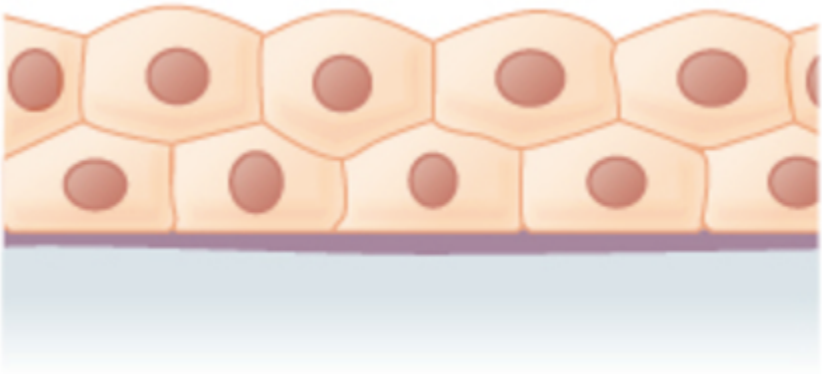
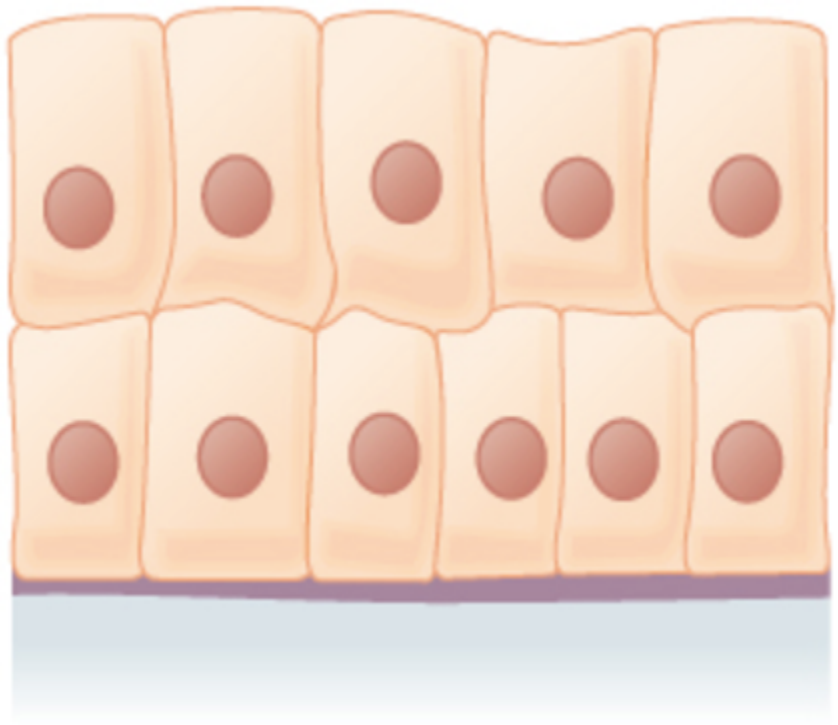
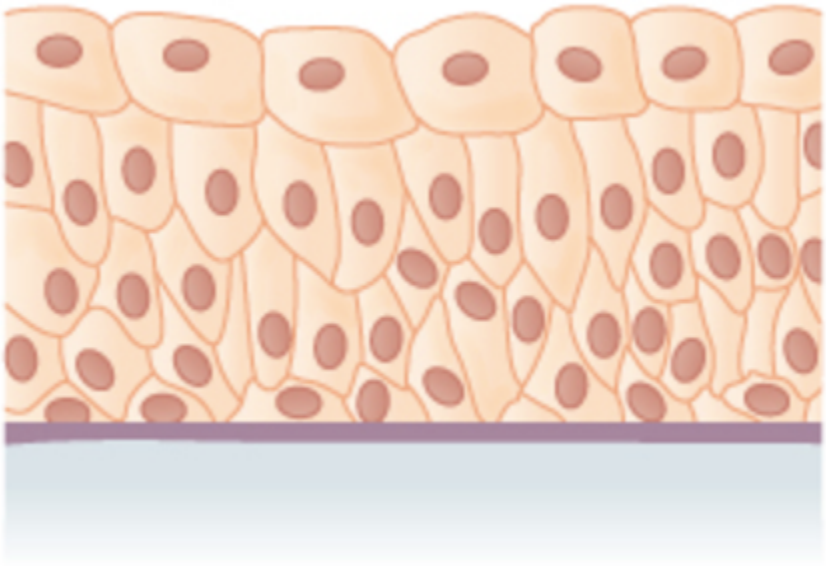
Table 1. Epithelial Tissue Cells		
Cells	Locations	Function
		
Stratified cuboidal epithelium 	Sweat glands, salivary glands, and mammary glands	Protective tissue
Stratified columnar epithelium	The male urethra and the ducts of some glands.	Secretes and protects

Table 1. Epithelial Tissue Cells		
Cells	Locations	Function
		
Transitional epithelium 	Lines the bladder, urethra and ureters	Allows the urinary organs to expand and stretch

Watch this video to find out more about the anatomy of epithelial tissues. Where in the body would one find non-keratinizing stratified squamous epithelium?

Watch this video online: https://youtu.be/7z2vYr5YjD8

Glandular Epithelium

A gland is a structure made up of one or more cells modified to synthesize and secrete chemical substances. Most glands consist of groups of epithelial cells. A gland can be classified as an **endocrine gland**, a ductless gland that releases secretions directly into surrounding tissues and fluids (endo- = “inside”), or an **exocrine gland** whose secretions leave through a duct that opens directly, or indirectly, to the external environment (exo- = “outside”).

Endocrine Glands

The secretions of endocrine glands are called hormones. Hormones are released into the interstitial fluid, diffused into the bloodstream, and delivered to targets, in other words, cells that have receptors to bind the hormones. The endocrine system is part of a major regulatory system coordinating the regulation and integration of body responses. A few examples of endocrine glands include the anterior pituitary, thymus, adrenal cortex, and gonads.

Exocrine Glands

Exocrine glands release their contents through a duct that leads to the epithelial surface. Mucous, sweat, saliva, and breast milk are all examples of secretions from exocrine glands. They are all discharged through tubular ducts. Secretions into the lumen of the gastrointestinal tract, technically outside of the body, are of the exocrine category.

Glandular Structure

Exocrine glands are classified as either unicellular or multicellular. The unicellular glands are scattered single cells, such as goblet cells, found in the mucous membranes of the small and large intestine.

The multicellular exocrine glands known as serous glands develop from simple epithelium to form a secretory surface that secretes directly into an inner cavity. These glands line the internal cavities of the abdomen and chest and release their secretions directly into the cavities. Other multicellular exocrine glands release their contents through a tubular duct. The duct is single in a simple gland but in compound glands is divided into one or more branches (Figure 4). In tubular glands, the ducts can be straight or coiled, whereas tubes that form pockets are alveolar (acinar), such as the exocrine portion of the pancreas. Combinations of tubes and pockets are known as tubuloalveolar (tubuloacinar) compound glands. In a branched gland, a duct is connected to more than one secretory group of cells.

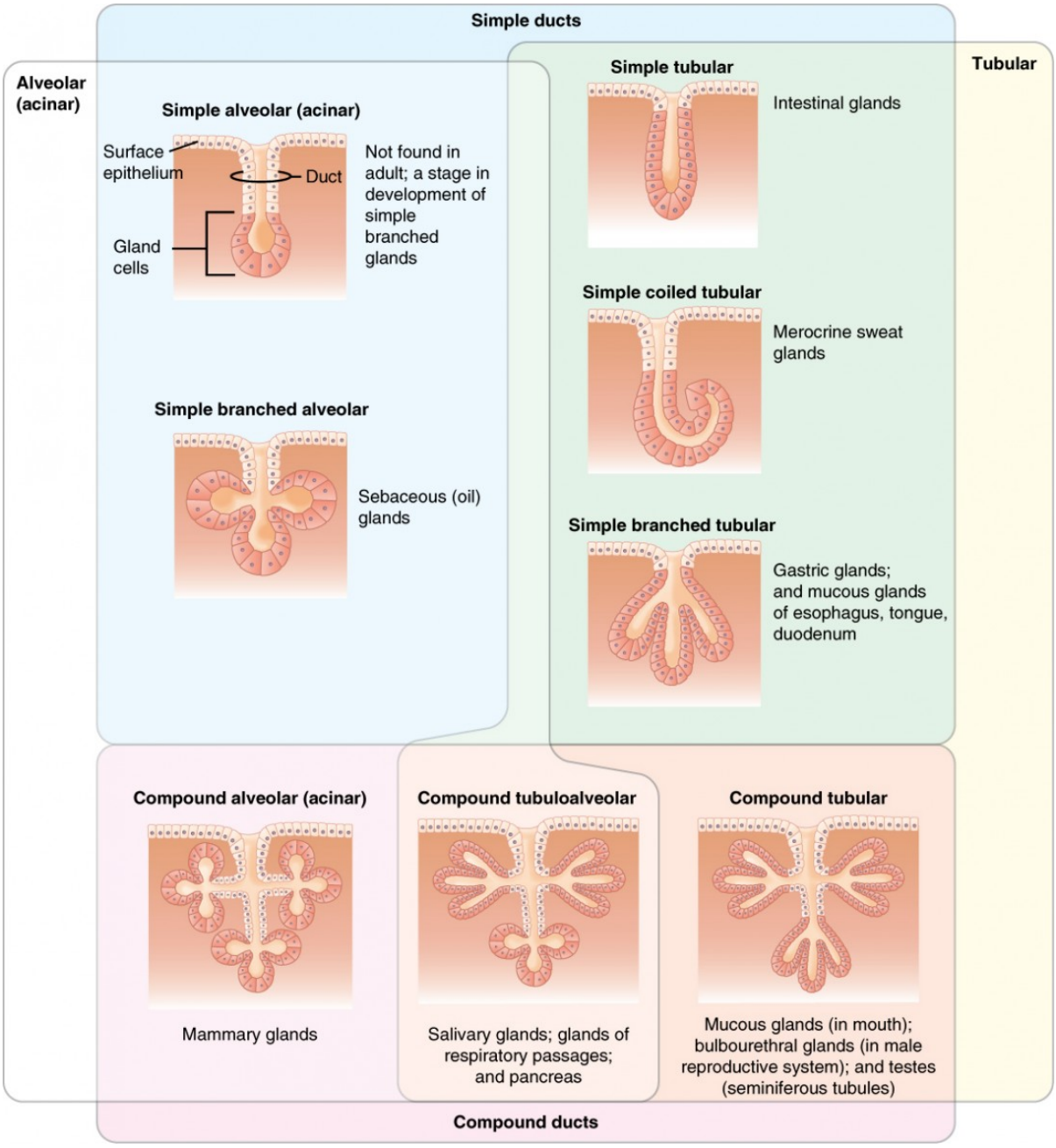


Figure 4. Types of Exocrine Glands. *Exocrine glands are classified by their structure.*

Methods and Types of Secretion

Exocrine glands can be classified by their mode of secretion and the nature of the substances released, as well as by the structure of the glands and shape of ducts (Figure 5). Merocrine secretion is the most common type of exocrine secretion. The secretions are enclosed in vesicles that move to the apical surface of the cell where the contents are released by exocytosis. For example, watery mucous containing the glycoprotein mucin, a lubricant that offers some pathogen protection is a merocrine secretion. The eccrine glands that produce and secrete sweat are another example.

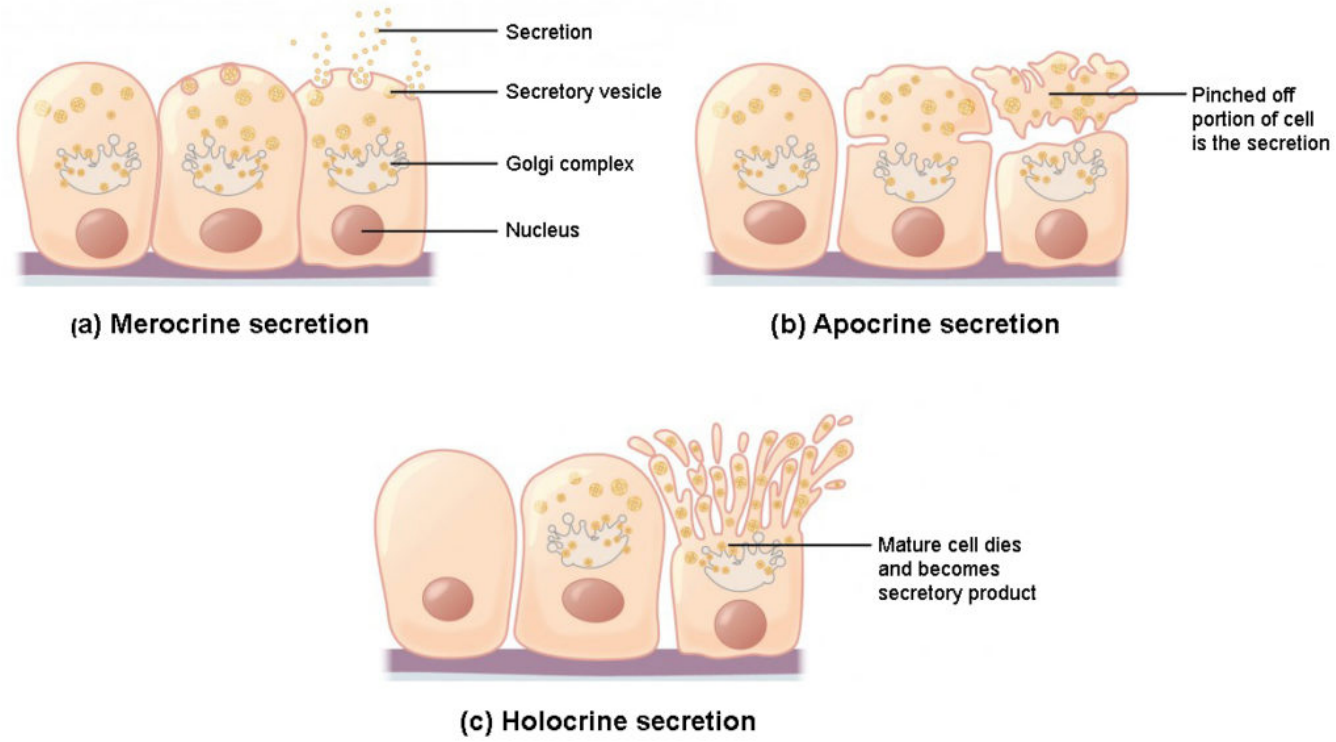


Figure 5. Modes of Glandular Secretion. *(a) In merocrine secretion, the cell remains intact. (b) In apocrine secretion, the apical portion of the cell is released, as well. (c) In holocrine secretion, the cell is destroyed as it releases its product and the cell itself becomes part of the secretion.*

Apocrine secretion accumulates near the apical portion of the cell. That portion of the cell and its secretory contents pinch off from the cell and are released. The sweat glands of the armpit are classified as apocrine glands. Both merocrine and apocrine glands continue to produce and secrete their contents with little damage caused to the cell because the nucleus and golgi regions remain intact after secretion.

In contrast, the process of holocrine secretion involves the rupture and destruction of the entire gland cell. The cell accumulates its secretory products and releases them only when it bursts. New gland cells differentiate from cells in the surrounding tissue to replace those lost by secretion. The sebaceous glands that produce the oils on the skin and hair are holocrine glands/cells (Figure 6).

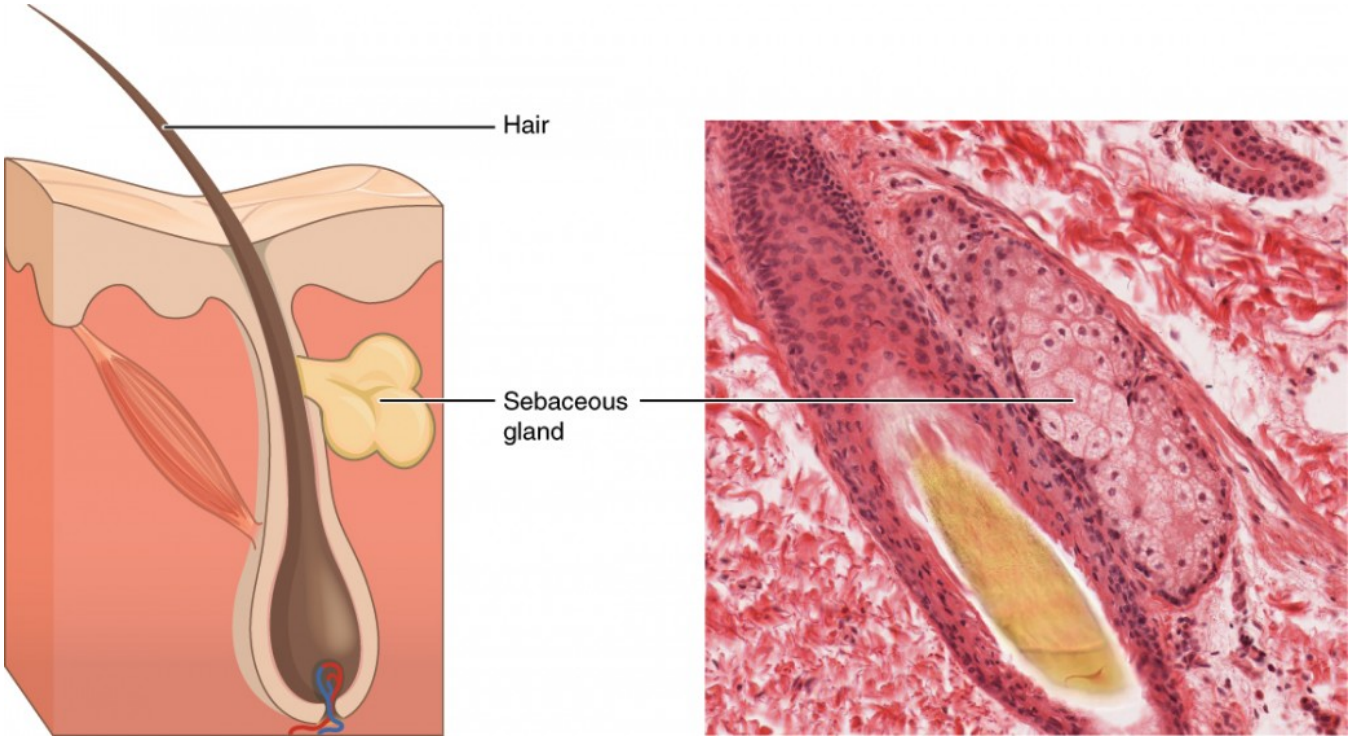


Figure 6. Sebaceous Glands. *These glands secrete oils that lubricate and protect the skin. They are holocrine glands and they are destroyed after releasing their contents. New glandular cells form to replace the cells that are lost. LM × 400. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

Glands are also named after the products they produce. The **serous gland** produces watery, blood-plasma-like secretions rich in enzymes such as alpha amylase, whereas the **mucous gland** releases watery to viscous products rich in the glycoprotein mucin. Both serous and mucous glands are common in the salivary glands of the mouth. Mixed exocrine glands contain both serous and mucous glands and release both types of secretions.

Self-Check Questions

Visit your course online to take a quiz to check your understanding of Epithelial Tissue:

CONNECTIVE TISSUE SUPPORTS AND PROTECTS

Learning Objectives

- Identify and distinguish between the types of connective tissue: proper, supportive, and fluid
- Explain the functions of connective tissues

As may be obvious from its name, one of the major functions of connective tissue is to connect tissues and organs. Unlike epithelial tissue, which is composed of cells closely packed with little or no extracellular space in between, connective tissue cells are dispersed in a **matrix**. The matrix usually includes a large amount of extracellular material produced by the connective tissue cells that are embedded within it. The matrix plays a major role in the functioning of this tissue. The major component of the matrix is a **ground substance** often crisscrossed by protein fibers. This ground substance is usually a fluid, but it can also be mineralized and solid, as in bones. Connective tissues come in a vast variety of forms, yet they typically have in common three characteristic components: cells, large amounts of amorphous ground substance, and protein fibers. The amount and structure of each component correlates with the function of the tissue, from the rigid ground substance in bones supporting the body to the inclusion of specialized cells; for example, a phagocytic cell that engulfs pathogens and also rids tissue of cellular debris.

Functions of Connective Tissues

Connective tissues perform many functions in the body, but most importantly, they support and connect other tissues; from the connective tissue sheath that surrounds muscle cells, to the tendons that attach muscles to bones, and to the skeleton that supports the positions of the body. Protection is another major function of connective tissue, in the form of fibrous capsules and bones that protect delicate organs and, of course, the skeletal system. Specialized cells in connective tissue defend the body from microorganisms that enter the body. Transport of fluid, nutrients, waste, and chemical messengers is ensured by specialized fluid connective tissues, such as blood and lymph. Adipose cells store surplus energy in the form of fat and contribute to the thermal insulation of the body.

Embryonic Connective Tissue

All connective tissues derive from the mesodermal layer of the embryo. The first connective tissue to develop in the embryo is **mesenchyme**, the stem cell line from which all connective tissues are later derived. Clusters of mesenchymal cells are scattered throughout adult tissue and supply the cells needed for replacement and repair after a connective tissue injury. A second type of embryonic connective tissue forms in the umbilical cord, called **mucous connective tissue** or Wharton's jelly. This tissue is no longer present after birth, leaving only scattered mesenchymal cells throughout the body.

Classification of Connective Tissues

The three broad categories of connective tissue are classified according to the characteristics of their ground substance and the types of fibers found within the matrix (Table 1). **Connective tissue proper** includes **loose connective tissue** and **dense connective tissue**. Both tissues have a variety of cell types and protein fibers suspended in a viscous ground substance. Dense connective tissue is reinforced by bundles of fibers that provide tensile strength, elasticity, and protection. In loose connective tissue, the fibers are loosely organized, leaving large spaces in between. **Supportive connective tissue**—bone and cartilage—provide structure and strength to the body and protect soft tissues. A few distinct cell types and densely packed fibers in a matrix characterize these tissues. In bone, the matrix is rigid and described as calcified because of the deposited calcium salts. In **fluid connective tissue**, in other words, lymph and blood, various specialized cells circulate in a watery fluid containing salts, nutrients, and dissolved proteins.

Table 1. Connective Tissue Examples

Connective tissue proper	Supportive connective tissue	Fluid connective tissue
Loose connective tissue • Areolar • Adipose • Reticular	Cartilage • Hyaline • Fibrocartilage • Elastic	Blood

Table 1. Connective Tissue Examples		
Connective tissue proper	**Supportive connective tissue**	**Fluid connective tissue**
Dense connective tissue • Regular elastic • Irregular elastic	Bones • Compact bone • Cancellous bone	Lymph

Connective Tissue Proper

Fibroblasts are present in all connective tissue proper (Figure 1). Fibrocytes, adipocytes, and mesenchymal cells are fixed cells, which means they remain within the connective tissue. Other cells move in and out of the connective tissue in response to chemical signals. Macrophages, mast cells, lymphocytes, plasma cells, and phagocytic cells are found in connective tissue proper but are actually part of the immune system protecting the body.

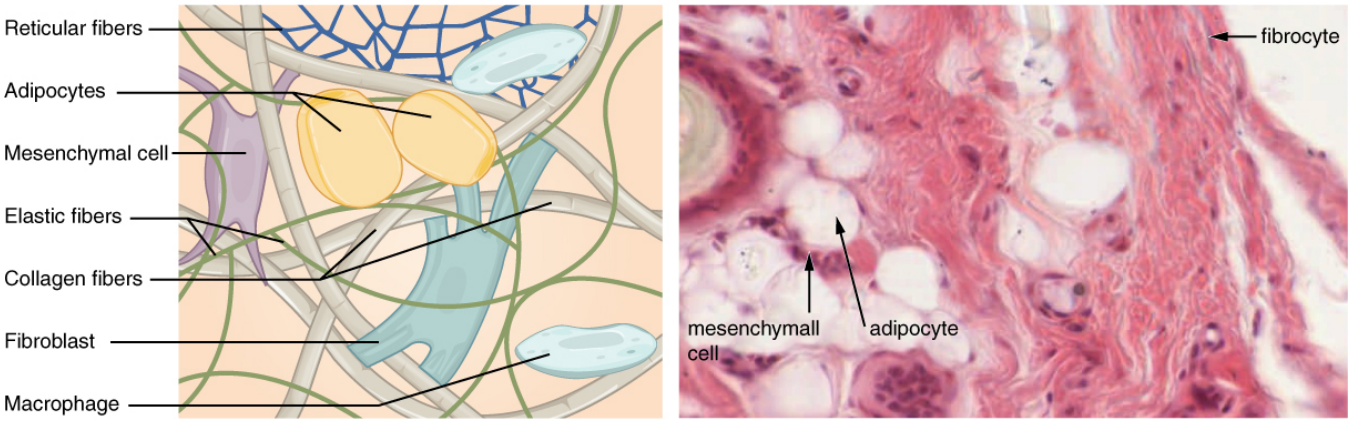


Figure 1. Connective Tissue Proper. *Fibroblasts produce this fibrous tissue. Connective tissue proper includes the fixed cells fibrocytes, adipocytes, and mesenchymal cells. LM × 400. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

Cell Types

The most abundant cell in connective tissue proper is the **fibroblast**. Polysaccharides and proteins secreted by fibroblasts combine with extra-cellular fluids to produce a viscous ground substance that, with embedded fibrous proteins, forms the extra-cellular matrix. As you might expect, a **fibrocyte**, a less active form of fibroblast, is the second most common cell type in connective tissue proper.

Adipocytes are cells that store lipids as droplets that fill most of the cytoplasm. There are two basic types of adipocytes: white and brown. The brown adipocytes store lipids as many droplets, and have high metabolic activity. In contrast, white fat adipocytes store lipids as a single large drop and are metabolically less active. Their effectiveness at storing large amounts of fat is witnessed in obese individuals. The number and type of adipocytes depends on the tissue and location, and vary among individuals in the population.

The **mesenchymal cell** is a multipotent adult stem cell. These cells can differentiate into any type of connective tissue cells needed for repair and healing of damaged tissue.

The macrophage cell is a large cell derived from a monocyte, a type of blood cell, which enters the connective tissue matrix from the blood vessels. The macrophage cells are an essential component of the immune system, which is the body's defense against potential pathogens and degraded host cells. When stimulated, macrophages release cytokines, small proteins that act as chemical messengers. Cytokines recruit other cells of the immune system to infected sites and stimulate their activities. Roaming, or free, macrophages move rapidly by amoeboid

movement, engulfing infectious agents and cellular debris. In contrast, fixed macrophages are permanent residents of their tissues.

The mast cell, found in connective tissue proper, has many cytoplasmic granules. These granules contain the chemical signals histamine and heparin. When irritated or damaged, mast cells release histamine, an inflammatory mediator, which causes vasodilation and increased blood flow at a site of injury or infection, along with itching, swelling, and redness you recognize as an allergic response. Like blood cells, mast cells are derived from hematopoietic stem cells and are part of the immune system.

Connective Tissue Fibers and Ground Substance

Three main types of fibers are secreted by fibroblasts: collagen fibers, elastic fibers, and reticular fibers. **Collagen fiber** is made from fibrous protein subunits linked together to form a long and straight fiber. Collagen fibers, while flexible, have great tensile strength, resist stretching, and give ligaments and tendons their characteristic resilience and strength. These fibers hold connective tissues together, even during the movement of the body.

Elastic fiber contains the protein elastin along with lesser amounts of other proteins and glycoproteins. The main property of elastin is that after being stretched or compressed, it will return to its original shape. Elastic fibers are prominent in elastic tissues found in skin and the elastic ligaments of the vertebral column.

Reticular fiber is also formed from the same protein subunits as collagen fibers; however, these fibers remain narrow and are arrayed in a branching network. They are found throughout the body, but are most abundant in the reticular tissue of soft organs, such as liver and spleen, where they anchor and provide structural support to the **parenchyma** (the functional cells, blood vessels, and nerves of the organ).

All of these fiber types are embedded in ground substance. Secreted by fibroblasts, ground substance is made of polysaccharides, specifically hyaluronic acid, and proteins. These combine to form a proteoglycan with a protein core and polysaccharide branches. The proteoglycan attracts and traps available moisture forming the clear, viscous, colorless matrix you now know as ground substance.

Loose Connective Tissue

Loose connective tissue is found between many organs where it acts both to absorb shock and bind tissues together. It allows water, salts, and various nutrients to diffuse through to adjacent or imbedded cells and tissues.

Adipose tissue consists mostly of fat storage cells, with little extracellular matrix (Figure 2). A large number of capillaries allow rapid storage and mobilization of lipid molecules. White adipose tissue is most abundant. It can appear yellow and owes its color to carotene and related pigments from plant food. White fat contributes mostly to lipid storage and can serve as insulation from cold temperatures and mechanical injuries. White adipose tissue can be found protecting the kidneys and cushioning the back of the eye. Brown adipose tissue is more common in infants, hence the term “baby fat.” In adults, there is a reduced amount of brown fat and it is found mainly in the neck and clavicular regions of the body. The many mitochondria in the cytoplasm of brown adipose tissue help explain its efficiency at metabolizing stored fat. Brown adipose tissue is thermogenic, meaning that as it breaks down fats, it releases metabolic heat, rather than producing adenosine triphosphate (ATP), a key molecule used in metabolism.

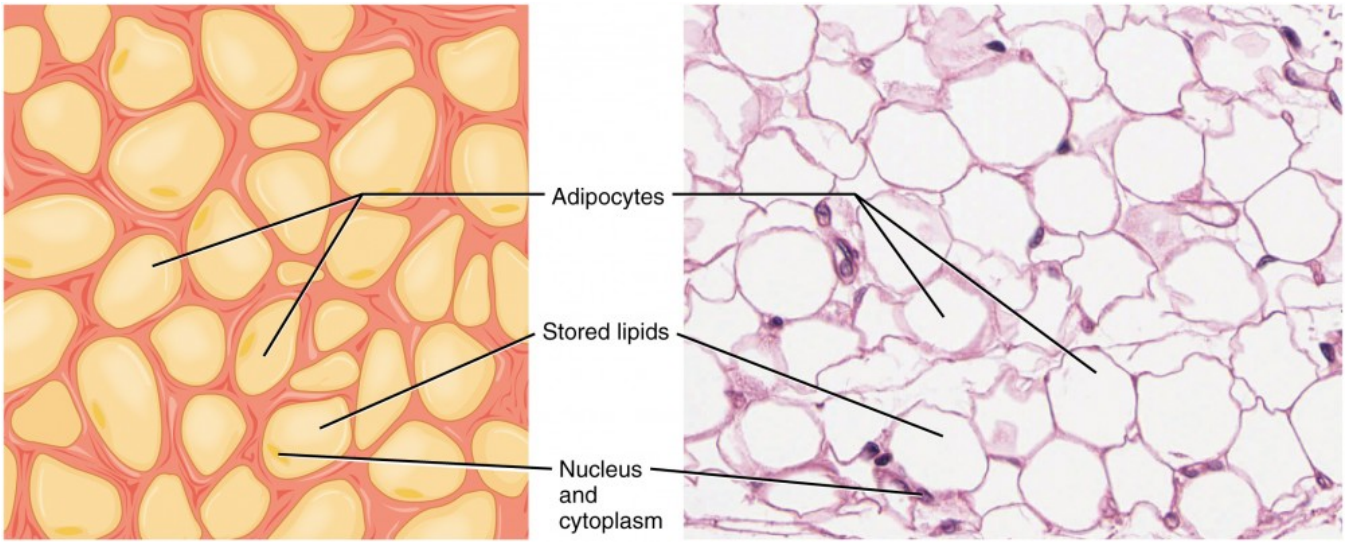


Figure 2. Adipose Tissue. *This is a loose connective tissue that consists of fat cells with little extracellular matrix. It stores fat for energy and provides insulation. LM × 800. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

Areolar tissue shows little specialization. It contains all the cell types and fibers previously described and is distributed in a random, web-like fashion. It fills the spaces between muscle fibers, surrounds blood and lymph vessels, and supports organs in the abdominal cavity. Areolar tissue underlies most epithelia and represents the connective tissue component of epithelial membranes, which are described further in a later section.

Reticular tissue is a mesh-like, supportive framework for soft organs such as lymphatic tissue, the spleen, and the liver (Figure 3). Reticular cells produce the reticular fibers that form the network onto which other cells attach. It derives its name from the Latin *reticulus*, which means “little net.”

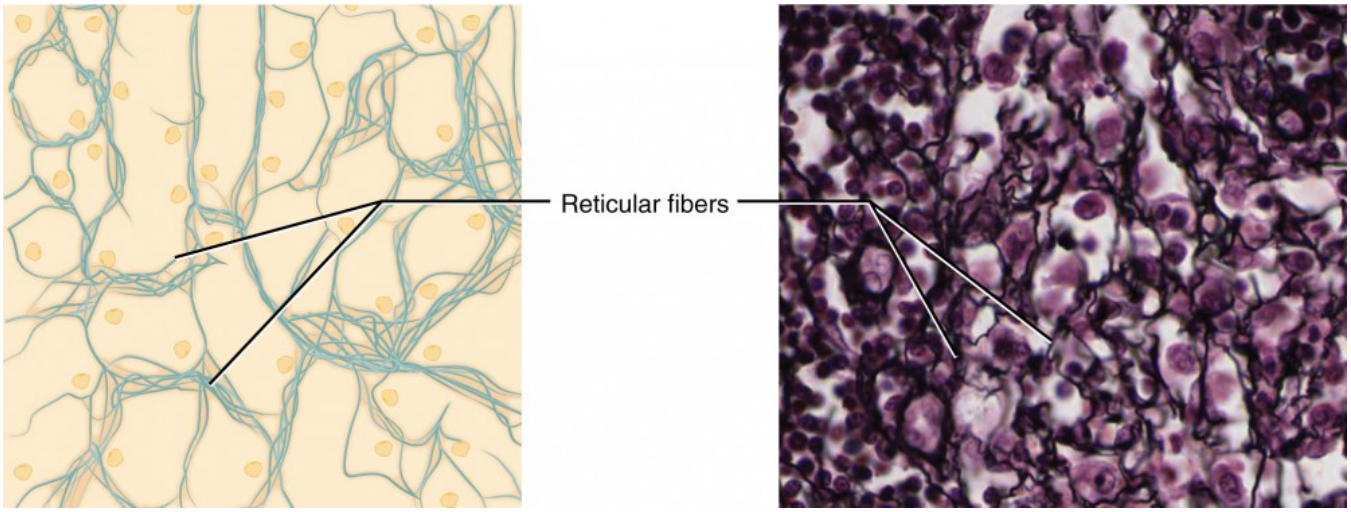


Figure 3. Reticular Tissue. *This is a loose connective tissue made up of a network of reticular fibers that provides a supportive framework for soft organs. LM × 1600. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

Dense Connective Tissue

Dense connective tissue contains more collagen fibers than does loose connective tissue. As a consequence, it displays greater resistance to stretching. There are two major categories of dense connective tissue: regular and irregular. Dense regular connective tissue fibers are parallel to each other, enhancing tensile strength and resistance to stretching in the direction of the fiber orientations. Ligaments and tendons are made of dense regular connective tissue, but in ligaments not all fibers are parallel. Dense regular elastic tissue contains elastin fibers in addition to collagen fibers, which allows the ligament to return to its original length after stretching. The ligaments in the vocal folds and between the vertebrae in the vertebral column are elastic.

In dense irregular connective tissue, the direction of fibers is random. This arrangement gives the tissue greater strength in all directions and less strength in one particular direction. In some tissues, fibers crisscross and form a mesh. In other tissues, stretching in several directions is achieved by alternating layers where fibers run in the same orientation in each layer, and it is the layers themselves that are stacked at an angle. The dermis of the skin is an example of dense irregular connective tissue rich in collagen fibers. Dense irregular elastic tissues give arterial walls the strength and the ability to regain original shape after stretching (Figure 4).

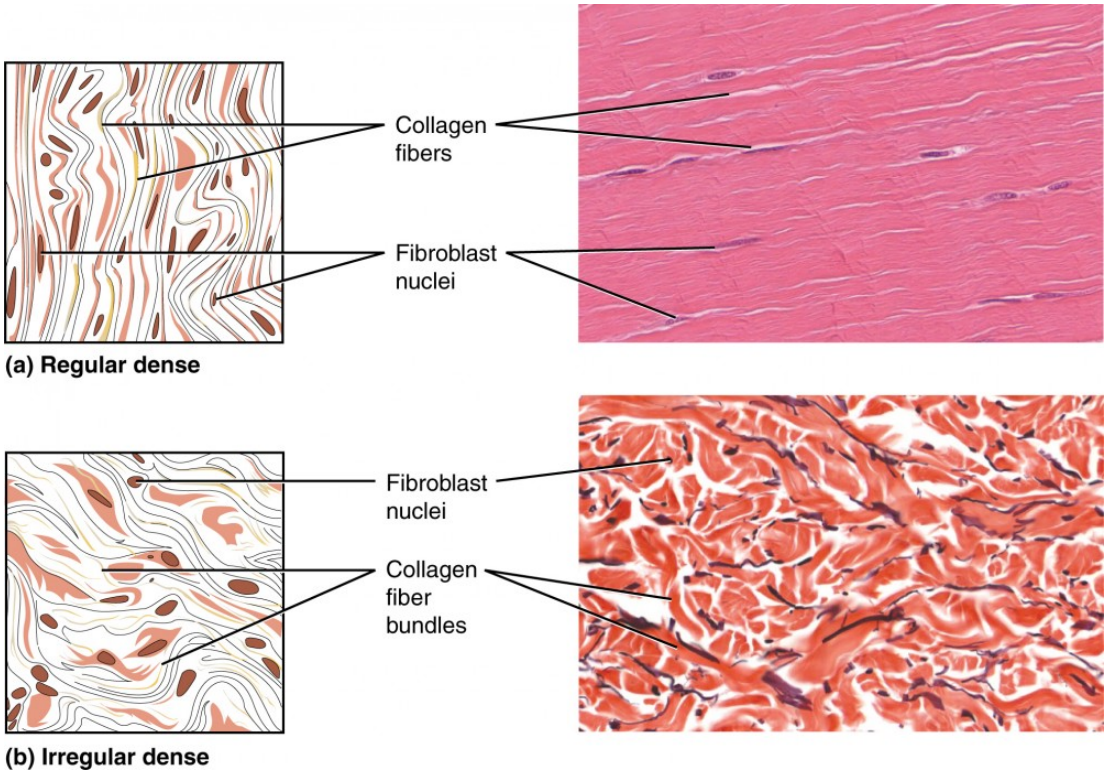


Figure 4. Dense Connective Tissue. *(a) Dense regular connective tissue consists of collagenous fibers packed into parallel bundles. (b) Dense irregular connective tissue consists of collagenous fibers interwoven into a mesh-like network. From top, LM × 1000, LM × 200. (Micrographs provided by the Regents of University of Michigan Medical School © 2012)*

Disorders of the Connective Tissue: Tendinitis

Your opponent stands ready as you prepare to hit the serve, but you are confident that you will smash the ball past your opponent. As you toss the ball high in the air, a burning pain shoots across your wrist and you drop the tennis racket. That dull ache in the wrist that you ignored through the summer is now an unbearable pain. The game is over for now.

After examining your swollen wrist, the doctor in the emergency room announces that you have developed wrist tendinitis. She recommends icing the tender area, taking non-steroidal anti-inflammatory medication to ease the pain and to reduce swelling, and complete rest for a few weeks. She interrupts your protests that you cannot stop playing. She issues a stern warning about the risk of aggravating the condition and the possibility of surgery. She consoles you by mentioning that well known tennis players such as Venus and Serena Williams and Rafael Nadal have also suffered from tendinitis related injuries.

What is tendinitis and how did it happen? Tendinitis is the inflammation of a tendon, the thick band of fibrous connective tissue that attaches a muscle to a bone. The condition causes pain and tenderness in the area around a joint. On rare occasions, a sudden serious injury will cause tendinitis. Most often, the condition results from repetitive motions over time that strain the tendons needed to perform the tasks.

Persons whose jobs and hobbies involve performing the same movements over and over again are often at the greatest risk of tendinitis. You hear of tennis and golfer's elbow, jumper's knee, and swimmer's shoulder. In all cases, overuse of the joint causes a microtrauma that initiates the inflammatory response. Tendinitis is

routinely diagnosed through a clinical examination. In case of severe pain, X-rays can be examined to rule out the possibility of a bone injury. Severe cases of tendinitis can even tear loose a tendon. Surgical repair of a tendon is painful. Connective tissue in the tendon does not have abundant blood supply and heals slowly.

While older adults are at risk for tendinitis because the elasticity of tendon tissue decreases with age, active people of all ages can develop tendinitis. Young athletes, dancers, and computer operators; anyone who performs the same movements constantly is at risk for tendinitis. Although repetitive motions are unavoidable in many activities and may lead to tendinitis, precautions can be taken that can lessen the probability of developing tendinitis. For active individuals, stretches before exercising and cross training or changing exercises are recommended. For the passionate athlete, it may be time to take some lessons to improve technique. All of the preventive measures aim to increase the strength of the tendon and decrease the stress put on it. With proper rest and managed care, you will be back on the court to hit that slice-spin serve over the net.

Watch this animation to learn more about tendonitis, a painful condition caused by swollen or injured tendons.

Watch this video online: https://youtu.be/p5vnf0VLvxQ

Supportive Connective Tissues

Two major forms of supportive connective tissue, cartilage and bone, allow the body to maintain its posture and protect internal organs.

Cartilage

The distinctive appearance of cartilage is due to polysaccharides called chondroitin sulfates, which bind with ground substance proteins to form proteoglycans. Embedded within the cartilage matrix are **chondrocytes**, or cartilage cells, and the space they occupy are called **lacunae** (singular = lacuna). A layer of dense irregular connective tissue, the perichondrium, encapsulates the cartilage. Cartilaginous tissue is avascular, thus all nutrients need to diffuse through the matrix to reach the chondrocytes. This is a factor contributing to the very slow healing of cartilaginous tissues.

The three main types of cartilage tissue are hyaline cartilage, fibrocartilage, and elastic cartilage (Figure 5). **Hyaline cartilage**, the most common type of cartilage in the body, consists of short and dispersed collagen fibers and contains large amounts of proteoglycans. Under the microscope, tissue samples appear clear. The surface of hyaline cartilage is smooth. Both strong and flexible, it is found in the rib cage and nose and covers bones where they meet to form moveable joints. It makes up a template of the embryonic skeleton before bone formation. A plate of hyaline cartilage at the ends of bone allows continued growth until adulthood. **Fibrocartilage** is tough because it has thick bundles of collagen fibers dispersed through its matrix. The knee and jaw joints and the the intervertebral discs are examples of fibrocartilage. **Elastic cartilage** contains elastic fibers as well as collagen and proteoglycans. This tissue gives rigid support as well as elasticity. Tug gently at your ear lobes, and notice that the lobes return to their initial shape. The external ear contains elastic cartilage.

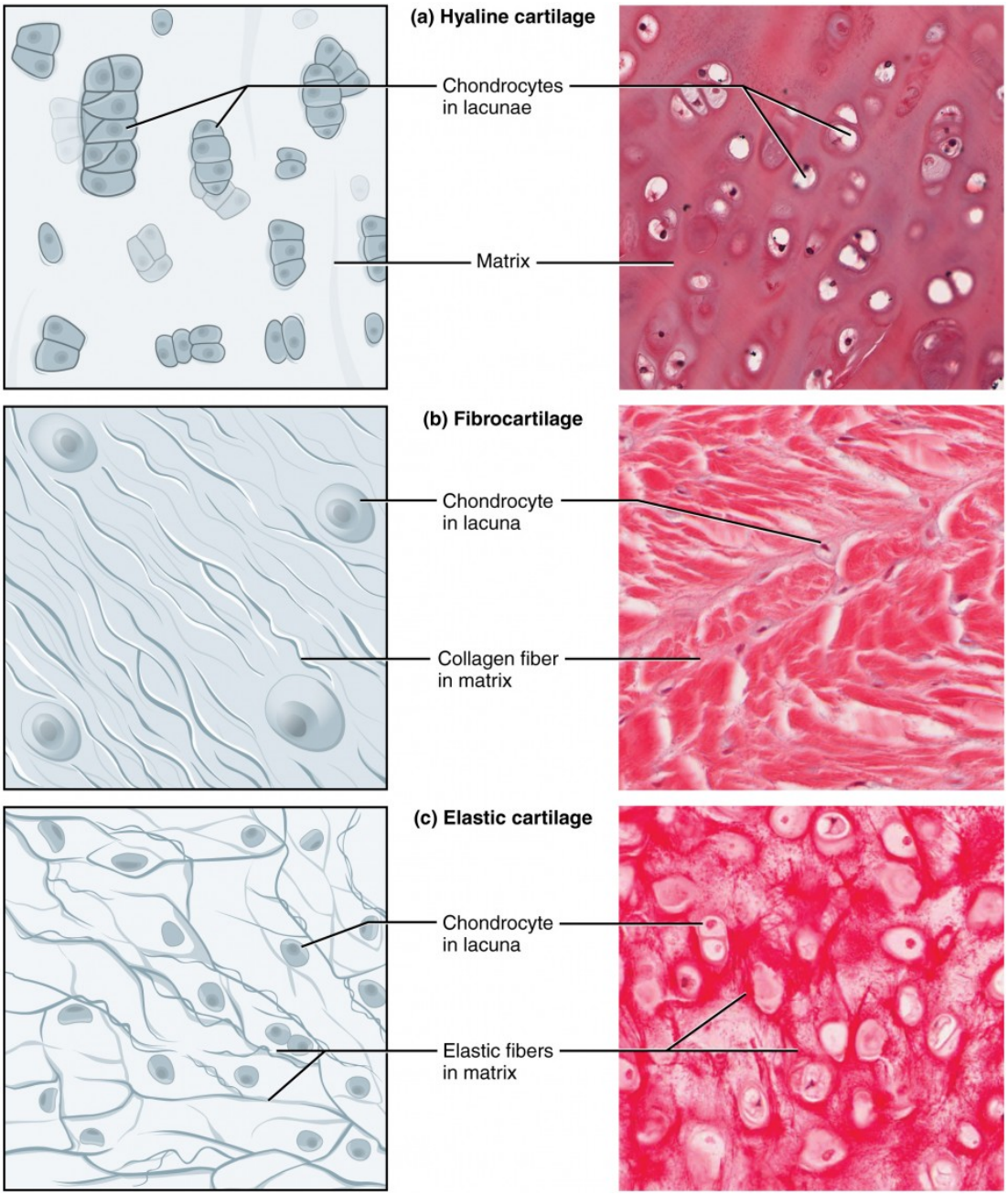


Figure 5. Types of Cartilage. *Cartilage is a connective tissue consisting of collagenous fibers embedded in a firm matrix of chondroitin sulfates. (a) Hyaline cartilage provides support with some flexibility. The example is from dog tissue. (b) Fibrocartilage provides some compressibility and can absorb pressure. (c) Elastic cartilage provides firm but elastic support. From top, LM × 300, LM × 1200, LM × 1016. (Micrographs provided by the Regents of University of Michigan Medical School © 2012)*

Bone

Bone is the hardest connective tissue. It provides protection to internal organs and supports the body. Bone's rigid extracellular matrix contains mostly collagen fibers embedded in a mineralized ground substance containing hydroxyapatite, a form of calcium phosphate. Both components of the matrix, organic and inorganic, contribute to the unusual properties of bone. Without collagen, bones would be brittle and shatter easily. Without mineral crystals, bones would flex and provide little support. Osteocytes, bone cells like chondrocytes, are located within lacunae. The histology of transverse tissue from long bone shows a typical arrangement of osteocytes in

concentric circles around a central canal. Bone is a highly vascularized tissue. Unlike cartilage, bone tissue can recover from injuries in a relatively short time.

Cancellous bone looks like a sponge under the microscope and contains empty spaces between trabeculae, or arches of bone proper. It is lighter than compact bone and found in the interior of some bones and at the end of long bones. Compact bone is solid and has greater structural strength.

Fluid Connective Tissue

Blood and lymph are fluid connective tissues. Cells circulate in a liquid extracellular matrix. The formed elements circulating in blood are all derived from hematopoietic stem cells located in bone marrow (Figure 6). Erythrocytes, red blood cells, transport oxygen and some carbon dioxide. Leukocytes, white blood cells, are responsible for defending against potentially harmful microorganisms or molecules. Platelets are cell fragments involved in blood clotting. Some white blood cells have the ability to cross the endothelial layer that lines blood vessels and enter adjacent tissues. Nutrients, salts, and wastes are dissolved in the liquid matrix and transported through the body.

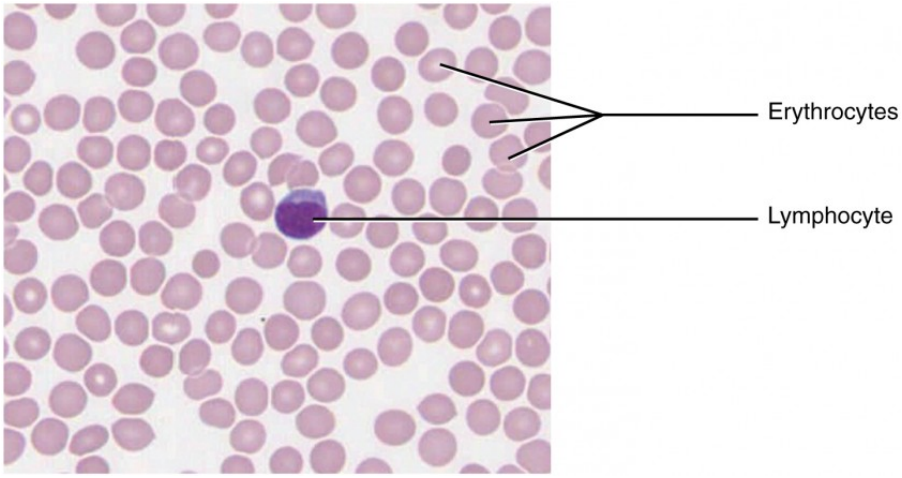


Figure 6. Blood: A Fluid Connective Tissue. *Blood is a fluid connective tissue containing erythrocytes and various types of leukocytes that circulate in a liquid extracellular matrix. LM × 1600. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

Lymph contains a liquid matrix and white blood cells. Lymphatic capillaries are extremely permeable, allowing larger molecules and excess fluid from interstitial spaces to enter the lymphatic vessels. Lymph drains into blood vessels, delivering molecules to the blood that could not otherwise directly enter the bloodstream. In this way, specialized lymphatic capillaries transport absorbed fats away from the intestine and deliver these molecules to the blood.

View the University of Michigan Webscope to explore the tissue sample in greater detail.

Self-Check Questions

Visit your course online to take a quiz to check your understanding of Connective Tissue:

MUSCLE TISSUE AND MOTION

Learning Objectives

- Identify the three types of muscle tissue
- Compare and contrast the functions of each muscle tissue type
- Explain how muscle tissue can enable motion

Muscle tissue is characterized by properties that allow movement. Muscle cells are excitable; they respond to a stimulus. They are contractile, meaning they can shorten and generate a pulling force. When attached between two movable objects, in other words, bones, contractions of the muscles cause the bones to move. Some muscle movement is voluntary, which means it is under conscious control. For example, a person decides to open a book and read a chapter on anatomy. Other movements are involuntary, meaning they are not under conscious control, such as the contraction of your pupil in bright light. Muscle tissue is classified into three types according to structure and function: skeletal, cardiac, and smooth (Table 1).

Table 1. Comparison of Structure and Properties of Muscle Tissue Types

Tissue	Histology	Function	Location
Skeletal	Long cylindrical fiber, striated, many peripherally located nuclei	Voluntary movement, produces heat, protects organs	Attached to bones and around entrance points to body (e.g., mouth, anus)
Cardiac	Short, branched, striated, single central nucleus	Contracts to pump blood	Heart
Smooth	Short, spindle-shaped, no evident striation, single nucleus in each fiber	Involuntary movement, moves food, involuntary control of respiration, moves secretions, regulates flow of blood in arteries by contraction	Walls of major organs and passageways

Skeletal muscle is attached to bones and its contraction makes possible locomotion, facial expressions, posture, and other voluntary movements of the body. Forty percent of your body mass is made up of skeletal muscle. Skeletal muscles generate heat as a byproduct of their contraction and thus participate in thermal homeostasis. Shivering is an involuntary contraction of skeletal muscles in response to perceived lower than normal body temperature. The muscle cell, or **myocyte**, develops from myoblasts derived from the mesoderm. Myocytes and their numbers remain relatively constant throughout life. Skeletal muscle tissue is arranged in bundles surrounded by connective tissue. Under the light microscope, muscle cells appear striated with many nuclei squeezed along the membranes. The **striation** is due to the regular alternation of the contractile proteins actin and myosin, along with the structural proteins that couple the contractile proteins to connective tissues. The cells are multinucleated as a result of the fusion of the many myoblasts that fuse to form each long muscle fiber.

Cardiac muscle forms the contractile walls of the heart. The cells of cardiac muscle, known as cardiomyocytes, also appear striated under the microscope. Unlike skeletal muscle fibers, cardiomyocytes are single cells typically with a single centrally located nucleus. A principal characteristic of cardiomyocytes is that they contract on their own intrinsic rhythms without any external stimulation. Cardiomyocyte attach to one another with specialized cell junctions called intercalated discs. Intercalated discs have both anchoring junctions and gap junctions. Attached cells form long, branching cardiac muscle fibers that are, essentially, a mechanical and electrochemical syncytium

allowing the cells to synchronize their actions. The cardiac muscle pumps blood through the body and is under involuntary control. The attachment junctions hold adjacent cells together across the dynamic pressures changes of the cardiac cycle.

Smooth muscle tissue contraction is responsible for involuntary movements in the internal organs. It forms the contractile component of the digestive, urinary, and reproductive systems as well as the airways and arteries. Each cell is spindle shaped with a single nucleus and no visible striations (Figure 1).

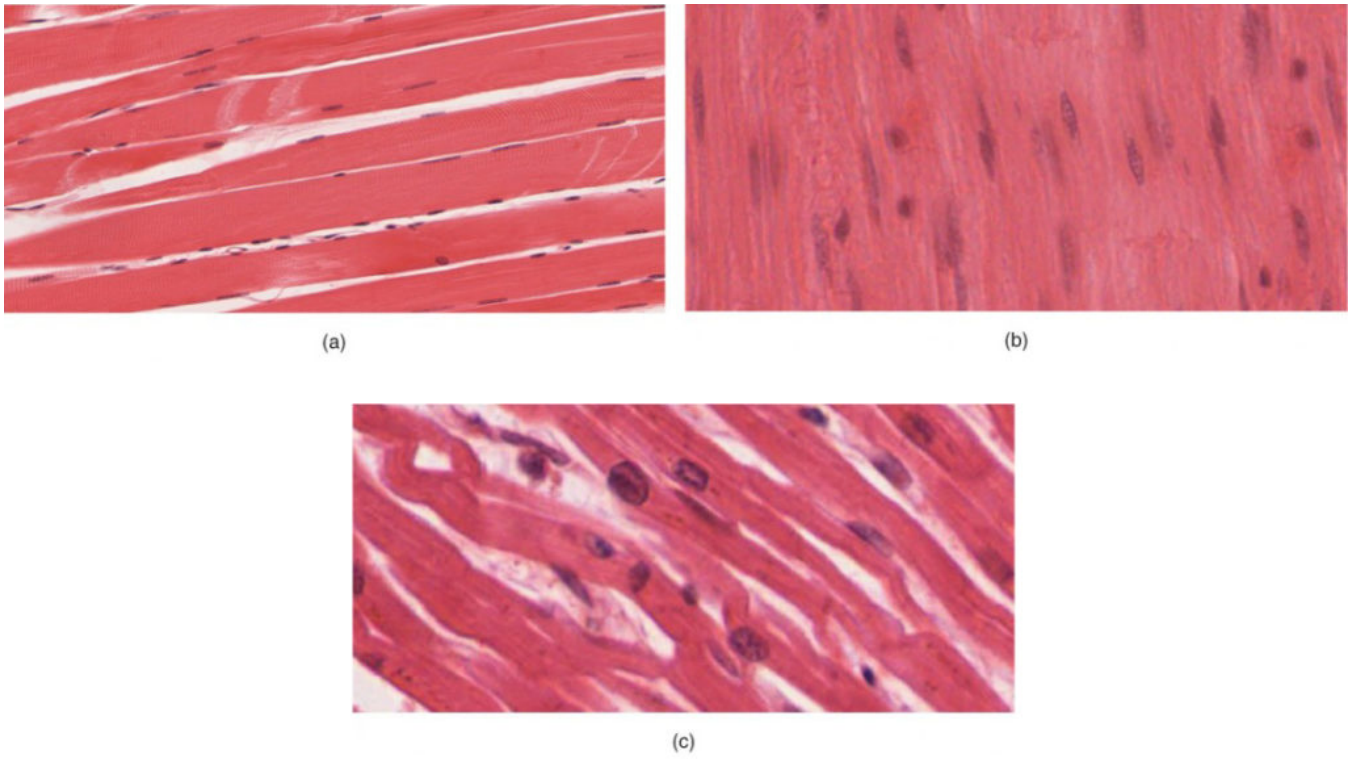


Figure 1. Muscle Tissue. *(a) Skeletal muscle cells have prominent striation and nuclei on their periphery. (b) Smooth muscle cells have a single nucleus and no visible striations. (c) Cardiac muscle cells appear striated and have a single nucleus. From top, LM × 1600, LM × 1600, LM × 1600. (Micrographs provided by the Regents of University of Michigan Medical School © 2012)*

Watch this video to learn more about muscle tissue. In looking through a microscope how could you distinguish skeletal muscle tissue from smooth muscle?

Watch this video online: https://youtu.be/raGl8bLkaAw

Self-Check Questions

Visit your course online to take a quiz to check your understanding of Muscle Tissues:

NERVOUS TISSUE MEDIATES PERCEPTION AND RESPONSE

Learning Objectives

- Identify the classes of cells that make up nervous tissue
- Discuss how nervous tissue mediates perception and response

Nervous tissue is characterized as being excitable and capable of sending and receiving electrochemical signals that provide the body with information. Two main classes of cells make up nervous tissue: the **neuron** and **neuroglia** (Figure 1). Neurons propagate information via electrochemical impulses, called action potentials, which are biochemically linked to the release of chemical signals. Neuroglia play an essential role in supporting neurons and modulating their information propagation.

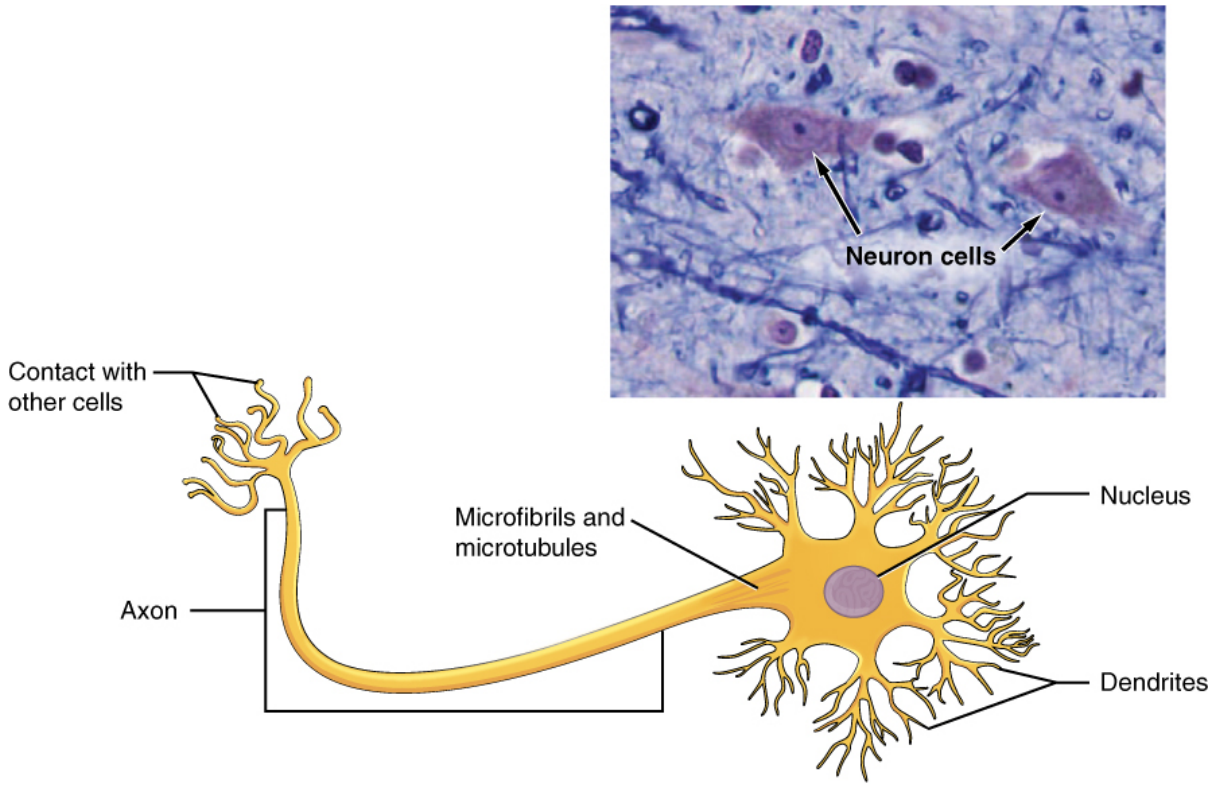


Figure 1. The Neuron. *The cell body of a neuron, also called the soma, contains the nucleus and mitochondria. The dendrites transfer the nerve impulse to the soma. The axon carries the action potential away to another excitable cell. LM × 1600. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

Follow this link to learn more about nervous tissue. What are the main parts of a nerve cell?

Neurons display distinctive morphology, well suited to their role as conducting cells, with three main parts. The cell body includes most of the cytoplasm, the organelles, and the nucleus. Dendrites branch off the cell body and appear as thin extensions. A long “tail,” the axon, extends from the neuron body and can be wrapped in an

insulating layer known as **myelin**, which is formed by accessory cells. The synapse is the gap between nerve cells, or between a nerve cell and its target, for example, a muscle or a gland, across which the impulse is transmitted by chemical compounds known as neurotransmitters. Neurons categorized as multipolar neurons have several dendrites and a single prominent axon. Bipolar neurons possess a single dendrite and axon with the cell body, while unipolar neurons have only a single process extending out from the cell body, which divides into a functional dendrite and into a functional axon. When a neuron is sufficiently stimulated, it generates an action potential that propagates down the axon towards the synapse. If enough neurotransmitters are released at the synapse to stimulate the next neuron or target, a response is generated.

The second class of neural cells comprises the neuroglia or glial cells, which have been characterized as having a simple support role. The word “glia” comes from the Greek word for glue. Recent research is shedding light on the more complex role of neuroglia in the function of the brain and nervous system. **Astrocyte** cells, named for their distinctive star shape, are abundant in the central nervous system. The astrocytes have many functions, including regulation of ion concentration in the intercellular space, uptake and/or breakdown of some neurotransmitters, and formation of the blood-brain barrier, the membrane that separates the circulatory system from the brain. Microglia protect the nervous system against infection but are not nervous tissue because they are related to macrophages. **Oligodendrocyte** cells produce myelin in the central nervous system (brain and spinal cord) while the **Schwann cell** produces myelin in the peripheral nervous system (Figure 2).

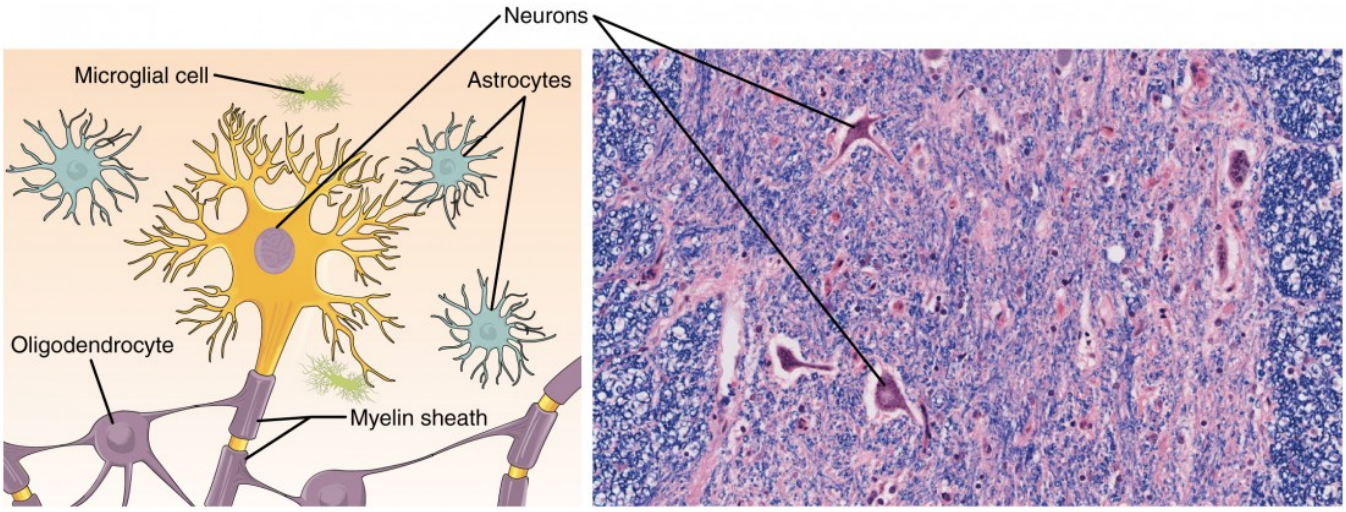


Figure 2. Nervous Tissue. Nervous tissue is made up of neurons and neuroglia. The cells of nervous tissue are specialized to transmit and receive impulses. LM × 872. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

Self-Check Questions

Visit your course online to take a quiz to check your understanding of Nervous Tissue:

TISSUE INJURY AND AGING

Learning Objectives

- Identify the cardinal signs of inflammation
- List the body's response to tissue injury
- Explain the process of tissue repair
- Discuss the progressive impact of aging on tissue
- Describe cancerous mutations' effect on tissue

Tissues of all types are vulnerable to injury and, inevitably, aging. In the former case, understanding how tissues respond to damage can guide strategies to aid repair. In the latter case, understanding the impact of aging can help in the search for ways to diminish its effects.

Tissue Injury and Repair

Inflammation is the standard, initial response of the body to injury. Whether biological, chemical, physical, or radiation burns, all injuries lead to the same sequence of physiological events. Inflammation limits the extent of injury, partially or fully eliminates the cause of injury, and initiates repair and regeneration of damaged tissue. **Necrosis**, or accidental cell death, causes inflammation. **Apoptosis** is programmed cell death, a normal step-by-step process that destroys cells no longer needed by the body. By mechanisms still under investigation, apoptosis does not initiate the inflammatory response. Acute inflammation resolves over time by the healing of tissue. If inflammation persists, it becomes chronic and leads to diseased conditions. Arthritis and tuberculosis are examples of chronic inflammation. The suffix "-*itis*" denotes inflammation of a specific organ or type, for example, peritonitis is the inflammation of the peritoneum, and meningitis refers to the inflammation of the meninges, the tough membranes that surround the central nervous system

The four cardinal signs of inflammation—redness, swelling, pain, and local heat—were first recorded in antiquity. Cornelius Celsus is credited with documenting these signs during the days of the Roman Empire, as early as the first century AD. A fifth sign, loss of function, may also accompany inflammation.

Upon tissue injury, damaged cells release inflammatory chemical signals that evoke local **vasodilation**, the widening of the blood vessels. Increased blood flow results in apparent redness and heat. In response to injury, mast cells present in tissue degranulate, releasing the potent vasodilator **histamine**. Increased blood flow and inflammatory mediators recruit white blood cells to the site of inflammation. The endothelium lining the local blood vessel becomes "leaky" under the influence of histamine and other inflammatory mediators allowing neutrophils, macrophages, and fluid to move from the blood into the interstitial tissue spaces. The excess liquid in tissue causes swelling, more properly called edema. The swollen tissues squeezing pain receptors cause the sensation of pain. Prostaglandins released from injured cells also activate pain neurons. Non-steroidal anti-inflammatory drugs (NSAIDs) reduce pain because they inhibit the synthesis of prostaglandins. High levels of NSAIDs reduce inflammation. Antihistamines decrease allergies by blocking histamine receptors and as a result the histamine response.

After containment of an injury, the tissue repair phase starts with removal of toxins and waste products. **Clotting** (coagulation) reduces blood loss from damaged blood vessels and forms a network of fibrin proteins that trap blood cells and bind the edges of the wound together. A scab forms when the clot dries, reducing the risk of infection. Sometimes a mixture of dead leukocytes and fluid called pus accumulates in the wound. As healing progresses, fibroblasts from the surrounding connective tissues replace the collagen and extracellular material lost by the injury. Angiogenesis, the growth of new blood vessels, results in vascularization of the new tissue known as granulation tissue. The clot retracts pulling the edges of the wound together, and it slowly dissolves as the tissue is repaired. When a large amount of granulation tissue forms and capillaries

disappear, a pale scar is often visible in the healed area. A **primary union** describes the healing of a wound where the edges are close together. When there is a gaping wound, it takes longer to refill the area with cells and collagen. The process called **secondary union** occurs as the edges of the wound are pulled together by what is called **wound contraction**. When a wound is more than one quarter of an inch deep, sutures (stitches) are recommended to promote a primary union and avoid the formation of a disfiguring scar. Regeneration is the addition of new cells of the same type as the ones that were injured (Figure 1).

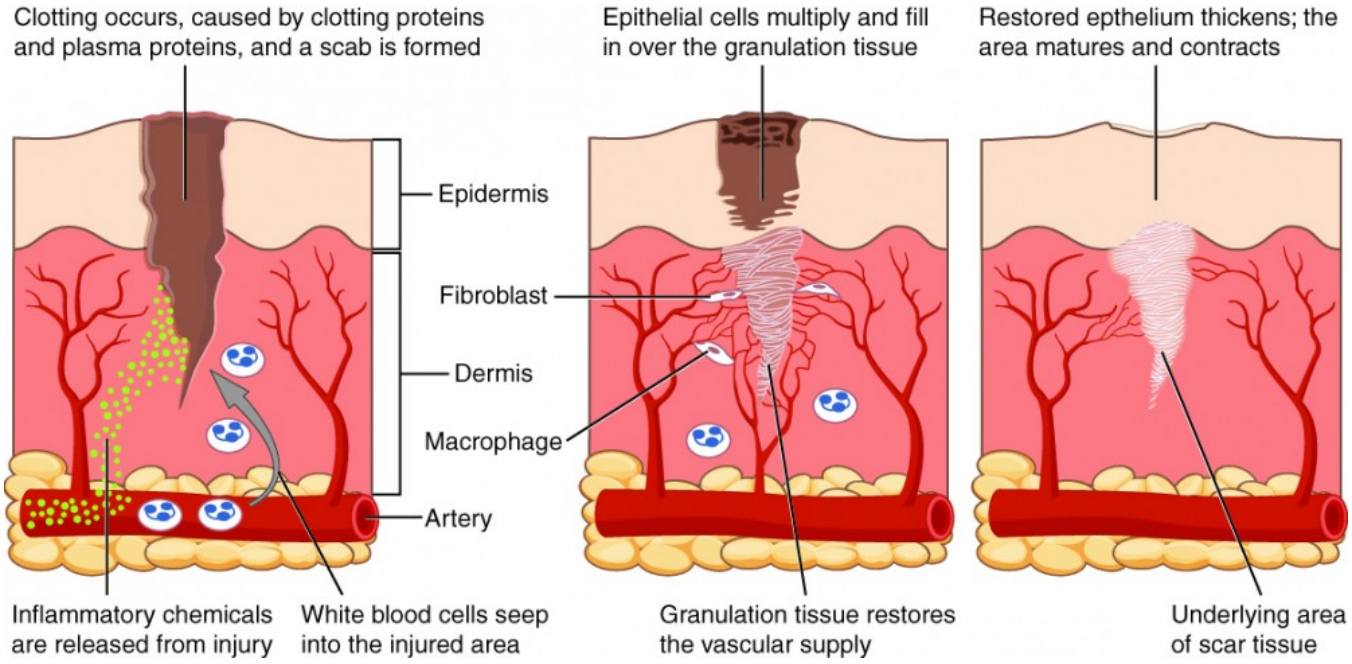


Figure 1. Tissue Healing. *During wound repair, collagen fibers are laid down randomly by fibroblasts that move into repair the area.*

Watch this video to see a hand heal. Over what period of time do you think these images were taken?
Watch this video online: https://youtu.be/7jWSLHHtHt0

Tissue and Aging

According to poet Ralph Waldo Emerson, “The surest poison is time.” In fact, biology confirms that many functions of the body decline with age. All the cells, tissues, and organs are affected by senescence, with noticeable variability between individuals owing to different genetic makeup and lifestyles. The outward signs of aging are easily recognizable. The skin and other tissues become thinner and drier, reducing their elasticity, contributing to wrinkles and high blood pressure. Hair turns gray because follicles produce less melanin, the brown pigment of hair and the iris of the eye. The face looks flabby because elastic and collagen fibers decrease in connective tissue and muscle tone is lost. Glasses and hearing aids may become parts of life as the senses slowly deteriorate, all due to reduced elasticity. Overall height decreases as the bones lose calcium and other minerals. With age, fluid decreases in the fibrous cartilage disks intercalated between the vertebrae in the spine. Joints lose cartilage and stiffen. Many tissues, including those in muscles, lose mass through a process called **atrophy**. Lumps and rigidity become more widespread. As a consequence, the passageways, blood vessels, and airways become more rigid. The brain and spinal cord lose mass. Nerves do not transmit impulses with the same speed and frequency as in the past. Some loss of thought clarity and memory can accompany aging. More severe problems are not necessarily associated with the aging process and may be symptoms of underlying illness.

As exterior signs of aging increase, so do the interior signs, which are not as noticeable. The incidence of heart diseases, respiratory syndromes, and type 2 diabetes increases with age, though these are not necessarily age-dependent effects. Wound healing is slower in the elderly, accompanied by a higher frequency of infection as the capacity of the immune system to fend off pathogen declines.

Aging is also apparent at the cellular level because all cells experience changes with aging. Telomeres, regions of the chromosomes necessary for cell division, shorten each time cells divide. As they do, cells are less able to divide and regenerate. Because of alterations in cell membranes, transport of oxygen and nutrients into the cell and removal of carbon dioxide and waste products from the cell are not as efficient in the elderly. Cells may begin to function abnormally, which may lead to diseases associated with aging, including arthritis, memory issues, and some cancers.

The progressive impact of aging on the body varies considerably among individuals, but Studies indicate, however, that exercise and healthy lifestyle choices can slow down the deterioration of the body that comes with old age.

Homeostatic Imbalances: Tissues and Cancer

Cancer is a generic term for many diseases in which cells escape regulatory signals. Uncontrolled growth, invasion into adjacent tissues, and colonization of other organs, if not treated early enough, are its hallmarks. Health suffers when tumors "rob" blood supply from the "normal" organs.

A mutation is defined as a permanent change in the DNA of a cell. Epigenetic modifications, changes that do not affect the code of the DNA but alter how the DNA is decoded, are also known to generate abnormal cells. Alterations in the genetic material may be caused by environmental agents, infectious agents, or errors in the replication of DNA that accumulate with age. Many mutations do not cause any noticeable change in the functions of a cell; however, if the modification affects key proteins that have an impact on the cell's ability to proliferate in an orderly fashion, the cell starts to divide abnormally.

As changes in cells accumulate, they lose their ability to form regular tissues. A tumor, a mass of cells displaying abnormal architecture, forms in the tissue. Many tumors are benign, meaning they do not metastasize nor cause disease. A tumor becomes malignant, or cancerous, when it breaches the confines of its tissue, promotes angiogenesis, attracts the growth of capillaries, and metastasizes to other organs (Figure 2).

The specific names of cancers reflect the tissue of origin. Cancers derived from epithelial cells are referred to as carcinomas. Cancer in myeloid tissue or blood cells form myelomas. Leukemias are cancers of white blood cells, whereas sarcomas derive from connective tissue. Cells in tumors differ both in structure and function. Some cells, called cancer stem cells, appear to be a subtype of cell responsible for uncontrolled growth. Recent research shows that contrary to what was previously assumed, tumors are not disorganized masses of cells, but have their own structures.

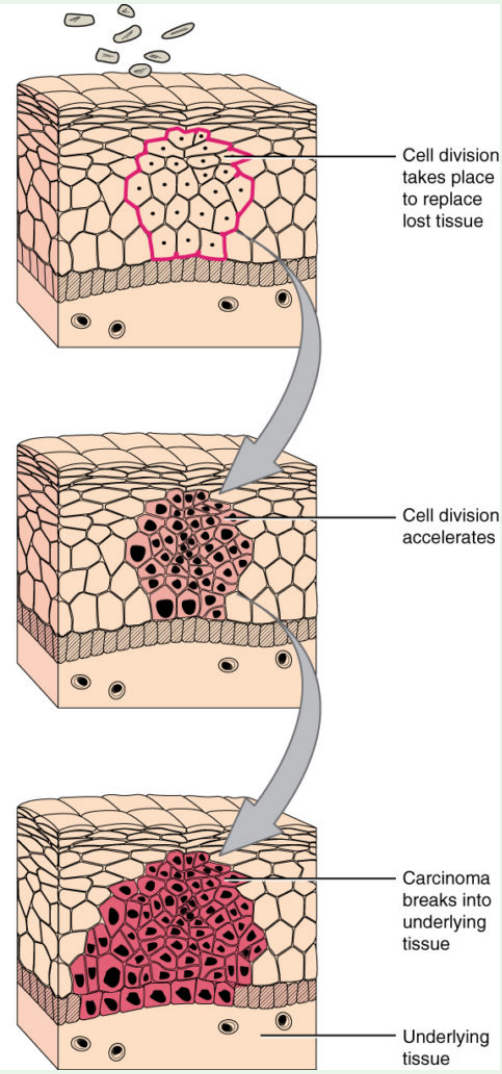


Figure 2. Development of Cancer. *Note the change in cell size, nucleus size, and organization in the tissue.*

Watch this video to learn more about tumors. What is a tumor?

Watch this video online: https://youtu.be/LEpTTolebqo

Cancer treatments vary depending on the disease's type and stage. Traditional approaches, including surgery, radiation, chemotherapy, and hormonal therapy, aim to remove or kill rapidly dividing cancer cells, but these strategies have their limitations. Depending on a tumor's location, for example, cancer surgeons may be unable to remove it. Radiation and chemotherapy are difficult, and it is often impossible to target only the cancer cells. The

treatments inevitably destroy healthy tissue as well. To address this, researchers are working on pharmaceuticals that can target specific proteins implicated in cancer-associated molecular pathways.

GLOSSARY: THE TISSUE LEVEL OF ORGANIZATION

adipocytes: lipid storage cells

adipose tissue: specialized areolar tissue rich in stored fat

anchoring junction: mechanically attaches adjacent cells to each other or to the basement membrane

apical: that part of a cell or tissue which, in general, faces an open space

apocrine secretion: release of a substance along with the apical portion of the cell

apoptosis: programmed cell death

areolar tissue: (also, loose connective tissue) a type of connective tissue proper that shows little specialization with cells dispersed in the matrix

astrocyte: star-shaped cell in the central nervous system that regulates ions and uptake and/or breakdown of some neurotransmitters and contributes to the formation of the blood-brain barrier

atrophy: loss of mass and function

basal lamina: thin extracellular layer that lies underneath epithelial cells and separates them from other tissues

basement membrane: in epithelial tissue, a thin layer of fibrous material that anchors the epithelial tissue to the underlying connective tissue; made up of the basal lamina and reticular lamina

cardiac muscle: heart muscle, under involuntary control, composed of striated cells that attach to form fibers, each cell contains a single nucleus, contracts autonomously

cell junction: point of cell-to-cell contact that connects one cell to another in a tissue

chondrocytes: cells of the cartilage

clotting: also called coagulation; complex process by which blood components form a plug to stop bleeding

collagen fiber: flexible fibrous proteins that give connective tissue tensile strength

connective tissue membrane: connective tissue that encapsulates organs and lines movable joints

connective tissue proper: connective tissue containing a viscous matrix, fibers, and cells.

connective tissue: type of tissue that serves to hold in place, connect, and integrate the body's organs and systems

cutaneous membrane: skin; epithelial tissue made up of a stratified squamous epithelial cells that cover the outside of the body

dense connective tissue: connective tissue proper that contains many fibers that provide both elasticity and protection

ectoderm: outermost embryonic germ layer from which the epidermis and the nervous tissue derive

elastic cartilage: type of cartilage, with elastin as the major protein, characterized by rigid support as well as elasticity

elastic fiber: fibrous protein within connective tissue that contains a high percentage of the protein elastin that allows the fibers to stretch and return to original size

endocrine gland: groups of cells that release chemical signals into the intercellular fluid to be picked up and transported to their target organs by blood

endoderm: innermost embryonic germ layer from which most of the digestive system and lower respiratory system derive

endothelium: tissue that lines vessels of the lymphatic and cardiovascular system, made up of a simple squamous epithelium

epithelial membrane: epithelium attached to a layer of connective tissue

epithelial tissue: type of tissue that serves primarily as a covering or lining of body parts, protecting the body; it also functions in absorption, transport, and secretion

exocrine gland: group of epithelial cells that secrete substances through ducts that open to the skin or to internal body surfaces that lead to the exterior of the body

fibroblast: most abundant cell type in connective tissue, secretes protein fibers and matrix into the extracellular space

fibrocartilage: tough form of cartilage, made of thick bundles of collagen fibers embedded in chondroitin sulfate ground substance

fibrocyte: less active form of fibroblast

fluid connective tissue: specialized cells that circulate in a watery fluid containing salts, nutrients, and dissolved proteins

gap junction: allows cytoplasmic communications to occur between cells

goblet cell: unicellular gland found in columnar epithelium that secretes mucous

ground substance: fluid or semi-fluid portion of the matrix

histamine: chemical compound released by mast cells in response to injury that causes vasodilation and endothelium permeability

histology: microscopic study of tissue architecture, organization, and function

holocrine secretion: release of a substance caused by the rupture of a gland cell, which becomes part of the secretion

hyaline cartilage: most common type of cartilage, smooth and made of short collagen fibers embedded in a chondroitin sulfate ground substance

inflammation: response of tissue to injury

lacunae: (singular = lacuna) small spaces in bone or cartilage tissue that cells occupy

lamina propria: areolar connective tissue underlying a mucous membrane

loose connective tissue: (also, areolar tissue) type of connective tissue proper that shows little specialization with cells dispersed in the matrix

matrix: extracellular material which is produced by the cells embedded in it, containing ground substance and fibers

merocrine secretion: release of a substance from a gland via exocytosis

mesenchymal cell: adult stem cell from which most connective tissue cells are derived

mesenchyme: embryonic tissue from which connective tissue cells derive

mesoderm: middle embryonic germ layer from which connective tissue, muscle tissue, and some epithelial tissue derive

mesothelium: simple squamous epithelial tissue which covers the major body cavities and is the epithelial portion of serous membranes

mucous connective tissue: specialized loose connective tissue present in the umbilical cord

mucous gland: group of cells that secrete mucous, a thick, slippery substance that keeps tissues moist and acts as a lubricant

mucous membrane: tissue membrane that is covered by protective mucous and lines tissue exposed to the outside environment

muscle tissue: type of tissue that is capable of contracting and generating tension in response to stimulation; produces movement.

myelin: layer of lipid inside some neuroglial cells that wraps around the axons of some neurons

myocyte: muscle cells

necrosis: accidental death of cells and tissues

nervous tissue: type of tissue that is capable of sending and receiving impulses through electrochemical signals.

neuroglia: supportive neural cells

neuron: excitable neural cell that transfer nerve impulses

oligodendrocyte: neuroglial cell that produces myelin in the brain

parenchyma: functional cells of a gland or organ, in contrast with the supportive or connective tissue of a gland or organ

primary union: edges of a wound are close enough together to promote healing without the use of stitches to hold them close

pseudostratified columnar epithelium: tissue that consists of a single layer of irregularly shaped and sized cells that give the appearance of multiple layers; found in ducts of certain glands and the upper respiratory tract

reticular fiber: fine fibrous protein, made of collagen subunits, which cross-link to form supporting “nets” within connective tissue

reticular lamina: matrix containing collagen and elastin secreted by connective tissue; a component of the basement membrane

reticular tissue: type of loose connective tissue that provides a supportive framework to soft organs, such as lymphatic tissue, spleen, and the liver

Schwann cell: neuroglial cell that produces myelin in the peripheral nervous system

secondary union: wound healing facilitated by wound contraction

serous gland: group of cells within the serous membrane that secrete a lubricating substance onto the surface

serous membrane: type of tissue membrane that lines body cavities and lubricates them with serous fluid

simple columnar epithelium: tissue that consists of a single layer of column-like cells; promotes secretion and absorption in tissues and organs

simple cuboidal epithelium: tissue that consists of a single layer of cube-shaped cells; promotes secretion and absorption in ducts and tubules

simple squamous epithelium: tissue that consists of a single layer of flat scale-like cells; promotes diffusion and filtration across surface

skeletal muscle: usually attached to bone, under voluntary control, each cell is a fiber that is multinucleated and striated

smooth muscle: under involuntary control, moves internal organs, cells contain a single nucleus, are spindle-shaped, and do not appear striated; each cell is a fiber

stratified columnar epithelium: tissue that consists of two or more layers of column-like cells, contains glands and is found in some ducts

stratified cuboidal epithelium: tissue that consists of two or more layers of cube-shaped cells, found in some ducts

stratified squamous epithelium: tissue that consists of multiple layers of cells with the most apical being flat scale-like cells; protects surfaces from abrasion

striation: alignment of parallel actin and myosin filaments which form a banded pattern

supportive connective tissue: type of connective tissue that provides strength to the body and protects soft tissue

synovial membrane: connective tissue membrane that lines the cavities of freely movable joints, producing synovial fluid for lubrication

tight junction: forms an impermeable barrier between cells

tissue membrane: thin layer or sheet of cells that covers the outside of the body, organs, and internal cavities

tissue: group of cells that are similar in form and perform related functions

totipotent: embryonic cells that have the ability to differentiate into any type of cell and organ in the body

transitional epithelium: form of stratified epithelium found in the urinary tract, characterized by an apical layer of cells that change shape in response to the presence of urine

vasodilation: widening of blood vessels

wound contraction: process whereby the borders of a wound are physically drawn together

ADDITIONAL LINKS

See examples and magnified views of various tissues here:

- https://www.mesacc.edu/departments/life-science/anatomy-physiology/resources

To check your understanding of connective tissue histology, download the free SecondLook App for the ipad:

- http://www.med.umich.edu/lrc/secondlook/

PRACTICE TEST: THE TISSUE LEVEL OF ORGANIZATION

Review the material from this module by completing the practice in course online.

REVIEW: HISTOLOGY

Click on this resource from “Ed the Pathology Guy” to review the information you’ve learned about Histology. Use the “Next” arrow in the upper corner of the screen to learn more.

http://www.pathguy.com/histo/001.htm

SLIDES OF HISTOLOGY

Learning Objectives

- Be able to describe the functions of cells commonly found in connective tissue and identify them.
- Be able to recognize interstitial (fibrillar) collagens and elastic fibers at the light and electron microscopic levels.
- Be able to distinguish between type I collagen, type III (reticular) collagen, and elastic fibers when appropriately stained material is presented.

- Be able to use knowledge about the physical characteristics of collagen and elastin in explaining the functions of tissue where these molecules occur in large quantities (*e.g.*, coarse type I collagen fibrils present in dense connective tissue compared to more delicate type III fibers found closer to the interface of cells and the extracellular matrix).
- Be able to recognize different types of connective tissue (*e.g.*, dense irregular, dense regular, loose, adipose) and provide examples where they are found in the body.
- Be able to recognize a basement membrane (or basal lamina) in sections or micrographs where the structure is conspicuously present and understand its functions.

The information below can also be accessed here.

Loose Connective Tissue

- **Slide 29 (small intestine, H&E)** WebScope ImageScope

Look at the connective tissue in the **submucosa** which is the lighter staining area [example] between the intestinal epithelium and the smooth muscle layer. In this area note the irregular, wavy collagen fibers arranged singly or in small groups. The collagen of fibrous supporting tissues, the dermis of the skin, tendon, ligaments and bone is type I collagen, which provides tensile strength. The background will be clear, reflecting a "ground substance"-rich connective tissue. Look for elongated nuclei, usually solitary, from which a modest amount of tapered cytoplasm extends from either one or both poles of the nucleus. These are fibroblasts [example](as opposed to clusters of similar appearing elongate nuclei that are usually smooth muscle cells or Schwann cells in a nerve that you will learn to recognize soon). Note that the nucleoplasm of a fibroblast has a generally fine stippled (dot-like) chromatin pattern with occasional coarse chromatin clumps (heterochomatin) and one or two nucleoli. Look for more examples of fibroblasts and note that you rarely see much cytoplasm and that the nuclei of these cells can be quite condensed and hyperchromatic depending upon the plane of section or the metabolic state. You should be able to recognize a range of nuclear morphologies and be able to identify the cells as fibroblasts. Most of the rounded cells you may see in the submucosa are likely white blood cells (monocytes, macrophages, and occasional neutrophils) that have migrated out into the tissue.

Now look at the region **immediately underneath the intestinal epithelium** *(*which is called the ***lamina propria*** [example]). This region is also a **loose, irregular connective tissue** but can be so extensively infiltrated by white blood cells and plasma cells that the supporting fibers and ground substance are obscured. Neutrophils and macrophages are also present and both are discussed below.

Plasma Cells

- **Slide 29 (small intestine, H&E)** WebScope ImageScope
- **Slide 40 (trachea, H&E)** WebScope ImageScope

Look for plasma cells within the **lamina propria** of **slide 29** [example]. They are round to oval shaped cells with a distinct cell boundary and a nucleus set to one side. Note the coarse chromatin clumps organzed as radial spokes in the round nuclei which is therefore often described as having a "clockface" or "wagon-wheel" appearance. You should note that the cytoplasm is quite basophilic (i.e. "base loving" so it binds hematoxylin and stains dark blue/purple), and, in well fixed tissue, the cytoplasm in many of the plasma cells is frequently granular (the rough endoplasmic reticulum, really) rather than smooth or even in appearance.

Find the Golgi complex, a pale or slightly eosinophilic (=*eosin* "loving", an area rich in membranes containing basic amino acids, syn. = acidophilic) region adjacent to the cell nucleus. The Golgi complex in these particular plasma cells is usually in the form of a fine crescent adjacent to the nucleus and it takes some practice to recognize.

Recall that the primary function of plasma cells is antibody secretion, so they are a prominent constituent of loose connective tissue wherever antigens may enter the body, such as the **gastrointestinal, urogenital, and respiratory tracts**. Plasma cells may also be found **within the connective tissue** of many of the **glands** that secrete into these regions. An excellent example of this is **slide 40** from the trachea (part of the respiratory tract). Look at the areas

outlined in the orientation diagram of the trachea and locate the loose, cellular connective tissue within the glands (the “glands” are coiled tubes of columnar epithelial cells; some the epithelial cells are tall and eosinophilic, whereas others are shorter and more basophilic). In addition to some fibroblasts and a few delicate collagen fibers, you should see quite a few plasma cells [example] amongst the epithelial tubes.

Slide 40 is also a very good specimen to examine the pseudostratified, ciliated columnar epithelium of the trachea. Note also that the basement membrane underlying this particular epithelium is especially prominent. Type IV collagen, which does not form fibrils, but rather a fine meshwork, is present in all basement membranes. The basal lamina is anchored to the underlying connective tissue by fine fibrils of type VII collagen (you obviously can’t tell this looking at it in the light microscope, but you should recall this from lecture).

Neutrophils

- Slide 29 (small intestine, H&E) WebScope ImageScope

Look in the lamina propria amongst the plasma cells and you will find neutrophils that have emigrated from the bloodstream into the tissue space as part of the immune response. Neutrophils can be identified by their granular cytoplasm and their multilobular, condensed nuclei. Because of their nuclear morphology, they are frequently also called “polymorphonuclear leukocytes” (aka “PMNs” or “polys”). Neutrophils generally enter tissues in large numbers only in response to a disease stimulus. However, as seen in this slide, it is quite normal to find them in tissues such as the gut where foreign substances frequently invoke an inflammatory response. You will study neutrophils in much greater detail in other sequences and in your histopathology course, but it is useful for now to at least be able to recognize them in various tissues and organs.

Macrophages

- Slide 26 (lymph node, H&E) WebScope ImageScope

With low power, locate the **medulla** (the interior) of the lymph node. Look for a region characterized by interlacing cords of cells. Macrophages are the biggest, rounded cells that are floating free in the spaces between the cords of cells. Many of the free cells in these medullary sinuses cannot be identified; however, the large rounded cells, with eccentrically placed, vesicular nuclei are the ones you should try to find.

Many of these macrophages contain phagocytosed red blood cells or the brownish breakdown pigment, hemosiderin (which is the result of lysosomal action on the ingested red blood cells.). Be sure you can identify a macrophage and not just a bunch of cells superimposed upon one another. Macrophages can be seen also in the **subcapsular sinus** (the lighter staining area just under the capsule at the periphery of the lymph node).

The “mononuclear phagocyte system” (also called the “reticuloendothelial system” for historic reasons) consists of free and fixed macrophages throughout the body. These cells are important in removing all kinds of debris from the body as well as playing a major role in the immune response.

Fat Cells

- Slide 152 (pharynx, H&E) WebScope ImageScope
- Slide 30 (mesentery, H&E) WebScope ImageScope
- Slide H2 (fetal thorax, H&E) WebScope ImageScope (virtual slide courtesy of Western University)

Slide 152 is a section from the pharynx. Locate the **large clear** circles [example] in the connective tissue that sits beneath the epithelium. These are fat cells (or adipocytes). In white or unilocular adipose tissue, lipids are stored as a single, non-membrane bound droplet in these cells. A fatty tissue called brown or multilocular fat, produced during fetal development, has adipocytes that contain **multiple** fat droplets. Brown fat is important for thermoregulation in newborns and hibernating mammals. In humans, brown fat is widely distributed throughout the body in the first decade of life, but it then disappears except for regions around the kidney, suprarenal glands, aorta, neck and mediastinum. None of our slides of adult tissue shows any brown fat, however this rather unique tissue can be seen in **slide H2** [example], which is from a developing fetus.

Look for adipose tissue in **Slide #30** which is taken from abdominal mesentery (the connective tissue that suspends the viscera within the abdominal cavity). Some of the individual fat cells are often broken during tissue preparation, but the overall impression of what the tissue looks like is the important point.

Mast Cells

- **Slide 160 (stomach, PAS & Azure II)** WebScope ImageScope

Mast cells can only be definitively recognized with special stains such as **Azure II** and **toluoidine blue** that identify the heparin storage granules (Azure metachromatically stains the heparin purple). Mast cells are most abundant in the connective tissue associated with the lining of the digestive and respiratory systems, and your collection just so happens to contain a tissue section from the stomach that has been stained with PAS and Azure II. As you look at this section, you will see a very obvious layer of mucous epithelial cells (PAS also reacts with the carbohydrate-rich mucin). However, to see the mast cells, you will need to look deeper in the **submucosa**where you should find small, ovoid cells amongst the collagen fibers with spherical, eccentric nuclei and **intensely basophilic** (dark purple to black) **granules** [example]. The granules are often so dark that they obscure the nucleus.

Reticular tissue

- **Slide 27 (lymph node, H&E)** WebScope ImageScope
- **Slide 28 (lymph node, silver stain)** WebScope ImageScope

The fine collagenous network that provides support in the bone marrow, lymphatic organs, around individual smooth muscle cells, and beneath most epithelia is composed mainly of Type III collagen. The collagen has an associated carbohydrate moiety (uncharacterized) that can reduce Ag+ to metallic Ag revealing a network (reticulum) of fine, black fibrils. These are termed reticular (or rarely, argyrophilic= “silver loving”) fibers. On **slide #27** look at the accumulations of**darkly stained cells** (lymphocytes in a lymph node). Note at high power that fibrils or fibers of any type cannot be readily observed. Now with **slide #28** (make sure your slide is stained with silver; it should say “Ag” on the label!), note how a network of **fine black fibrils** is present in this same tissue following silver staining. These are reticular fibers, found in skin, muscle and blood vessels. The reticular fibers provide physical support for all the cells present in tissues subject to stretching. You are not responsible for recognizing reticular fibers unless a silver stain is used.

Please remember that virtually all cells (except for those in the brain and spinal cord) are provided with some degree of support by collagen (reticular fibers) even though that may not be apparent with H&E staining. (Masson Trichrome and silver staining are frequently used in pathology to determine if connective tissue has proliferated–a sign of damage and attempted repair–in the liver, kidney and lung.)

Dense Connective Tissue

Dense Irregular Connective Tissue

- **Slide 33 (skin, Verhoeff stain)** WebScope ImageScope
- **Slide 250-1 (vagina, H&E)** WebScope ImageScope
- **Slide 250-2 (vagina, trichrome)** WebScope ImageScope

The area beneath the stratified squamous epithelium shown in **slide 33** is the dermis, which is composed of dense irregular connective tissue. In this section, the fibers clearly predominate. This slide has been stained with iron hematoxylin and eosin so you can see collagen fibers(orange) as well as elastic fibers (purple/black) in the dermis [example]. Note how the diameter of the fibers varies with location. In the region immediately beneath the epidermis you can see how the elastic fibers are interconnected forming an elaborate, **delicate** net of fibers [example]amongst thin strands of collagen. However, deeper in the dermis, the collagen and elastic fibers are much thicker.

Slide 250 which you used to look at stratified squamous non-keratinizing epithelium is also useful for the study of connective tissue (we will also use this slide to study smooth muscle and peripheral ganglia). Be sure you look at both the H&E and Masson trichrome-stained slides as they provide an excellent opportunity to see how collagen stains in connective tissue when either stain is applied. When we study smooth muscle and peripheral nerve tissue we will come back to this slide to try and distinguish between collagen fibers and fascicles of smooth muscle and/or nerve fibers and ganglia.

NOTE: Slide 250 illustrates a point about the limits of classification schemes. Even though we try to set up rigid categories (e.g. "loose" versus "dense" connective tissue), sometimes it is not always possible to classify connective tissue in a given section; it may be a little loose, a little dense, a little fatty, etc. In these particular instances, don't worry so much about trying to **exactly classify** the tissue per se, but at least try to identify the cellular and extracelluar components that you can (also bear in mind that you can't always definitely identify **every** cell) and think how its overall appearance reflects its **function**.

Dense Regular Connective Tissue

Collagenous

- **Slide 106 (plantar skin and tendon, H&E)** WebScope ImageScope
- **Slide 112 (plantar skin and tendon, H&E)** WebScope ImageScope

Slide 106 and 112 have bits of well preserved flexor tendon at the top of the section (the tissue at the **very top** of slide 112 is actually skeletal muscle -which you'll study in the next lab; the tendon is just below it). Note the **regular orientation** of the collagen fibers (there's a bit a "waviness" but you should get the idea). You should also observe that there aren't a lot of cells, a characteristic of "dense" connective tissue. The very small cracks between the fibers are just artifacts of shrinkage that occured during tissue preparation. Of course, there are some places where there are breaks in the dense regular connective tissue of the tendon containing loose connective tissue associated with nerves and blood vessels or the occasional bit of adipose tissue.

Elastic tissue

- **slide 36 (Aorta, aldehyde fuchsin)** WebScope ImageScope
- **slide 88 (Aorta, H&E)** WebScope ImageScope

These slides are examples of regularly arranged sheets (lamellae) of elastin. Slide 36 is stained with aldehyde fuchsin and Masson trichrome (Aldehyde Fuchsin, Fe. Hem. & Mass.), so the elastic lamellae are **purple**. Slide 88 is stained with H&E where the concentric rings of elastic lamellae are intensely stained with eosin giving a **glassy red appearance** [example] (one of the few places where elastin is easy to recognize in H&E sections).

Two other locations where elastic fibers can be readily seen in H&E sections are in the lamina propria of the pharynx (**slide 152** WebScope ImageScope) and the trachea (**slide 40** WebScopeImageScope). *Unlike the tissue of the aorta which would be classified as "regular," these tissues are obviously **irregular** but they're mentioned here for the purpose of illustrating how aggregates of elastic fibers appear in H&E-stained sections.* Just as in the H&E-stained aorta, the elastic fibers in the pharynx and trachea are glassy and orange-red –they appear as stippled dots because they've been cut in cross section.

Electron Micrographs

- **26 Connective Tissue – Dense Irregular** Webscope Imagescope

Dense Connective Tissue. Note the alternating layers of fibroblasts and collagenous fiber bundles. Make sure you can see the difference between cross sectioned and longitudinally sectioned collagenous fibrils. In dense connective tissue, which type of cell is most common? (CT7)

- **18 Loose Connective Tissue – Lamina propria of tracheal mucosa** Webscope Imagescope

Loose Connective Tissue. In this micrograph of loose connective tissue of the tracheal mucosa numerous (labeled) cells of the connective tissue are present. Note the relative size of the different cell types, their shapes, amount of rough ER and variously sized granules and inclusions. Then use your text and atlas to review the diagnostic features of each connective tissue cell present in the micrograph. Note the paucity of collagen fibrils. What was present in the “empty” looking intercellular space? (CT10)

- 27 Elastic Connective Tissue – Junction of Media and Adventilia of artery Webscope Imagescope

Observe the branching nature of the elastic fiber and the “mantle” of elastic microfibrils. The cross banding of the collagenous fibrils is easily observed.

- 28 Collagen and Elastin – Cross section of Chorda Tendinea Webscope Imagescope

Observe the mixture of collagen and elastic fibers in this cross section of chorda tendinea. Although collagen fibers mostly fill the view, there are numerous elastic fibers, which provide the elasticity essential for the function of the tissue.

- 29 Tendon – Longitudinal section Webscope Imagescope

Note the uniform distribution of regularly arranged collagen fibers (type I).

- 25 Connective Tissue – Fibroblast Webscope Imagescope

Observe the large amount of rough endoplasmic reticulum (ER) in these cells. Is this an indication of an active or inactive cell? (CT9) Test your ability to identify different organelles at this magnification!

- 20 Mast cell – Human Webscope Imagescope

Mast cells contain a mixture of granule types reflective of the variety of substances they secrete. Histamine and heparin are found in the more “regular” looking granules (evenly dark and round). Other secretory products include leukotrienes and other phospholipid derivatives, which are made from the sheets of membranes arranged as lamella, whorls, or even scroll-like bodies within the more irregular appearing granules. What are the secretory products of the mast cell? (CT11)

- 63 Macrophage Webscope Imagescope

Tissue macrophages can be found in many different organs. As they have a phagocytic function, removing pathogens and cell debris, macrophages usually contain abundant primary and secondary lysosomes.

- 21 Plasma cell Webscope Imagescope

This electron micrograph shows a typical secretory cell, a plasma cell, which secretes immunoglobulin protein. Many of the major types of cellular organelles are visible in this image. In the nucleus, areas of euchromatin and heterochromatin can easily be identified. Use these micrographs to review the structure of organelles. Be sure you recognise favourable sections of the nucleas, mitochondria, and rough ER.

- 23 Fat Cells – Mature Webscope Imagescope

This electron micrograph depicts mature fat cells. You can see one large lipid droplet in the cytoplasm of each cell. The nuclei of many cells are not included in the field of view. Brown fat cells would have several small lipid droplets all of which would be roughly the same size. Remember that each fat cell is enclosed by a thin basal lamina (Unfortunately, in these examples you can’t see the basal lamina). Where are the nuclei of the fat cells? (CT8)

Review Questions

1. What type of epithelium lines the luminal surface of the intestine?

Answer

The luminal surface of the intestine is made up of a simple columnar epithelium.

2. Why is rough endoplasmic reticulum basophilic?

Answer

The ribosomes attached to rough ER are associated with both ribosomal and messenger RNA – these nucleic acids carry a net negative charge and bind basic dyes (which are positively charged).

3. What type of lining epithelium is present in the pharynx?

Answer

Stratified squamous non-keratinizing epithelium lines the pharynx.

4. Can you see a nucleus in each fat cell?

Answer

No, because not all nuclei are on the plane of section.

5. What do mast cells do?

Answer

Mast cells are actively involved in a host's immune response and produce many substances, some of which are heparin and histamine. The degranulation of these cells is responsible for triggering type I, immediate hypersensitivity reactions. Type I reactions, also called anaphylactic reactions, are something you will learn about while studying the immune system later on, but for now, here is a quick explanation. IgE is an antibody, produced by plasma cells, that has a high affinity for mast cells and basophils. The antibody binds mast cells and waits for a second exposure to whatever it happens to be responsive to (an allergen). When the IgE binds an appropriate molecule, it will trigger degranulation of the mast cell and the vasodilation, congestion, bronchiolar constriction, wheezing, etc. associated with allergies and other type I reactions.

6. Why do cells actively secreting proteins exhibit basophilic cytoplasm?

Answer

Protein secreting cells have a basophilic cytoplasm because they are full of rough ER, which stains with hematoxylin, a basic dye.

7. In dense connective tissue, which type of cell is most common?

Answer

Dense connective tissue is full of fibroblasts.

8. Where are the nuclei of fat cells?

Answer

Fat cell nuclei are on the periphery of the cell and may or may not be in the plane of section.

9. Is rough ER an indication of an active or an inactive cell?

Answer

Large amounts of rough ER indicate that the cell is active and is producing large amounts of proteins.

10. What was present in the “empty” looking intercellular space?

Answer

The empty space within connective tissue is ground substance.

11. What are the secretory products of the mast cell?

Answer

Heparin and histamine are just some of the contents of mast cell granules.

HISTOLOGY LINKS

Interactive Links

- Slides and practice quizzes
- Histology virtual microscope slides found here
- Graduate virtual histology course and practical exams
- Histology microscope slides and Histology Lecture Powerpoints
- Photos of histology microscope slides
- Histology slides including labels
- Introductory Histology Slides
    - SIU School of Medicine
    - University of Kansas Medial Center

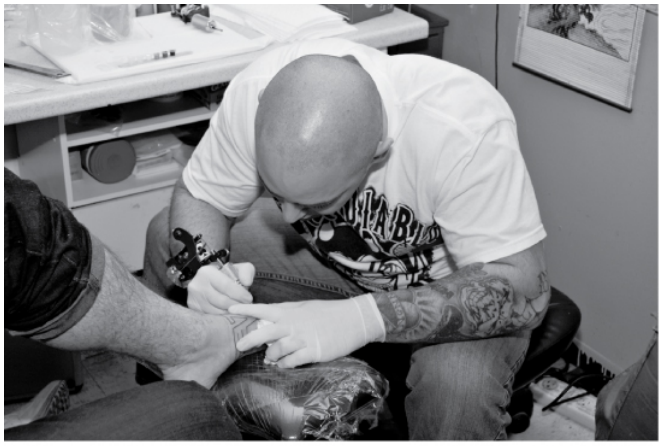
MODULE 6: THE INTEGUMENTARY SYSTEM

INTRODUCTION TO THE INTEGUMENTARY SYSTEM

Learning Objectives

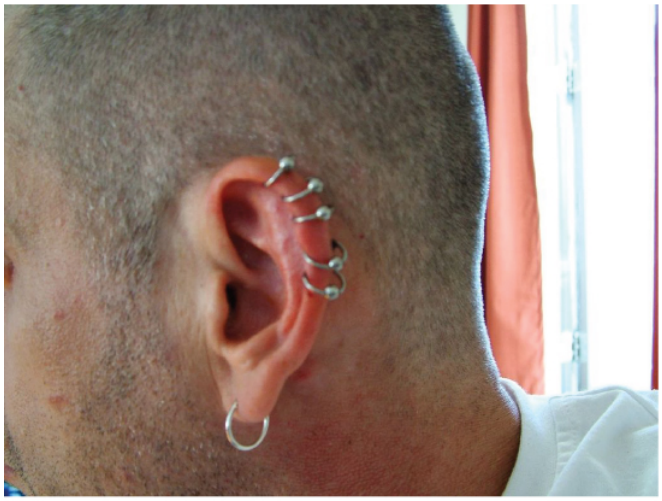
- Describe the integumentary system and the role it plays in homeostasis
- Describe the layers of the skin and the functions of each layer
- Describe the accessory structures of the skin and the functions of each
- Describe the changes that occur in the integumentary system during the aging process
- Discuss several common diseases, disorders, and injuries that affect the integumentary system
- Explain treatments for some common diseases, disorders, and injuries of the integumentary system

What do you think when you look at your skin in the mirror? Do you think about covering it with makeup, adding a tattoo, or maybe a body piercing? Or do you think about the fact that the skin belongs to one of the body's most essential and dynamic systems: the integumentary system? The integumentary system refers to the skin and its accessory structures, and it is responsible for much more than simply lending to your outward appearance. In the adult human body, the skin makes up about 16 percent of body weight and covers an area of 1.5 to 2 m^2. In fact, the skin and accessory structures are the largest organ system in the human body. As such, the skin protects your inner organs and it is in need of daily care and protection to maintain its health. This chapter will introduce the structure and functions of the integumentary system, as well as some of the diseases, disorders, and injuries that can affect this system.



(a)

(b)



(c)

(d)

Figure 1. Functions of Skin. *Your skin is a vital part of your life and appearance (a–d). Some people choose to embellish it with tattoos (a), makeup (b), and even piercings (c). (credit a: Steve Teo; credit b: "spaceodissey"/flickr; credit c: Mark/flickr; credit d: Lisa Schaffer)*

LAYERS OF THE SKIN

Learning Objectives

- Identify the components of the integumentary system
- Describe the layers of the skin and the functions of each layer
- Identify and describe the hypodermis and deep fascia
- Describe the role of keratinocytes and their life cycle
- Describe the role of melanocytes in skin pigmentation

Although you may not typically think of the skin as an organ, it is in fact made of tissues that work together as a single structure to perform unique and critical functions. The skin and its accessory structures make up

the **integumentary system**, which provides the body with overall protection. The skin is made of multiple layers of cells and tissues, which are held to underlying structures by connective tissue (Figure 1). The deeper layer of skin is well vascularized (has numerous blood vessels). It also has numerous sensory, and autonomic and sympathetic nerve fibers ensuring communication to and from the brain.

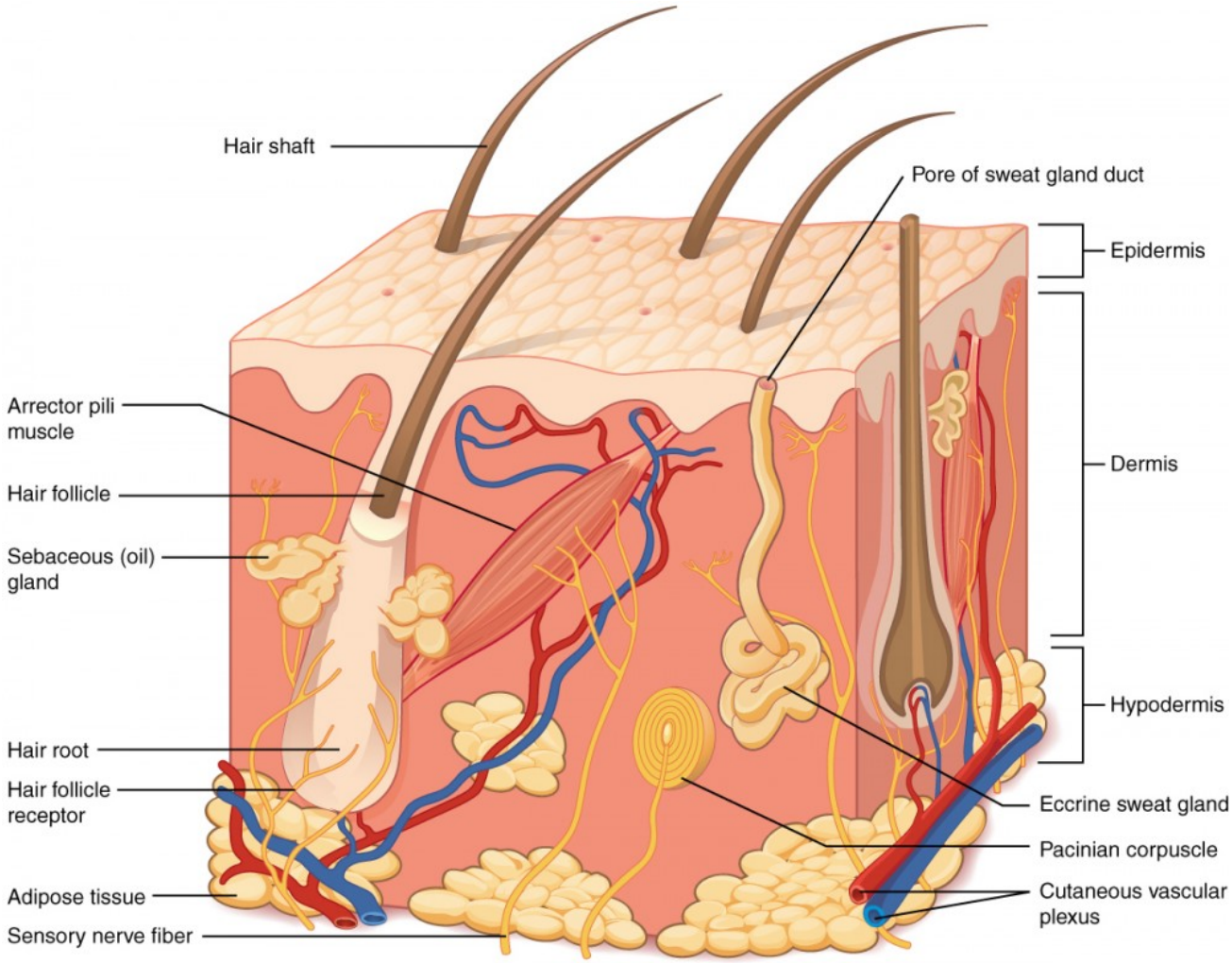


Figure 1. Layers of Skin. *The skin is composed of two main layers: the epidermis, made of closely packed epithelial cells, and the dermis, made of dense, irregular connective tissue that houses blood vessels, hair follicles, sweat glands, and other structures. Beneath the dermis lies the hypodermis, which is composed mainly of loose connective and fatty tissues.*

The skin consists of two main layers and a closely associated layer. View this animation to learn more about layers of the skin. What are the basic functions of each of these layers?

The Epidermis

The **epidermis** is composed of keratinized, stratified squamous epithelium. It is made of four or five layers of epithelial cells, depending on its location in the body. It does not have any blood vessels within it (i.e., it is avascular). Skin that has four layers of cells is referred to as “thin skin.” From deep to superficial, these layers are the stratum basale, stratum spinosum, stratum granulosum, and stratum corneum. Most of the skin can be classified as thin skin. “Thick skin” is found only on the palms of the hands and the soles of the feet. It has a fifth layer, called the stratum lucidum, located between the stratum corneum and the stratum granulosum (Figure 2).

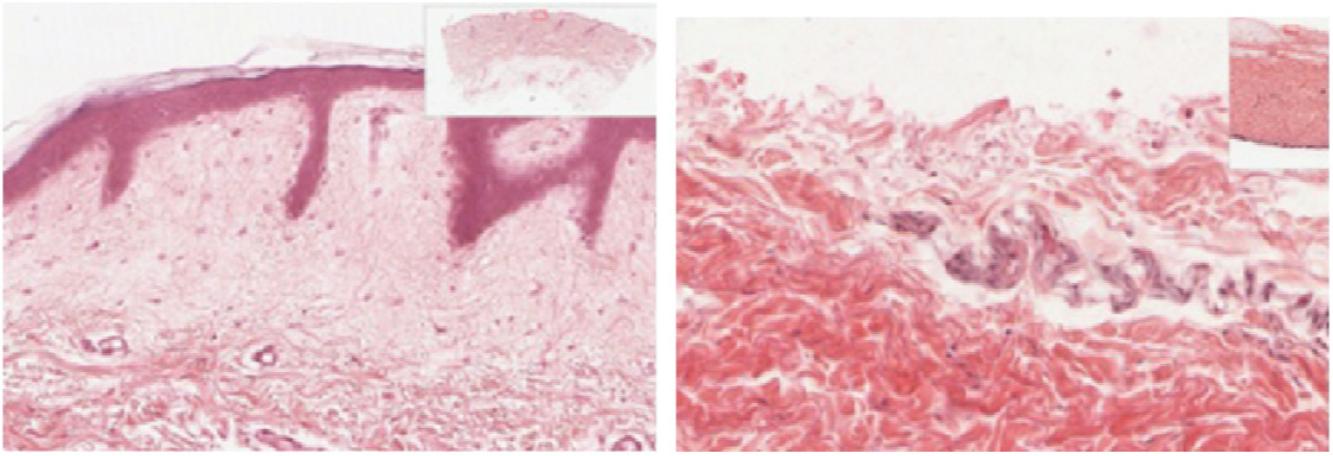


Figure 2. Thin Skin versus Thick Skin. *These slides show cross-sections of the epidermis and dermis of (a) thin and (b) thick skin. Note the significant difference in the thickness of the epithelial layer of the thick skin. From top, LM × 40, LM × 40. (Micrographs provided by the Regents of University of Michigan Medical School © 2012)*

The cells in all of the layers except the stratum basale are called keratinocytes. A **keratinocyte** is a cell that manufactures and stores the protein keratin. **Keratin** is an intracellular fibrous protein that gives hair, nails, and skin their hardness and water-resistant properties. The keratinocytes in the stratum corneum are dead and regularly slough away, being replaced by cells from the deeper layers (Figure 3).

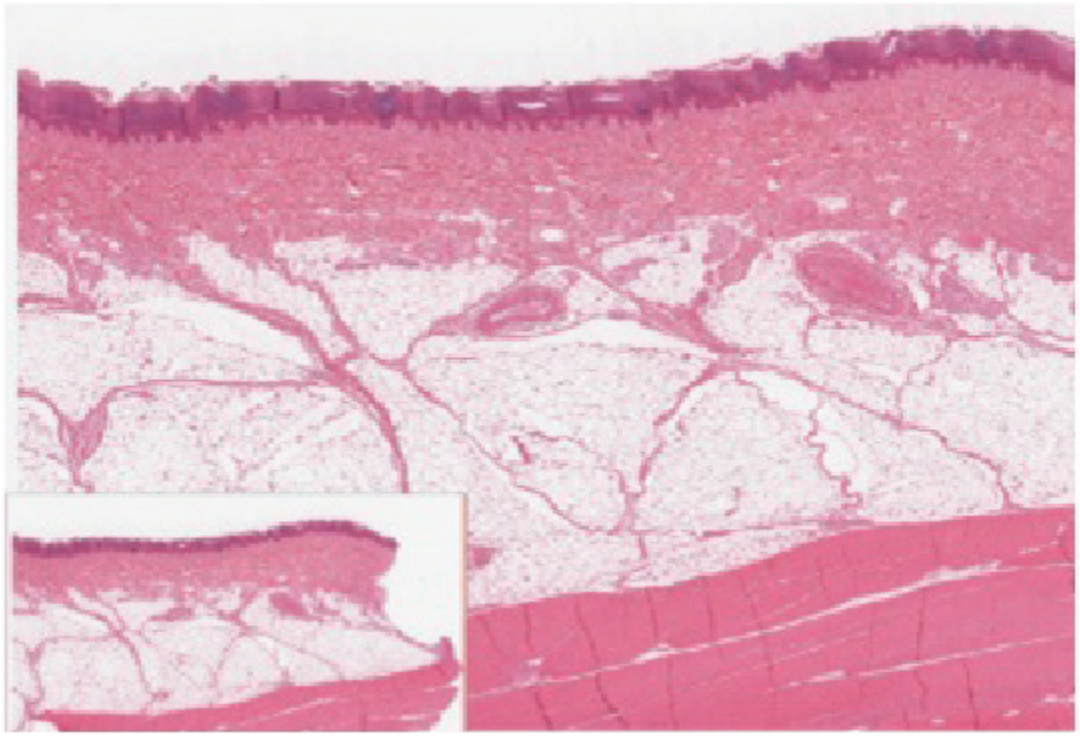


Figure 3. Epidermis. *The epidermis is epithelium composed of multiple layers of cells. The basal layer consists of cuboidal cells, whereas the outer layers are squamous, keratinized cells, so the whole epithelium is often described as being keratinized stratified squamous epithelium. LM × 40. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

View the University of Michigan WebScope at to explore the tissue sample in greater detail. If you zoom on the cells at the outermost layer of this section of skin, what do you notice about the cells?

Stratum Basale

The **stratum basale** (also called the stratum germinativum) is the deepest epidermal layer and attaches the epidermis to the basal lamina, below which lie the layers of the dermis. The cells in the stratum basale bond to the dermis via intertwining collagen fibers, referred to as the basement membrane. A finger-like projection, or fold, known as the **dermal papilla** (plural = *dermal papillae*) is found in the superficial portion of the dermis. Dermal papillae increase the strength of the connection between the epidermis and dermis; the greater the folding, the stronger the connections made (Figure 4).

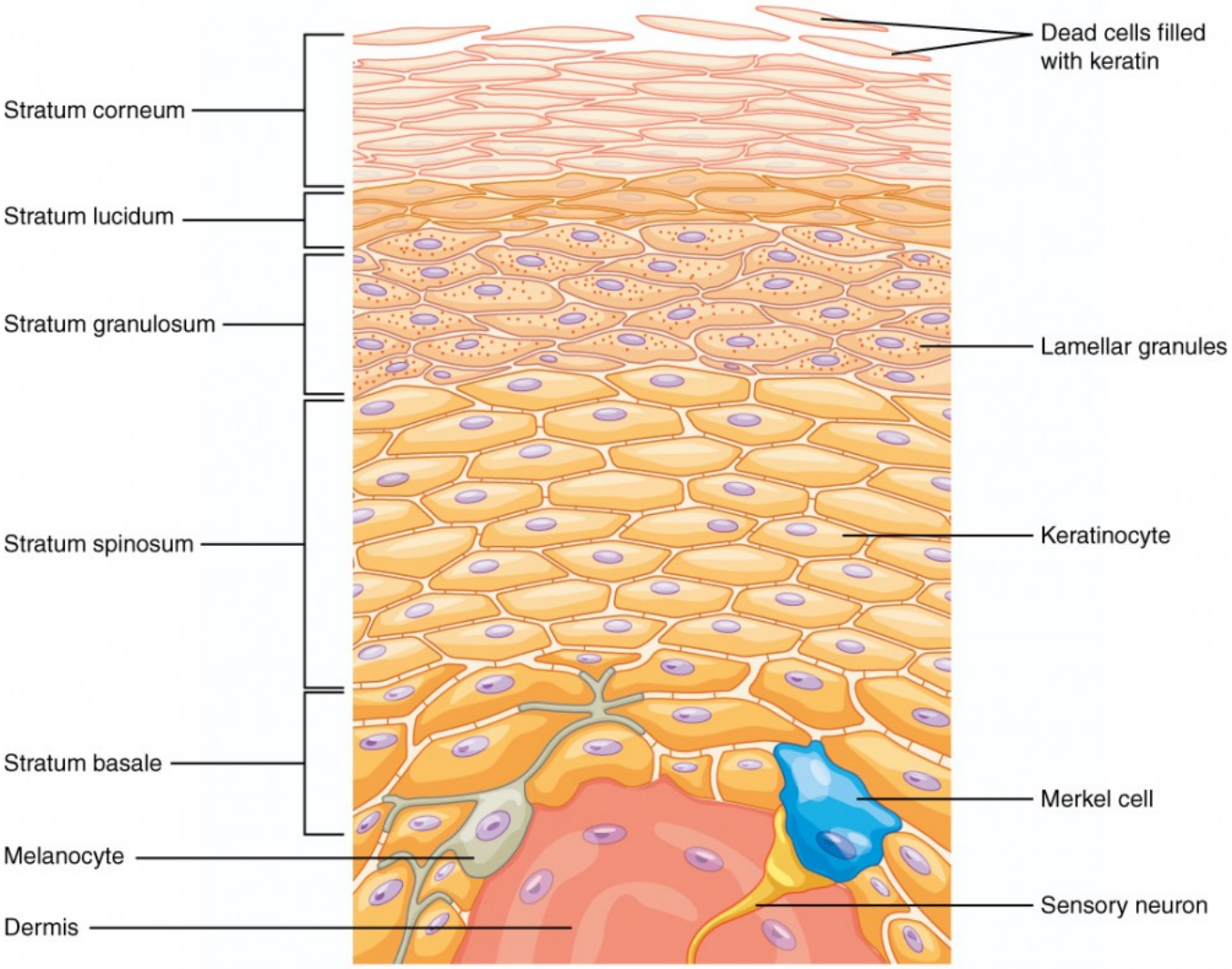


Figure 4. Layers of the Epidermis. *The epidermis of thick skin has five layers: stratum basale, stratum spinosum, stratum granulosum, stratum lucidum, and stratum corneum.*

The stratum basale is a single layer of cells primarily made of basal cells. A **basal cell** is a cuboidal-shaped stem cell that is a precursor of the keratinocytes of the epidermis. All of the keratinocytes are produced from this single layer of cells, which are constantly going through mitosis to produce new cells. As new cells are formed, the existing cells are pushed superficially away from the stratum basale. Two other cell types are found dispersed among the basal cells in the stratum basale. The first is a **Merkel cell**, which functions as a receptor and is responsible for stimulating sensory nerves that the brain perceives as touch. These cells are especially abundant on the surfaces of the hands and feet. The second is a **melanocyte**, a cell that produces the pigment melanin. **Melanin** gives hair and skin its color, and also helps protect the living cells of the epidermis from ultraviolet (UV) radiation damage.

In a growing fetus, fingerprints form where the cells of the stratum basale meet the papillae of the underlying dermal layer (papillary layer), resulting in the formation of the ridges on your fingers that you recognize as

fingerprints. Fingerprints are unique to each individual and are used for forensic analyses because the patterns do not change with the growth and aging processes.

Stratum Spinosum

As the name suggests, the **stratum spinosum** is spiny in appearance due to the protruding cell processes that join the cells via a structure called a **desmosome**. The desmosomes interlock with each other and strengthen the bond between the cells. It is interesting to note that the “spiny” nature of this layer is an artifact of the staining process. Unstained epidermis samples do not exhibit this characteristic appearance. The stratum spinosum is composed of eight to 10 layers of keratinocytes, formed as a result of cell division in the stratum basale (Figure 5). Interspersed among the keratinocytes of this layer is a type of dendritic cell called the **Langerhans cell**, which functions as a macrophage by engulfing bacteria, foreign particles, and damaged cells that occur in this layer.

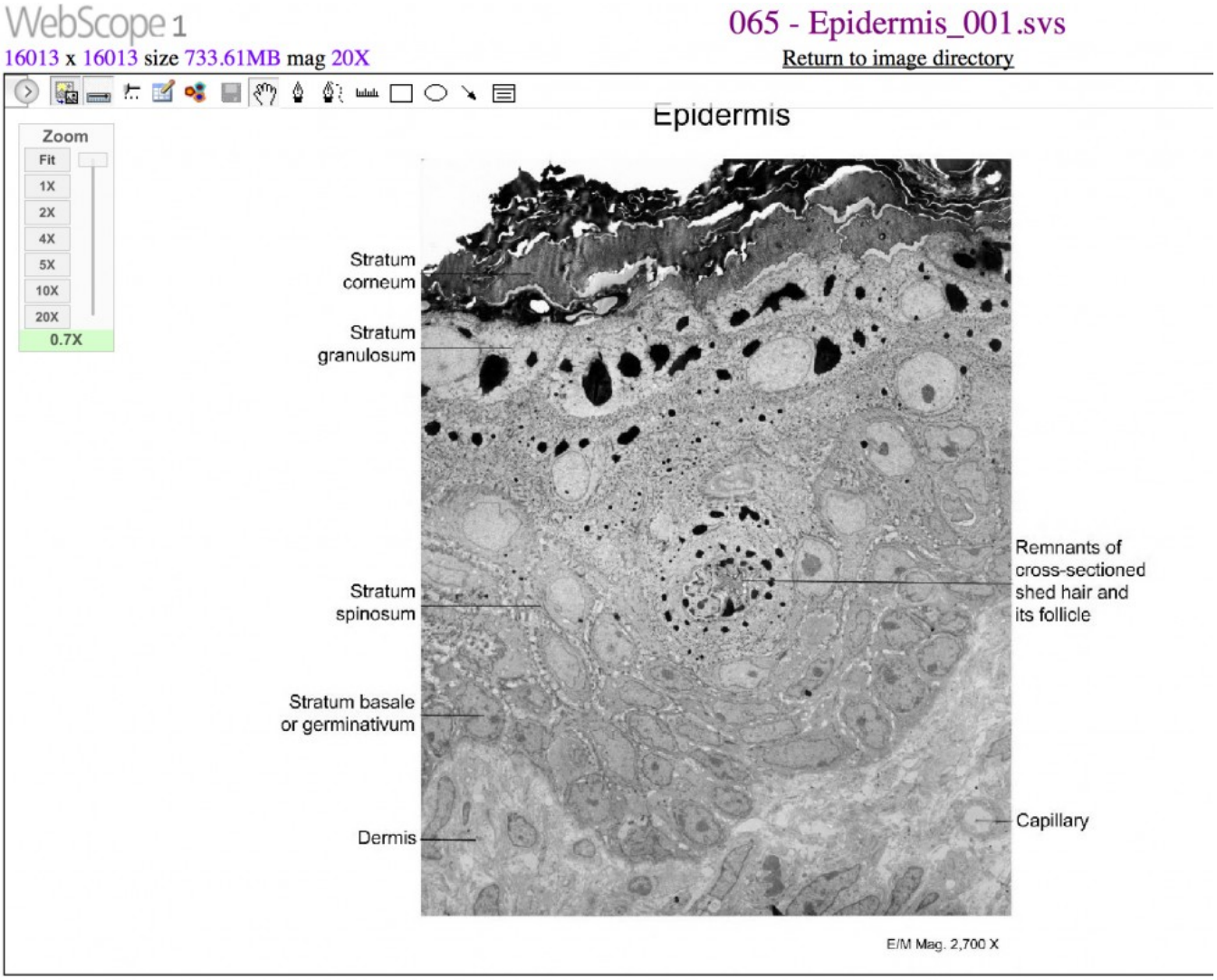


Figure 5. Cells of the Epidermis. *The cells in the different layers of the epidermis originate from basal cells located in the stratum basale, yet the cells of each layer are distinctively different. EM × 2700. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

View the University of Michigan WebScope to explore the tissue sample in greater detail. If you zoom on the cells at the outermost layer of this section of skin, what do you notice about the cells?

The keratinocytes in the stratum spinosum begin the synthesis of keratin and release a water-repelling glycolipid that helps prevent water loss from the body, making the skin relatively waterproof. As new keratinocytes are

produced atop the stratum basale, the keratinocytes of the stratum spinosum are pushed into the stratum granulosum.

Stratum Granulosum

The **stratum granulosum** has a grainy appearance due to further changes to the keratinocytes as they are pushed from the stratum spinosum. The cells (three to five layers deep) become flatter, their cell membranes thicken, and they generate large amounts of the proteins keratin, which is fibrous, and **keratohyalin**, which accumulates as lamellar granules within the cells (see Figure 4). These two proteins make up the bulk of the keratinocyte mass in the stratum granulosum and give the layer its grainy appearance. The nuclei and other cell organelles disintegrate as the cells die, leaving behind the keratin, keratohyalin, and cell membranes that will form the stratum lucidum, the stratum corneum, and the accessory structures of hair and nails.

Stratum Lucidum

The **stratum lucidum** is a smooth, seemingly translucent layer of the epidermis located just above the stratum granulosum and below the stratum corneum. This thin layer of cells is found only in the thick skin of the palms, soles, and digits. The keratinocytes that compose the stratum lucidum are dead and flattened (see Figure 4). These cells are densely packed with **eleiden**, a clear protein rich in lipids, derived from keratohyalin, which gives these cells their transparent (i.e., lucid) appearance and provides a barrier to water.

Stratum Corneum

The **stratum corneum** is the most superficial layer of the epidermis and is the layer exposed to the outside environment (see Figure 4). The increased keratinization (also called cornification) of the cells in this layer gives it its name. There are usually 15 to 30 layers of cells in the stratum corneum. This dry, dead layer helps prevent the penetration of microbes and the dehydration of underlying tissues, and provides a mechanical protection against abrasion for the more delicate, underlying layers. Cells in this layer are shed periodically and are replaced by cells pushed up from the stratum granulosum (or stratum lucidum in the case of the palms and soles of feet). The entire layer is replaced during a period of about 4 weeks. Cosmetic procedures, such as microdermabrasion, help remove some of the dry, upper layer and aim to keep the skin looking “fresh” and healthy.

Dermis

The **dermis** might be considered the “core” of the integumentary system (*derma–* = “skin”), as distinct from the **epidermis** (*epi–* = “upon” or “over”) and **hypodermis** (*hypo–* = “below”). It contains blood and lymph vessels, nerves, and other structures, such as hair follicles and sweat glands. The dermis is made of two layers of connective tissue that compose an interconnected mesh of elastin and collagenous fibers, produced by fibroblasts (Figure 6).

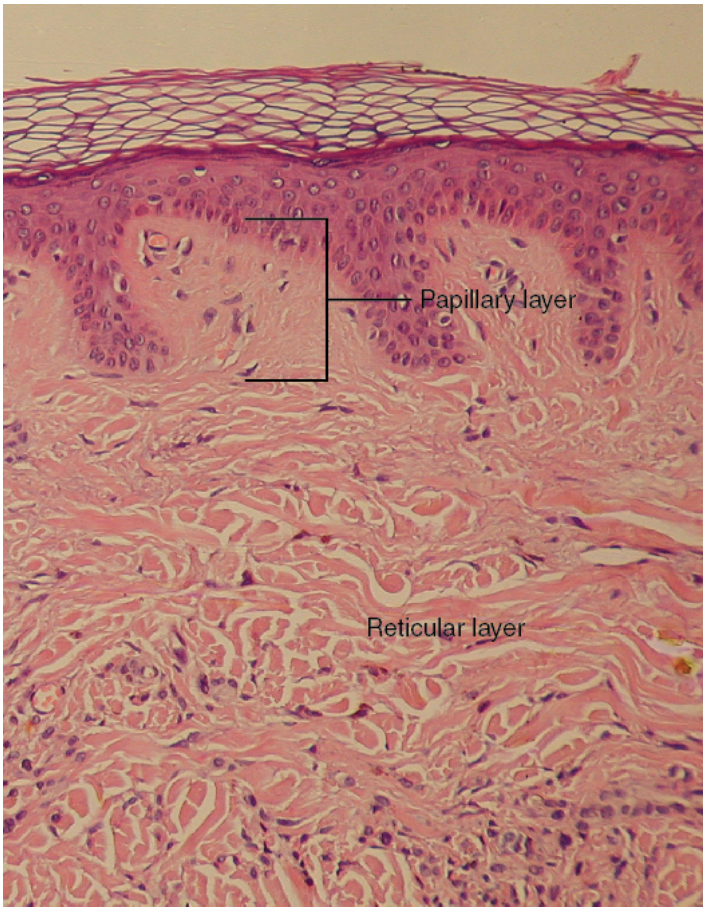


Figure 6. Layers of the Dermis. *This stained slide shows the two components of the dermis—the papillary layer and the reticular layer. Both are made of connective tissue with fibers of collagen extending from one to the other, making the border between the two somewhat indistinct. The dermal papillae extending into the epidermis belong to the papillary layer, whereas the dense collagen fiber bundles below belong to the reticular layer. LM × 10. (credit: modification of work by “kilbad”/Wikimedia Commons)*

Papillary Layer

The **papillary layer** is made of loose, areolar connective tissue, which means the collagen and elastin fibers of this layer form a loose mesh. This superficial layer of the dermis projects into the stratum basale of the epidermis to form finger-like dermal papillae (see Figure 6). Within the papillary layer are fibroblasts, a small number of fat cells (adipocytes), and an abundance of small blood vessels. In addition, the papillary layer contains phagocytes, defensive cells that help fight bacteria or other infections that have breached the skin. This layer also contains lymphatic capillaries, nerve fibers, and touch receptors called the Meissner corpuscles.

Reticular Layer

Underlying the papillary layer is the much thicker **reticular layer**, composed of dense, irregular connective tissue. This layer is well vascularized and has a rich sensory and sympathetic nerve supply. The reticular layer appears reticulated (net-like) due to a tight meshwork of fibers. **Elastin fibers** provide some elasticity to the skin, enabling movement. Collagen fibers provide structure and tensile strength, with strands of collagen extending into both the papillary layer and the hypodermis. In addition, collagen binds water to keep the skin hydrated. Collagen injections and Retin-A creams help restore skin turgor by either introducing collagen externally or stimulating blood flow and repair of the dermis, respectively.

Hypodermis

The **hypodermis** (also called the subcutaneous layer or superficial fascia) is a layer directly below the dermis and serves to connect the skin to the underlying fascia (fibrous tissue) of the bones and muscles. It is not strictly a part of the skin, although the border between the hypodermis and dermis can be difficult to distinguish. The hypodermis consists of well-vascularized, loose, areolar connective tissue and adipose tissue, which functions as a mode of fat storage and provides insulation and cushioning for the integument.

Everyday Connection: Lipid Storage

The hypodermis is home to most of the fat that concerns people when they are trying to keep their weight under control. Adipose tissue present in the hypodermis consists of fat-storing cells called adipocytes. This stored fat can serve as an energy reserve, insulate the body to prevent heat loss, and act as a cushion to protect underlying structures from trauma.

Where the fat is deposited and accumulates within the hypodermis depends on hormones (testosterone, estrogen, insulin, glucagon, leptin, and others), as well as genetic factors. Fat distribution changes as our bodies mature and age. Men tend to accumulate fat in different areas (neck, arms, lower back, and abdomen) than do women (breasts, hips, thighs, and buttocks). The body mass index (BMI) is often used as a measure of fat, although this measure is, in fact, derived from a mathematical formula that compares body weight (mass) to height. Therefore, its accuracy as a health indicator can be called into question in individuals who are extremely physically fit.

In many animals, there is a pattern of storing excess calories as fat to be used in times when food is not readily available. In much of the developed world, insufficient exercise coupled with the ready availability and consumption of high-calorie foods have resulted in unwanted accumulations of adipose tissue in many people. Although periodic accumulation of excess fat may have provided an evolutionary advantage to our ancestors, who experienced unpredictable bouts of famine, it is now becoming chronic and considered a major health threat. Recent studies indicate that a distressing percentage of our population is overweight and/or clinically obese. Not only is this a problem for the individuals affected, but it also has a severe impact on our healthcare system. Changes in lifestyle, specifically in diet and exercise, are the best ways to control body fat accumulation, especially when it reaches levels that increase the risk of heart disease and diabetes.

Pigmentation

The color of skin is influenced by a number of pigments, including melanin, carotene, and hemoglobin. Recall that melanin is produced by cells called melanocytes, which are found scattered throughout the stratum basale of the epidermis. The melanin is transferred into the keratinocytes via a cellular vesicle called a **melanosome** (Figure 7).

Melanin occurs in two primary forms. Eumelanin exists as black and brown, whereas pheomelanin provides a red color. Dark-skinned individuals produce more melanin than those with pale skin. Exposure to the UV rays of the sun or a tanning salon causes melanin to be manufactured and built up in keratinocytes, as sun exposure stimulates keratinocytes to secrete chemicals that stimulate melanocytes. The accumulation of melanin in keratinocytes results in the darkening of the skin, or a tan. This increased melanin accumulation protects the DNA of epidermal cells from UV ray damage and the breakdown of folic acid, a nutrient necessary for our health and well-being. In contrast, too much melanin can interfere with the production of vitamin D, an important nutrient involved in calcium absorption. Thus, the amount of melanin present in our skin is dependent on a balance between available sunlight and folic acid destruction, and protection from UV radiation and vitamin D production.

It requires about 10 days after initial sun exposure for melanin synthesis to peak, which is why pale-skinned individuals tend to suffer sunburns of the epidermis initially. Dark-skinned individuals can also get sunburns, but are more protected than are pale-skinned individuals. Melanosomes are temporary structures that are eventually destroyed by fusion with lysosomes; this fact, along with melanin-filled keratinocytes in the stratum corneum sloughing off, makes tanning impermanent.

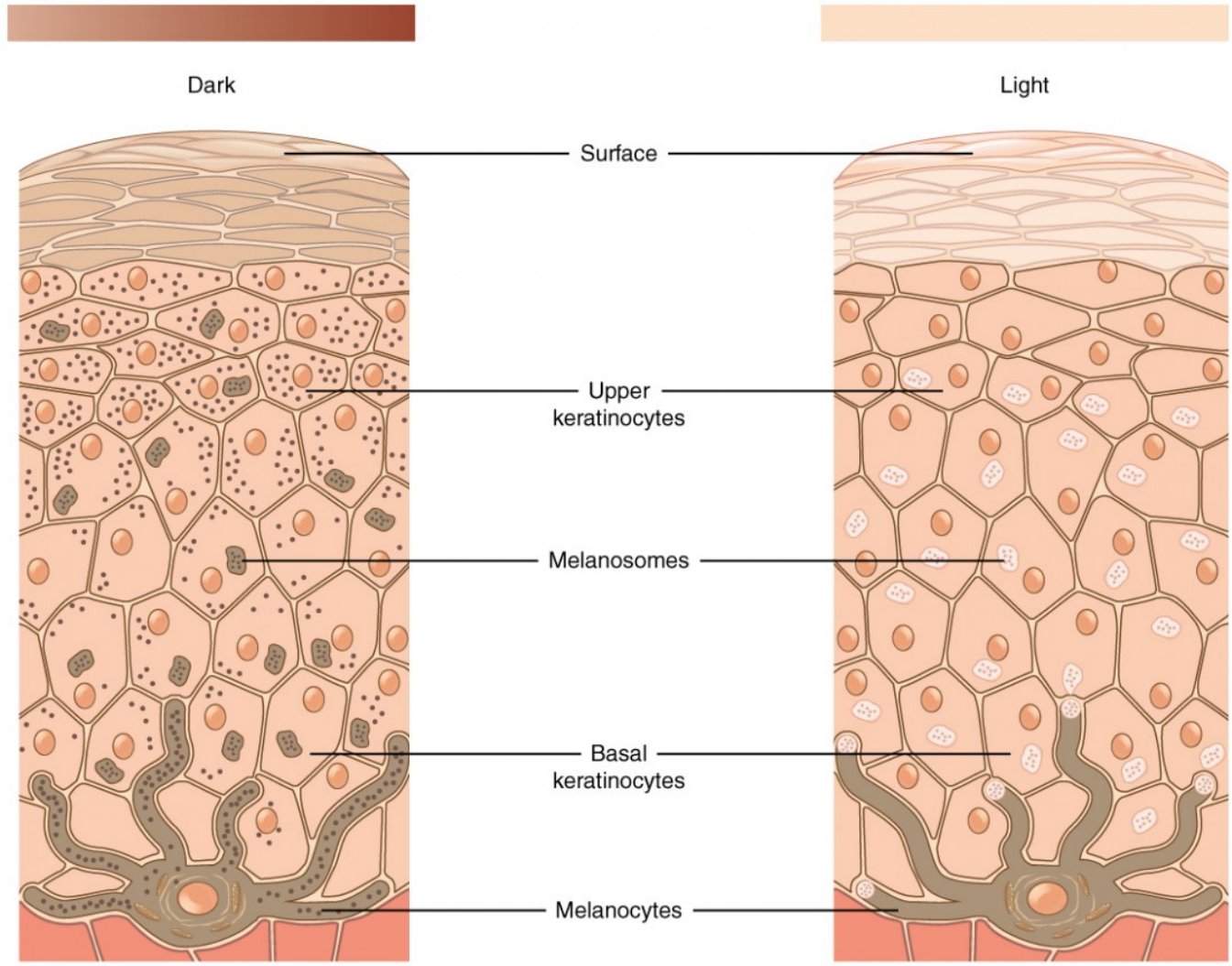


Figure 7. Skin Pigmentation. *The relative coloration of the skin depends of the amount of melanin produced by melanocytes in the stratum basale and taken up by keratinocytes.*

Too much sun exposure can eventually lead to wrinkling due to the destruction of the cellular structure of the skin, and in severe cases, can cause sufficient DNA damage to result in skin cancer. When there is an irregular accumulation of melanocytes in the skin, freckles appear. Moles are larger masses of melanocytes, and although most are benign, they should be monitored for changes that might indicate the presence of cancer (Figure 8).

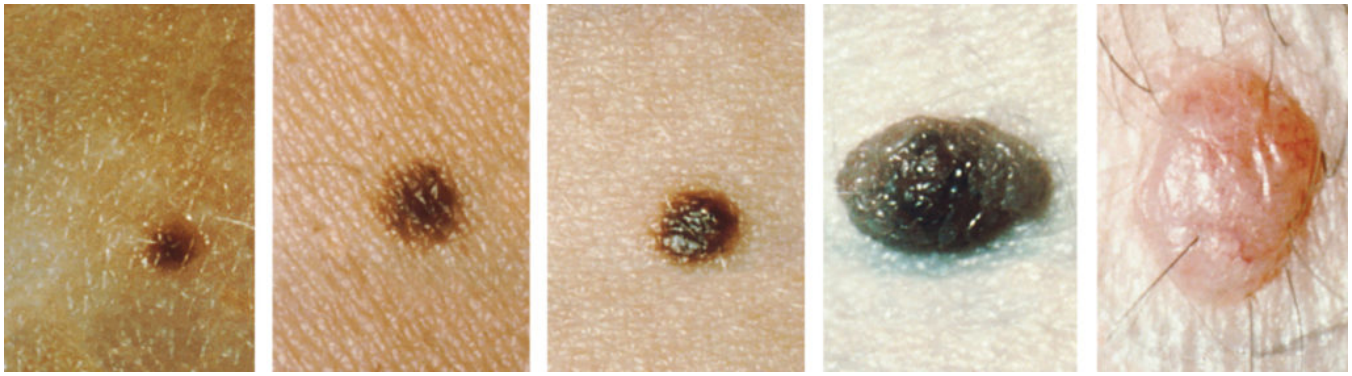


Figure 8. Moles range from benign accumulations of melanocytes to melanomas. These structures populate the landscape of our skin. (credit: the National Cancer Institute)

Key Takeaways

Disorders of the Integumentary System

The first thing a clinician sees is the skin, and so the examination of the skin should be part of any thorough physical examination. Most skin disorders are relatively benign, but a few, including melanomas, can be fatal if untreated. A couple of the more noticeable disorders, albinism and vitiligo, affect the appearance of the skin and its accessory organs. Although neither is fatal, it would be hard to claim that they are benign, at least to the individuals so afflicted.

Albinism is a genetic disorder that affects (completely or partially) the coloring of skin, hair, and eyes. The defect is primarily due to the inability of melanocytes to produce melanin. Individuals with albinism tend to appear white or very pale due to the lack of melanin in their skin and hair. Recall that melanin helps protect the skin from the harmful effects of UV radiation. Individuals with albinism tend to need more protection from UV radiation, as they are more prone to sunburns and skin cancer. They also tend to be more sensitive to light and have vision problems due to the lack of pigmentation on the retinal wall. Treatment of this disorder usually involves addressing the symptoms, such as limiting UV light exposure to the skin and eyes. In **vitiligo**, the melanocytes in certain areas lose their ability to produce melanin, possibly due to an autoimmune reaction. This leads to a loss of color in patches (Figure 9). Neither albinism nor vitiligo directly affects the lifespan of an individual.

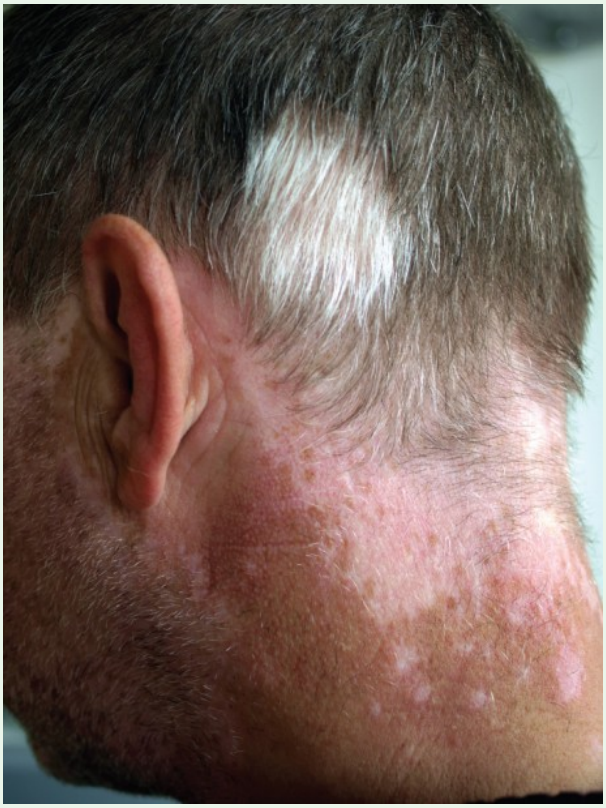


Figure 9. Vitiligo. *Individuals with vitiligo experience depigmentation that results in lighter colored patches of skin. The condition is especially noticeable on darker skin. (credit: Klaus D. Peter)*

Other changes in the appearance of skin coloration can be indicative of diseases associated with other body systems. Liver disease or liver cancer can cause the accumulation of bile and the yellow pigment bilirubin, leading to the skin appearing yellow or jaundiced (*jaune* is the French word for “yellow”). Tumors of the pituitary gland can result in the secretion of large amounts of melanocyte-stimulating hormone (MSH), which results in a darkening of the skin. Similarly, Addison’s disease can stimulate the release of excess amounts of adrenocorticotropic hormone (ACTH), which can give the skin a deep bronze color. A sudden drop in oxygenation can affect skin color, causing the skin to initially turn ashen (white). With a prolonged reduction in oxygen levels, dark red deoxyhemoglobin becomes dominant in the blood, making the skin appear blue, a condition referred to as cyanosis (*kyanos* is the Greek word for “blue”). This happens when the oxygen supply is restricted, as when someone is experiencing difficulty in breathing because of asthma or a heart attack. However, in these cases the effect on skin color has nothing do with the skin’s pigmentation.

This ABC video follows the story of a pair of fraternal African-American twins, one of whom is albino. Watch this video to learn about the challenges these children and their family face. Which ethnicities do you think are exempt from the possibility of albinism?

Self-Check Questions

Visit your course online to take a quiz to check your understanding of the Layers of the Skin:

ACCESSORY STRUCTURES OF THE SKIN

Learning Objectives

- Identify the accessory structures of the skin
- Describe the structure and function of hair and nails
- Describe the structure and function of sweat glands and sebaceous glands

Accessory structures of the skin include hair, nails, sweat glands, and sebaceous glands. These structures embryologically originate from the epidermis and can extend down through the dermis into the hypodermis.

Hair

Hair is a keratinous filament growing out of the epidermis. It is primarily made of dead, keratinized cells. Strands of hair originate in an epidermal penetration of the dermis called the **hair follicle**. The **hair shaft** is the part of the hair not anchored to the follicle, and much of this is exposed at the skin's surface. The rest of the hair, which is anchored in the follicle, lies below the surface of the skin and is referred to as the **hair root**. The hair root ends deep in the dermis at the **hair bulb**, and includes a layer of mitotically active basal cells called the **hair matrix**. The hair bulb surrounds the **hair papilla**, which is made of connective tissue and contains blood capillaries and nerve endings from the dermis (Figure 1).

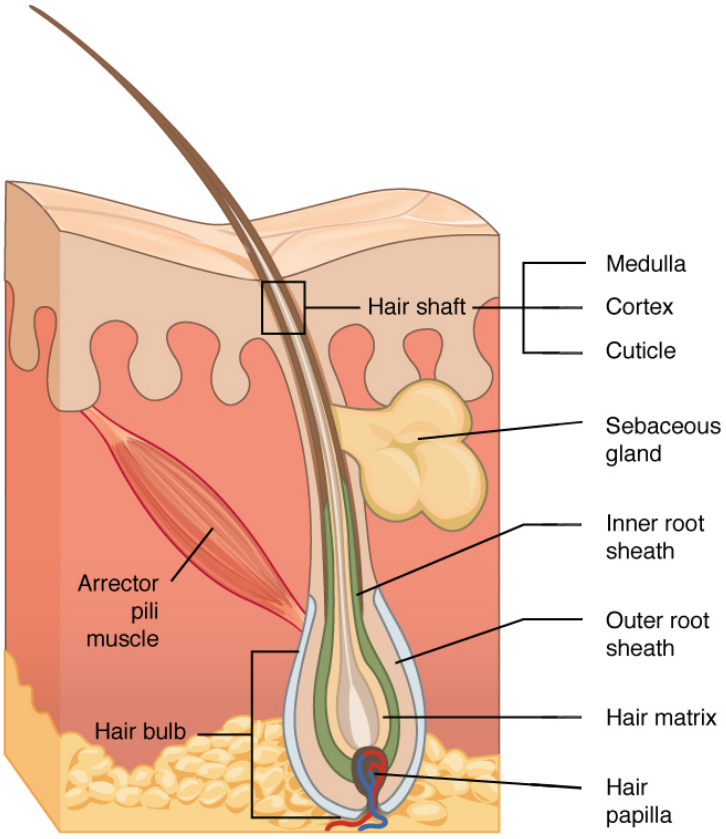


Figure 1. Hair follicles originate in the epidermis and have many different parts.

Just as the basal layer of the epidermis forms the layers of epidermis that get pushed to the surface as the dead skin on the surface sheds, the basal cells of the hair bulb divide and push cells outward in the hair root and shaft as the hair grows. The **medulla** forms the central core of the hair, which is surrounded by the **cortex**, a layer of compressed, keratinized cells that is covered by an outer layer of very hard, keratinized cells known as the **cuticle**. These layers are depicted in a longitudinal cross-section of the hair follicle (Figure 2), although not all hair has a medullary layer.

Hair texture (straight, curly) is determined by the shape and structure of the cortex, and to the extent that it is present, the medulla. The shape and structure of these layers are, in turn, determined by the shape of the hair follicle. Hair growth begins with the production of keratinocytes by the basal cells of the hair bulb. As new cells are deposited at the hair bulb, the hair shaft is pushed through the follicle toward the surface. Keratinization is completed as the cells are pushed to the skin surface to form the shaft of hair that is externally visible. The external hair is completely dead and composed entirely of keratin. For this reason, our hair does not have sensation. Furthermore, you can cut your hair or shave without damaging the hair structure because the cut is superficial. Most chemical hair removers also act superficially; however, electrolysis and yanking both attempt to destroy the hair bulb so hair cannot grow.

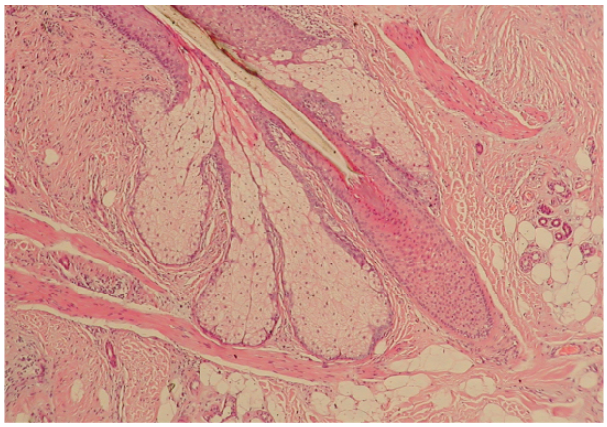


Figure 2. The slide shows a cross-section of a hair follicle. Basal cells of the hair matrix in the center differentiate into cells of the inner root sheath. Basal cells at the base of the hair root form the outer root sheath. LM × 4. (credit: modification of work by "kilbad"/Wikimedia Commons)

The wall of the hair follicle is made of three concentric layers of cells. The cells of the **internal root sheath** surround the root of the growing hair and extend just up to the hair shaft. They are derived from the basal cells of the hair matrix. The **external root sheath**, which is an extension of the epidermis, encloses the hair root. It is made of basal cells at the base of the hair root and tends to be more keratinous in the upper regions. The **glassy membrane** is a thick, clear connective tissue sheath covering the hair root, connecting it to the tissue of the dermis.

The hair follicle is made of multiple layers of cells that form from basal cells in the hair matrix and the hair root. Cells of the hair matrix divide and differentiate to form the layers of the hair. Watch this video to learn more about hair follicles.

Watch this video online: https://youtu.be/aLY4EzDXwSM

Hair serves a variety of functions, including protection, sensory input, thermoregulation, and communication. For example, hair on the head protects the skull from the sun. The hair in the nose and ears, and around the eyes (eyelashes) defends the body by trapping and excluding dust particles that may contain allergens and microbes. Hair of the eyebrows prevents sweat and other particles from dripping into and bothering the eyes. Hair also has a sensory function due to sensory innervation by a hair root plexus surrounding the base of each hair follicle. Hair is extremely sensitive to air movement or other disturbances in the environment, much more so than the skin surface. This feature is also useful for the detection of the presence of insects or other potentially damaging substances on the skin surface. Each hair root is connected to a smooth muscle called the **arrector pili** that contracts in response to nerve signals from the sympathetic nervous system, making the external hair shaft "stand up." The primary purpose for this is to trap a layer of air to add insulation. This is visible in humans as goose bumps and even more obvious in animals, such as when a frightened cat raises its fur. Of course, this is much more obvious in organisms with a heavier coat than most humans, such as dogs and cats.

Hair Growth

Hair grows and is eventually shed and replaced by new hair. This occurs in three phases. The first is the **anagen** phase, during which cells divide rapidly at the root of the hair, pushing the hair shaft up and out. The length of this phase is measured in years, typically from 2 to 7 years. The **catagen** phase lasts only 2 to 3 weeks, and marks a transition from the hair follicle's active growth. Finally, during the **telogen** phase, the hair follicle is at rest and no new growth occurs. At the end of this phase, which lasts about 2 to 4 months, another anagen phase begins. The basal cells in the hair matrix then produce a new hair follicle, which pushes the old hair out as the growth cycle repeats itself. Hair typically grows at the rate of 0.3 mm per day during the anagen phase. On average, 50 hairs are lost and replaced per day. Hair loss occurs if there is more hair shed than what is replaced and can happen due to hormonal or dietary changes. Hair loss can also result from the aging process, or the influence of hormones.

Hair Color

Similar to the skin, hair gets its color from the pigment melanin, produced by melanocytes in the hair papilla. Different hair color results from differences in the type of melanin, which is genetically determined. As a person ages, the melanin production decreases, and hair tends to lose its color and becomes gray and/or white.

Nails

The nail bed is a specialized structure of the epidermis that is found at the tips of our fingers and toes. The **nail body** is formed on the **nail bed**, and protects the tips of our fingers and toes as they are the farthest extremities and the parts of the body that experience the maximum mechanical stress (Figure 3).

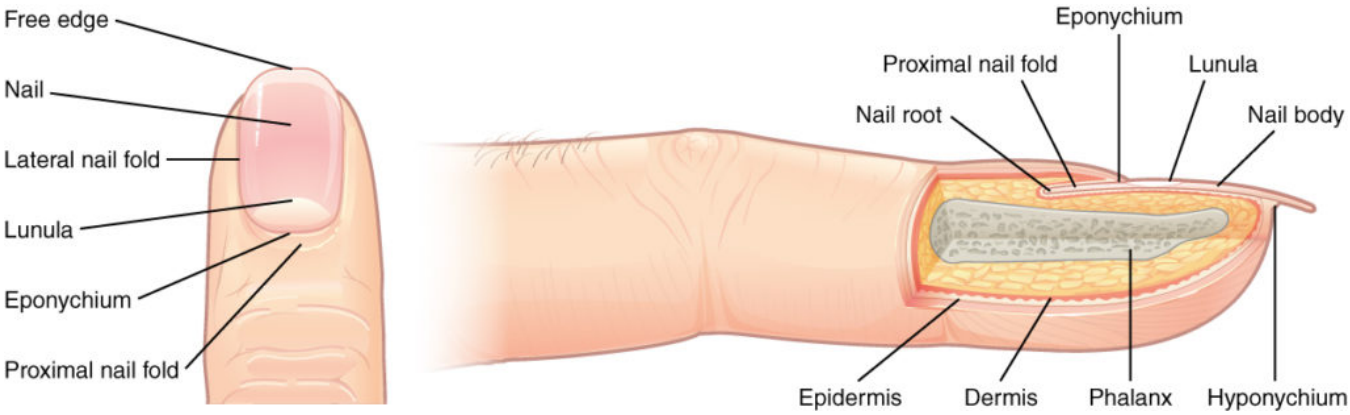


Figure 3. The nail is an accessory structure of the integumentary system.

In addition, the nail body forms a back-support for picking up small objects with the fingers. The nail body is composed of densely packed dead keratinocytes. The epidermis in this part of the body has evolved a specialized structure upon which nails can form. The nail body forms at the **nail root**, which has a matrix of proliferating cells from the stratum basale that enables the nail to grow continuously. The lateral **nail fold** overlaps the nail on the sides, helping to anchor the nail body. The nail fold that meets the proximal end of the nail body forms the **nail cuticle**, also called the **eponychium**. The nail bed is rich in blood vessels, making it appear pink, except at the base, where a thick layer of epithelium over the nail matrix forms a crescent-shaped region called the **lunula** (the "little moon"). The area beneath the free edge of the nail, furthest from the cuticle, is called the **hyponychium**. It consists of a thickened layer of stratum corneum.

Nails are accessory structures of the integumentary system. Watch this video to learn more about the origin and growth of fingernails.

Watch this video online: https://youtu.be/TxZWOXgnt3A

Sweat Glands

When the body becomes warm, **sudoriferous glands** produce sweat to cool the body. Sweat glands develop from epidermal projections into the dermis and are classified as merocrine glands; that is, the secretions are excreted by exocytosis through a duct without affecting the cells of the gland. There are two types of sweat glands, each secreting slightly different products.

An **eccrine sweat gland** is type of gland that produces a hypotonic sweat for thermoregulation. These glands are found all over the skin's surface, but are especially abundant on the palms of the hand, the soles of the feet, and the forehead (Figure 4). They are coiled glands lying deep in the dermis, with the duct rising up to a pore on the skin surface, where the sweat is released. This type of sweat, released by exocytosis, is hypotonic and composed mostly of water, with some salt, antibodies, traces of metabolic waste, and dermicidin, an antimicrobial peptide. Eccrine glands are a primary component of thermoregulation in humans and thus help to maintain homeostasis.

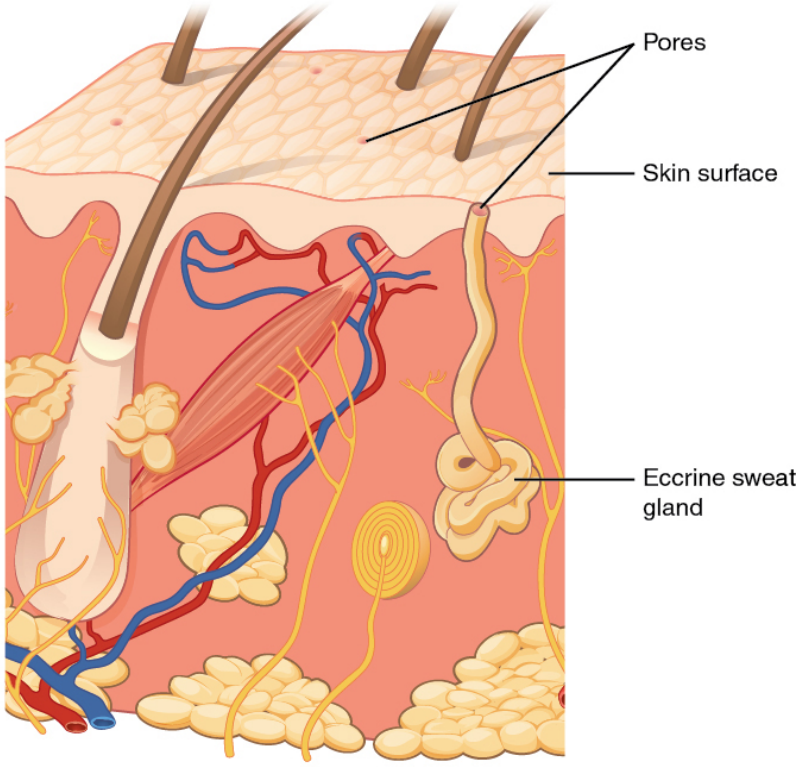


Figure 4. Eccrine glands are coiled glands in the dermis that release sweat that is mostly water.

An **apocrine sweat gland** is usually associated with hair follicles in densely hairy areas, such as armpits and genital regions. Apocrine sweat glands are larger than eccrine sweat glands and lie deeper in the dermis, sometimes even reaching the hypodermis, with the duct normally emptying into the hair follicle. In addition to water and salts, apocrine sweat includes organic compounds that make the sweat thicker and subject to bacterial decomposition and subsequent smell. The release of this sweat is under both nervous and hormonal control, and plays a role in the poorly understood human pheromone response. Most commercial antiperspirants use an aluminum-based compound as their primary active ingredient to stop sweat. When the antiperspirant enters the sweat gland duct, the aluminum-based compounds precipitate due to a change in pH and form a physical block in the duct, which prevents sweat from coming out of the pore.

Sweating regulates body temperature. The composition of the sweat determines whether body odor is a byproduct of sweating. Visit this link to learn more about sweating and body odor.

Sebaceous Glands

A **sebaceous gland** is a type of oil gland that is found all over the body and helps to lubricate and waterproof the skin and hair. Most sebaceous glands are associated with hair follicles. They generate and excrete **sebum**, a mixture of lipids, onto the skin surface, thereby naturally lubricating the dry and dead layer of keratinized cells of the stratum corneum, keeping it pliable. The fatty acids of sebum also have antibacterial properties, and prevent water loss from the skin in low-humidity environments. The secretion of sebum is stimulated by hormones, many of which do not become active until puberty. Thus, sebaceous glands are relatively inactive during childhood.

Self-Check Questions

Visit your course online to take a quiz to check your understanding of the Accessory Structures of the Skin:

FUNCTIONS OF THE INTEGUMENTARY SYSTEM

Learning Objectives

- Describe the different functions of the skin and the structures that enable them
- Explain how the skin helps maintain body temperature

The skin and accessory structures perform a variety of essential functions, such as protecting the body from invasion by microorganisms, chemicals, and other environmental factors; preventing dehydration; acting as a sensory organ; modulating body temperature and electrolyte balance; and synthesizing vitamin D. The underlying hypodermis has important roles in storing fats, forming a "cushion" over underlying structures, and providing insulation from cold temperatures.

Protection

The skin protects the rest of the body from the basic elements of nature such as wind, water, and UV sunlight. It acts as a protective barrier against water loss, due to the presence of layers of keratin and glycolipids in the stratum corneum. It also is the first line of defense against abrasive activity due to contact with grit, microbes, or harmful chemicals. Sweat excreted from sweat glands deters microbes from over-colonizing the skin surface by generating dermicidin, which has antibiotic properties.

Everyday Connection: Tattoos and Piercings

The word "armor" evokes several images. You might think of a Roman centurion or a medieval knight in a suit of armor. The skin, in its own way, functions as a form of armor—body armor. It provides a barrier between your vital, life-sustaining organs and the influence of outside elements that could potentially damage them.

For any form of armor, a breach in the protective barrier poses a danger. The skin can be breached when a child skins a knee or an adult has blood drawn—one is accidental and the other medically necessary. However, you also breach this barrier when you choose to "accessorize" your skin with a tattoo or body piercing. Because the needles involved in producing body art and piercings must penetrate the skin, there are dangers associated with the practice. These include allergic reactions; skin infections; blood-borne diseases, such as tetanus, hepatitis C, and hepatitis D; and the growth of scar tissue. Despite the risk, the practice of piercing the skin for decorative purposes has become increasingly popular. According to the American Academy of Dermatology, 24 percent of people from ages 18 to 50 have a tattoo.

Tattooing has a long history, dating back thousands of years ago. The dyes used in tattooing typically derive from metals. A person with tattoos should be cautious when having a magnetic resonance imaging (MRI) scan because an MRI machine uses powerful magnets to create images of the soft tissues of the body, which could react with the metals contained in the tattoo dyes. Read this article to learn more about tattooing.

Sensory Function

The fact that you can feel an ant crawling on your skin, allowing you to flick it off before it bites, is because the skin, and especially the hairs projecting from hair follicles in the skin, can sense changes in the environment. The hair root plexus surrounding the base of the hair follicle senses a disturbance, and then transmits the information to the central nervous system (brain and spinal cord), which can then respond by activating the skeletal muscles of your eyes to see the ant and the skeletal muscles of the body to act against the ant.

The skin acts as a sense organ because the epidermis, dermis, and the hypodermis contain specialized sensory nerve structures that detect touch, surface temperature, and pain. These receptors are more concentrated on the tips of the fingers, which are most sensitive to touch, especially the **Meissner corpuscle** (tactile corpuscle) (Figure 1), which responds to light touch, and the **Pacinian corpuscle** (lamellated corpuscle), which responds to vibration. Merkel cells, seen scattered in the stratum basale, are also touch receptors. In addition to these specialized receptors, there are sensory nerves connected to each hair follicle, pain and temperature receptors scattered throughout the skin, and motor nerves innervate the arrector pili muscles and glands. This rich innervation helps us sense our environment and react accordingly.

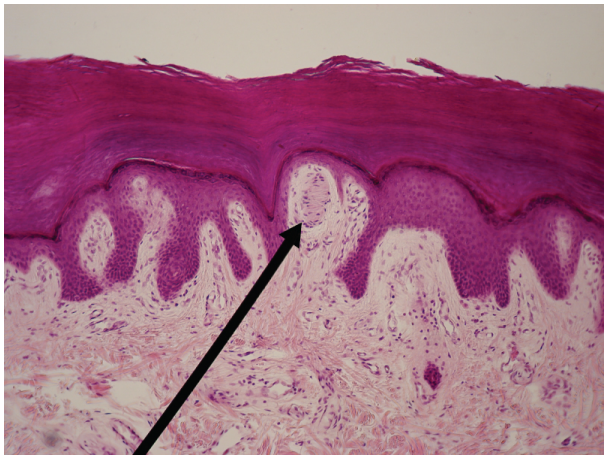


Figure 1. In this micrograph of a skin cross-section, you can see a Meissner corpuscle (arrow), a type of touch receptor located in a dermal papilla adjacent to the basement membrane and stratum basale of the overlying epidermis. LM × 100. (credit: "Wbensmith"/Wikimedia Commons)

Thermoregulation

The integumentary system helps regulate body temperature through its tight association with the sympathetic nervous system, the division of the nervous system involved in our fight-or-flight responses. The sympathetic nervous system is continuously monitoring body temperature and initiating appropriate motor responses. Recall that sweat glands, accessory structures to the skin, secrete water, salt, and other substances to cool the body when it becomes warm. Even when the body does not appear to be noticeably sweating, approximately 500 mL of sweat (insensible perspiration) are secreted a day. If the body becomes excessively warm due to high temperatures, vigorous activity (Figure 2), or a combination of the two, sweat glands will be stimulated by the sympathetic nervous system to produce large amounts of sweat, as much as 0.7 to 1.5 L per hour for an active person. When the sweat evaporates from the skin surface, the body is cooled as body heat is dissipated.

In addition to sweating, arterioles in the dermis dilate so that excess heat carried by the blood can dissipate through the skin and into the surrounding environment (Figure 2). This accounts for the skin redness that many people experience when exercising.

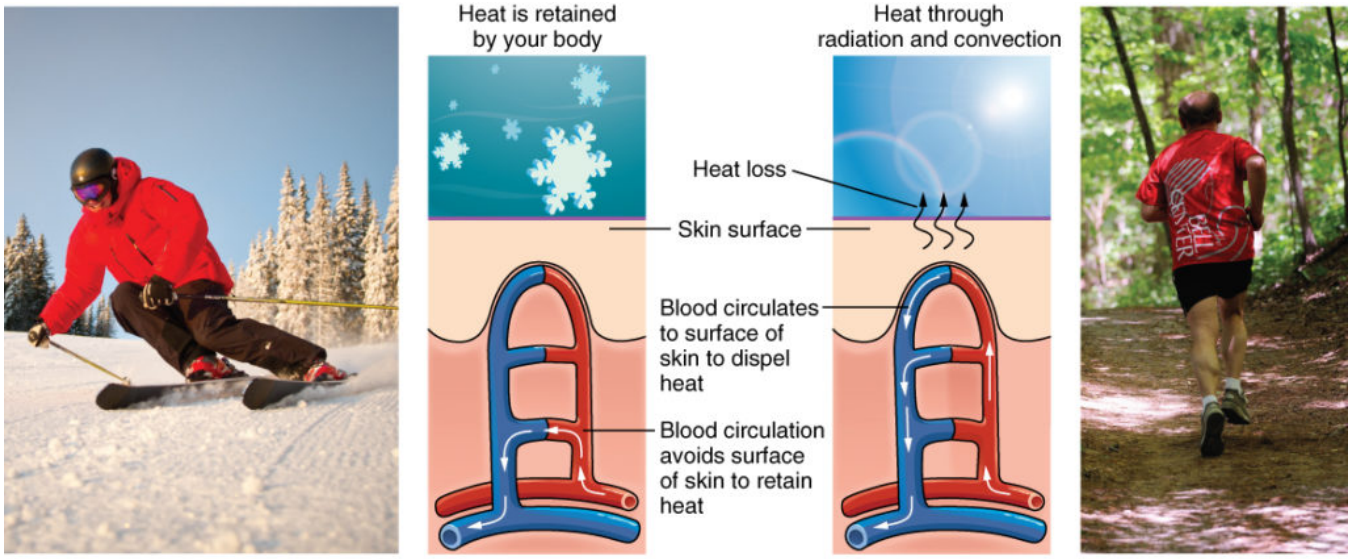


Figure 2. During strenuous physical activities, such as skiing (a) or running (c), the dermal blood vessels dilate and sweat secretion increases (b). These mechanisms prevent the body from overheating. In contrast, the dermal blood vessels constrict to minimize heat loss in response to low temperatures (b). (credit a: "Trysil"/flickr; credit c: Ralph Daily)

When body temperatures drop, the arterioles constrict to minimize heat loss, particularly in the ends of the digits and tip of the nose. This reduced circulation can result in the skin taking on a whitish hue. Although the temperature of the skin drops as a result, passive heat loss is prevented, and internal organs and structures remain warm. If the temperature of the skin drops too much (such as environmental temperatures below freezing), the conservation of body core heat can result in the skin actually freezing, a condition called frostbite.

Aging and the Integumentary System

All systems in the body accumulate subtle and some not-so-subtle changes as a person ages. Among these changes are reductions in cell division, metabolic activity, blood circulation, hormonal levels, and muscle strength (Figure 3). In the skin, these changes are reflected in decreased mitosis in the stratum basale, leading to a thinner epidermis. The dermis, which is responsible for the elasticity and resilience of the skin, exhibits a reduced ability to regenerate, which leads to slower wound healing. The hypodermis, with its fat stores, loses structure due to the reduction and redistribution of fat, which in turn contributes to the thinning and sagging of skin.

Figure 3. Generally, skin, especially on the face and hands, starts to display the first noticeable signs of aging, as it loses its elasticity over time. (credit: Janet Ramsden)

The accessory structures also have lowered activity, generating thinner hair and nails, and reduced amounts of sebum and sweat. A reduced sweating ability can cause some elderly to be intolerant to extreme heat. Other cells in the skin, such as melanocytes and dendritic cells, also become less active, leading to a paler skin tone and lowered immunity. Wrinkling of the skin occurs due to breakdown of its structure, which results from decreased collagen and elastin production in the dermis, weakening of muscles lying under the skin, and the inability of the skin to retain adequate moisture.

Many anti-aging products can be found in stores today. In general, these products try to rehydrate the skin and thereby fill out the wrinkles, and some stimulate skin growth using hormones and growth factors.

Additionally, invasive techniques include collagen injections to plump the tissue and injections of BOTOX® (the name brand of the botulinum neurotoxin) that paralyze the muscles that crease the skin and cause wrinkling.

Vitamin D Synthesis

The epidermal layer of human skin synthesizes **vitamin D** when exposed to UV radiation. In the presence of sunlight, a form of vitamin D_3 called cholecalciferol is synthesized from a derivative of the steroid cholesterol in the skin. The liver converts cholecalciferol to calcidiol, which is then converted to calcitriol (the active chemical form of the vitamin) in the kidneys. Vitamin D is essential for normal absorption of calcium and phosphorous, which are required for healthy bones. The absence of sun exposure can lead to a lack of vitamin D in the body, leading to a condition called **rickets**, a painful condition in children where the bones are misshapen due to a lack of calcium, causing bowleggedness. Elderly individuals who suffer from vitamin D deficiency can develop a condition called osteomalacia, a softening of the bones. In present day society, vitamin D is added as a supplement to many foods, including milk and orange juice, compensating for the need for sun exposure.

In addition to its essential role in bone health, vitamin D is essential for general immunity against bacterial, viral, and fungal infections. Recent studies are also finding a link between insufficient vitamin D and cancer.

Self-Check Questions

Visit your course online to take a quiz to check your understanding of the Functions of the Integumentary System:

DISEASES, DISORDERS, AND INJURIES

Learning Objectives

- Describe several different diseases and disorders of the skin
- Describe the effect of injury to the skin and the process of healing

The integumentary system is susceptible to a variety of diseases, disorders, and injuries. These range from annoying but relatively benign bacterial or fungal infections that are categorized as disorders, to skin cancer and severe burns, which can be fatal. In this section, you will learn several of the most common skin conditions.

Diseases

One of the most talked about diseases is skin cancer. Cancer is a broad term that describes diseases caused by abnormal cells in the body dividing uncontrollably. Most cancers are identified by the organ or tissue in which the cancer originates. One common form of cancer is skin cancer. The Skin Cancer Foundation reports that one in five Americans will experience some type of skin cancer in their lifetime. The degradation of the ozone layer in the atmosphere and the resulting increase in exposure to UV radiation has contributed to its rise. Overexposure to UV radiation damages DNA, which can lead to the formation of cancerous lesions. Although melanin offers some protection against DNA damage from the sun, often it is not enough. The fact that cancers can also occur on areas of the body that are normally not exposed to UV radiation suggests that there are additional factors that can lead to cancerous lesions.

In general, cancers result from an accumulation of DNA mutations. These mutations can result in cell populations that do not die when they should and uncontrolled cell proliferation that leads to tumors. Although many tumors are benign (harmless), some produce cells that can mobilize and establish tumors in other organs of the body; this process is referred to as **metastasis**. Cancers are characterized by their ability to metastasize.

Basal Cell Carcinoma

Basal cell carcinoma is a form of cancer that affects the mitotically active stem cells in the stratum basale of the epidermis. It is the most common of all cancers that occur in the United States and is frequently found on the head, neck, arms, and back, which are areas that are most susceptible to long-term sun exposure. Although UV rays are the main culprit, exposure to other agents, such as radiation and arsenic, can also lead to this type of cancer. Wounds on the skin due to open sores, tattoos, burns, etc. may be predisposing factors as well. Basal cell carcinomas start in the stratum basale and usually spread along this boundary. At some point, they begin to grow toward the surface and become an uneven patch, bump, growth, or scar on the skin surface (Figure 1). Like most cancers, basal cell carcinomas respond best to treatment when caught early. Treatment options include surgery, freezing (cryosurgery), and topical ointments (Mayo Clinic 2012).

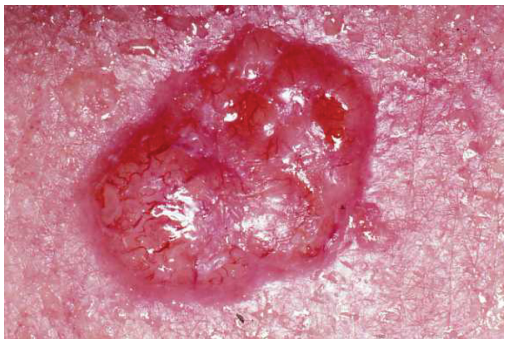


Figure 1. Basal cell carcinoma can take several different forms. Similar to other forms of skin cancer, it is readily cured if caught early and treated. (credit: John Hendrix, MD)

Squamous Cell Carcinoma

Squamous cell carcinoma is a cancer that affects the keratinocytes of the stratum spinosum and presents as lesions commonly found on the scalp, ears, and hands (Figure 2). It is the second most common skin cancer. The American Cancer Society reports that two of 10 skin cancers are squamous cell carcinomas, and it is more aggressive than basal cell carcinoma. If not removed, these carcinomas can metastasize. Surgery and radiation are used to cure squamous cell carcinoma.

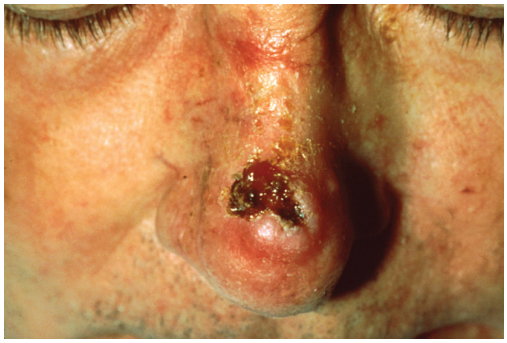


Figure 2. Squamous cell carcinoma presents here as a lesion on an individual's nose. (credit: the National Cancer Institute)

Melanoma

A **melanoma** is a cancer characterized by the uncontrolled growth of melanocytes, the pigment-producing cells in the epidermis. Typically, a melanoma develops from a mole. It is the most fatal of all skin cancers, as it is highly metastatic and can be difficult to detect before it has spread to other organs. Melanomas usually appear as asymmetrical brown and black patches with uneven borders and a raised surface (Figure 3). Treatment typically involves surgical excision and immunotherapy.

Doctors often give their patients the following ABCDE mnemonic to help with the diagnosis of early-stage melanoma. If you observe a mole on your body displaying these signs, consult a doctor.

- Asymmetry – the two sides are not symmetrical
- Borders – the edges are irregular in shape
- Color – the color is varied shades of brown or black
- Diameter – it is larger than 6 mm (0.24 in)
- Evolving – its shape has changed

Some specialists cite the following additional signs for the most serious form, nodular melanoma:

- Elevated – it is raised on the skin surface
- Firm – it feels hard to the touch
- Growing – it is getting larger

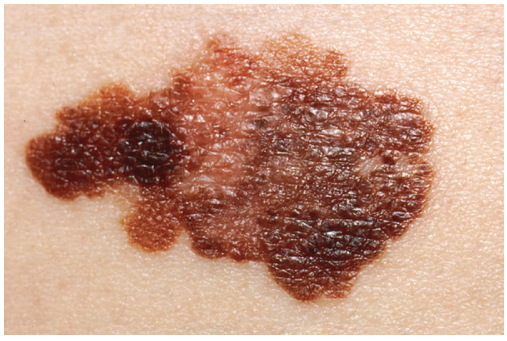


Figure 3. Melanomas typically present as large brown or black patches with uneven borders and a raised surface. (credit: the National Cancer Institute)

Skin Disorders

Two common skin disorders are eczema and acne. Eczema is an inflammatory condition and occurs in individuals of all ages. Acne involves the clogging of pores, which can lead to infection and inflammation, and is often seen in adolescents. Other disorders, not discussed here, include seborrheic dermatitis (on the scalp), psoriasis, cold sores, impetigo, scabies, hives, and warts.

Eczema

Eczema is an allergic reaction that manifests as dry, itchy patches of skin that resemble rashes (Figure 4). It may be accompanied by swelling of the skin, flaking, and in severe cases, bleeding. Many who suffer from eczema have antibodies against dust mites in their blood, but the link between eczema and allergy to dust mites has not been proven. Symptoms are usually managed with moisturizers, corticosteroid creams, and immunosuppressants.

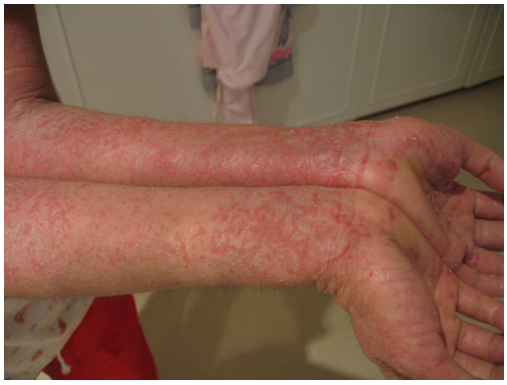


Figure 4. Eczema is a common skin disorder that presents as a red, flaky rash. (credit: "Jambula"/Wikimedia Commons)

Acne

Acne is a skin disturbance that typically occurs on areas of the skin that are rich in sebaceous glands (face and back). It is most common along with the onset of puberty due to associated hormonal changes, but can also occur in infants and continue into adulthood. Hormones, such as androgens, stimulate the release of sebum. An overproduction and accumulation of sebum along with keratin can block hair follicles. This plug is initially white. The sebum, when oxidized by exposure to air, turns black. Acne results from infection by acne-causing bacteria (*Propionibacterium* and *Staphylococcus*), which can lead to redness and potential scarring due to the natural wound healing process (Figure 5).

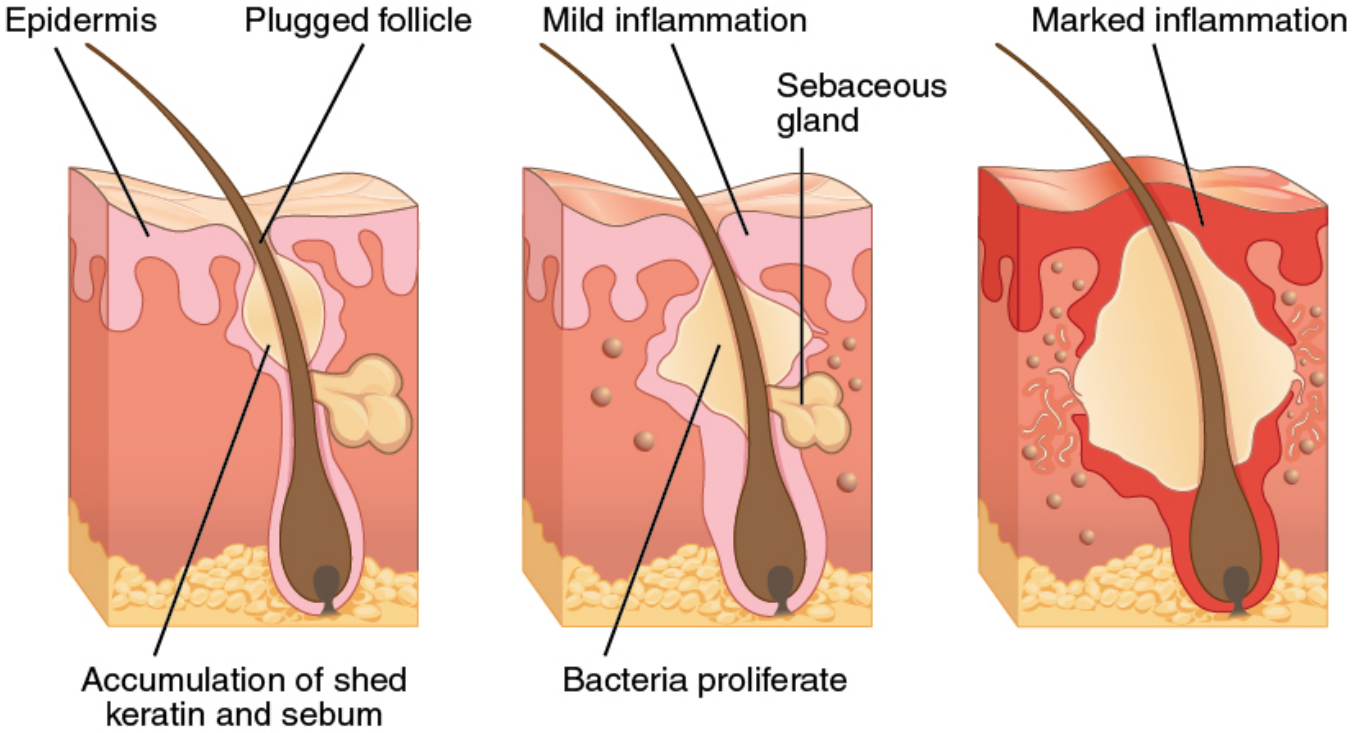


Figure 5. Acne is a result of over-productive sebaceous glands, which leads to formation of blackheads and inflammation of the skin.

Career Connection: Dermatologist

Have you ever had a skin rash that did not respond to over-the-counter creams, or a mole that you were concerned about? Dermatologists help patients with these types of problems and more, on a daily basis. Dermatologists are medical doctors who specialize in diagnosing and treating skin disorders. Like all medical doctors, dermatologists earn a medical degree and then complete several years of residency training. In addition, dermatologists may then participate in a dermatology fellowship or complete additional, specialized training in a dermatology practice. If practicing in the United States, dermatologists must pass the United States Medical Licensing Exam (USMLE), become licensed in their state of practice, and be certified by the American Board of Dermatology.

Most dermatologists work in a medical office or private-practice setting. They diagnose skin conditions and rashes, prescribe oral and topical medications to treat skin conditions, and may perform simple procedures, such as mole or wart removal. In addition, they may refer patients to an oncologist if skin cancer that has metastasized is suspected. Recently, cosmetic procedures have also become a prominent part of dermatology. Botox injections, laser treatments, and collagen and dermal filler injections are popular among patients, hoping to reduce the appearance of skin aging.

Dermatology is a competitive specialty in medicine. Limited openings in dermatology residency programs mean that many medical students compete for a few select spots. Dermatology is an appealing specialty to many prospective doctors, because unlike emergency room physicians or surgeons, dermatologists generally do not have to work excessive hours or be “on-call” weekends and holidays. Moreover, the popularity of cosmetic dermatology has made it a growing field with many lucrative opportunities. It is not unusual for dermatology clinics to market themselves exclusively as cosmetic dermatology centers, and for dermatologists to specialize exclusively in these procedures.

Consider visiting a dermatologist to talk about why he or she entered the field and what the field of dermatology is like.

Injuries

Because the skin is the part of our bodies that meets the world most directly, it is especially vulnerable to injury. Injuries include burns and wounds, as well as scars and calluses. They can be caused by sharp objects, heat, or excessive pressure or friction to the skin.

Skin injuries set off a healing process that occurs in several overlapping stages. The first step to repairing damaged skin is the formation of a blood clot that helps stop the flow of blood and scabs over with time. Many different types of cells are involved in wound repair, especially if the surface area that needs repair is extensive. Before the basal stem cells of the stratum basale can recreate the epidermis, fibroblasts mobilize and divide rapidly to repair the damaged tissue by collagen deposition, forming granulation tissue. Blood capillaries follow the fibroblasts and help increase blood circulation and oxygen supply to the area. Immune cells, such as macrophages, roam the area and engulf any foreign matter to reduce the chance of infection.

Burns

A burn results when the skin is damaged by intense heat, radiation, electricity, or chemicals. The damage results in the death of skin cells, which can lead to a massive loss of fluid. Dehydration, electrolyte imbalance, and renal and circulatory failure follow, which can be fatal. Burn patients are treated with intravenous fluids to offset dehydration, as well as intravenous nutrients that enable the body to repair tissues and replace lost proteins. Another serious threat to the lives of burn patients is infection. Burned skin is extremely susceptible to bacteria and other pathogens, due to the loss of protection by intact layers of skin.

Burns are sometimes measured in terms of the size of the total surface area affected. This is referred to as the “rule of nines,” which associates specific anatomical areas with a percentage that is a factor of nine (Figure 6). Burns are also classified by the degree of their severity. A **first-degree burn** is a superficial burn that affects only the epidermis. Although the skin may be painful and swollen, these burns typically heal on their own within a few days. Mild sunburn fits into the category of a first-degree burn. A **second-degree burn** goes deeper and affects both the epidermis and a portion of the dermis. These burns result in swelling and a painful blistering of the skin. It

is important to keep the burn site clean and sterile to prevent infection. If this is done, the burn will heal within several weeks. A **third-degree burn** fully extends into the epidermis and dermis, destroying the tissue and affecting the nerve endings and sensory function. These are serious burns that may appear white, red, or black; they require medical attention and will heal slowly without it. A **fourth-degree burn** is even more severe, affecting the underlying muscle and bone. Oddly, third and fourth-degree burns are usually not as painful because the nerve endings themselves are damaged. Full-thickness burns cannot be repaired by the body, because the local tissues used for repair are damaged and require excision (debridement), or amputation in severe cases, followed by grafting of the skin from an unaffected part of the body, or from skin grown in tissue culture for grafting purposes.

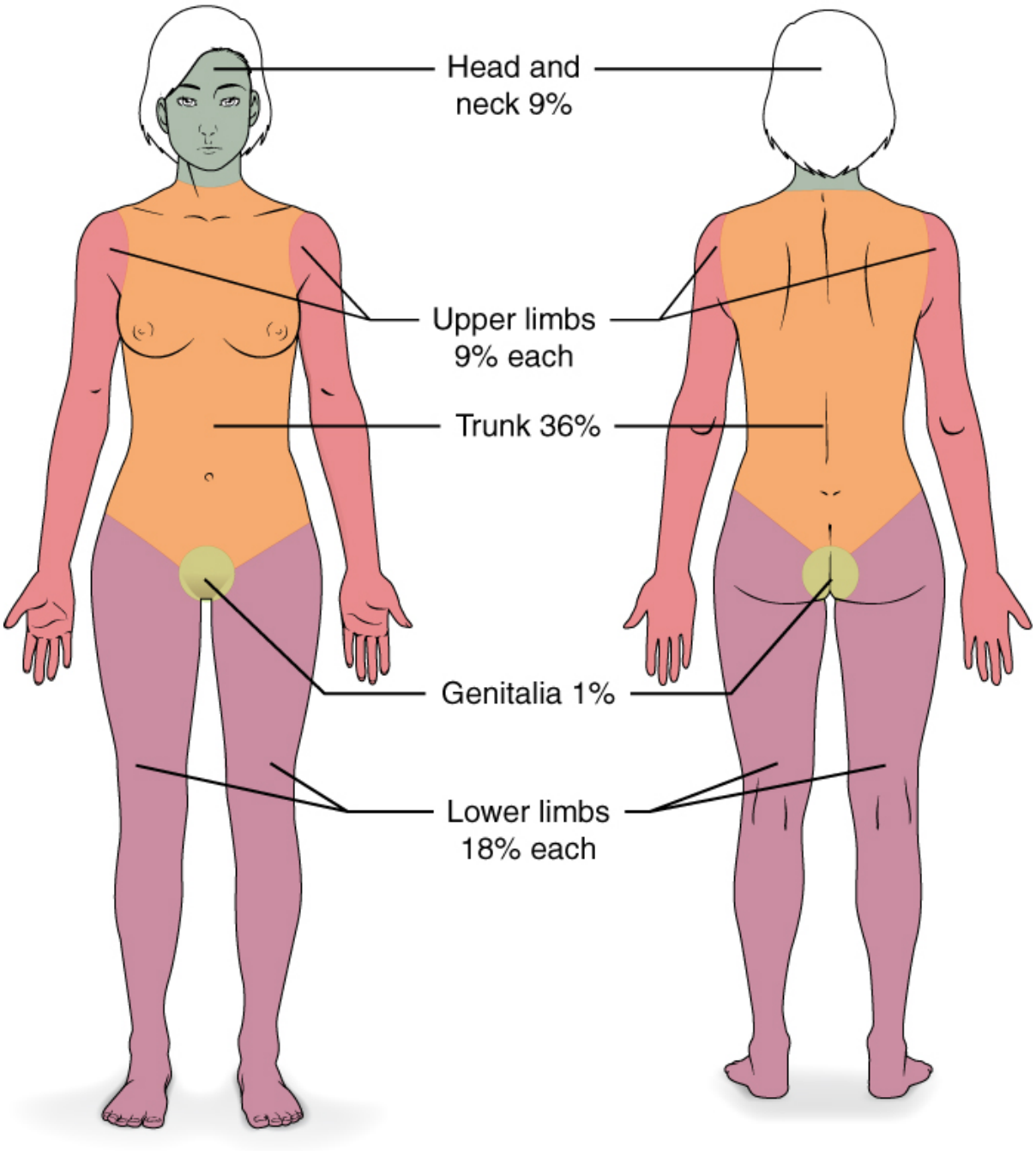


Figure 6. The size of a burn will guide decisions made about the need for specialized treatment. Specific parts of the body are associated with a percentage of body area.

Skin grafts are required when the damage from trauma or infection cannot be closed with sutures or staples. Watch this video to learn more about skin grafting procedures.

Watch this video online: https://youtu.be/bn9uMVxk8wI

Scars and Keloids

Most cuts or wounds, with the exception of ones that only scratch the surface (the epidermis), lead to scar formation. A **scar** is collagen-rich skin formed after the process of wound healing that differs from normal skin. Scarring occurs in cases in which there is repair of skin damage, but the skin fails to regenerate the original skin structure. Fibroblasts generate scar tissue in the form of collagen, and the bulk of repair is due to the basket-weave pattern generated by collagen fibers and does not result in regeneration of the typical cellular structure of skin. Instead, the tissue is fibrous in nature and does not allow for the regeneration of accessory structures, such as hair follicles, sweat glands, or sebaceous glands.

Sometimes, there is an overproduction of scar tissue, because the process of collagen formation does not stop when the wound is healed; this results in the formation of a raised or hypertrophic scar called a **keloid**. In contrast, scars that result from acne and chickenpox have a sunken appearance and are called atrophic scars.

Scarring of skin after wound healing is a natural process and does not need to be treated further. Application of mineral oil and lotions may reduce the formation of scar tissue. However, modern cosmetic procedures, such as dermabrasion, laser treatments, and filler injections have been invented as remedies for severe scarring. All of these procedures try to reorganize the structure of the epidermis and underlying collagen tissue to make it look more natural.

Bedsores and Stretch Marks

Skin and its underlying tissue can be affected by excessive pressure. One example of this is called a **bedsore**. Bedsores, also called decubitis ulcers, are caused by constant, long-term, unrelieved pressure on certain body parts that are bony, reducing blood flow to the area and leading to necrosis (tissue death). Bedsores are most common in elderly patients who have debilitating conditions that cause them to be immobile. Most hospitals and long-term care facilities have the practice of turning the patients every few hours to prevent the incidence of bedsores. If left untreated by removal of necrotized tissue, bedsores can be fatal if they become infected.

The skin can also be affected by pressure associated with rapid growth. A **stretch mark** results when the dermis is stretched beyond its limits of elasticity, as the skin stretches to accommodate the excess pressure. Stretch marks usually accompany rapid weight gain during puberty and pregnancy. They initially have a reddish hue, but lighten over time. Other than for cosmetic reasons, treatment of stretch marks is not required. They occur most commonly over the hips and abdomen.

Calluses

When you wear shoes that do not fit well and are a constant source of abrasion on your toes, you tend to form a **callus** at the point of contact. This occurs because the basal stem cells in the stratum basale are triggered to divide more often to increase the thickness of the skin at the point of abrasion to protect the rest of the body from further damage. This is an example of a minor or local injury, and the skin manages to react and treat the problem independent of the rest of the body. Calluses can also form on your fingers if they are subject to constant mechanical stress, such as long periods of writing, playing string instruments, or video games. A **corn** is a specialized form of callus. Corns form from abrasions on the skin that result from an elliptical-type motion.

Self-Check Questions

Visit your course online to take a quiz to check your understanding of Diseases of the Integumentary System:

SLIDES OF THE INTEGUMENTARY SYSTEM

Learning Objectives

- Be able to identify principal layers of the skin (epidermis, dermis and hypodermis) at the light microscope level and know the principal functions of each layer.
- Be able to identify the layers of the epidermis in thick and thin skin and describe the major cellular events that take place in each layer in the process of keratinization.
- Identify melanocytes and explain the process of pigment formation in the skin.
- Be able to identify eccrine and apocrine sweat glands at the light microscope level.
- Identify the components of the pilosebaceous apparatus and know the structural and developmental relationship between each component and the epidermis of the skin.

This material may also be accessed here.

Integumentary Structures

The skin and its associated structures, hair, sweat glands and nails make up the integumentary system.

Thick skin

- **106** *thick skin, sole of foot H&E* Webscope Imagescope
- **112** *thick skin, sole of foot H&E* Webscope Imagescope
- **112N** *thick skin, sole of foot H&E* Webscope Imagescope

In this slide the structure of skin, especially the epidermis, is exaggerated in response to the continued stress and abrasion applied to the plantar surface of the foot. Study the epidermis in **slides #106**, **#112**, and **#112N**. Identify the various strata:

1. Stratum basale (also known as S. germinativum): A single layer of cuboidal to columnar cells resting on and separated from the underlying dermis by a basal lamina. Mitotic figures occur in this layer.
2. Stratum spinosum: Several layers in thickness. In reduced light, the cells appear interconnected by "spinous" processes.
3. Stratum granulosum: A few layers of cells that are characterized by numerous, dense, basophilic granules. These are keratohyaline and membrane coating granules.
4. Stratum corneum: Note the striking change in cellular morphology. The cells are flattened, devoid of nuclei or cytoplasmic granules, and filled with mature keratin (**#112N**). In **#106** or **#112**, however, nuclei are still present in many cells of this layer, which are not normal. Because of differential dye penetration, the staining of the stratum corneum is variable and unpredictable. Sectioning artifacts are common.

The principal cell type of the epidermis is termed a keratinocyte and you will see this term used as a general descriptor for the epithelial cell found in any stratified squamous epithelium. Note the absence of blood vessels in the epidermis. Nourishment is obtained by diffusion from capillaries in the underlying dermis.

The interface of the epidermis and dermis is uneven. A pattern of ridges and grooves on the deep surface of the epidermis fit a complementary pattern of corrugations of the underlying dermis. The projections of the dermis are called dermal papillae and those of the epidermis, epidermal ridges (pegs), because of their appearance in vertical sections of the skin. However, these terms are not always accurately descriptive of the three dimensional configuration of the region of interdigitation. With low power, identify the epidermal ridges and dermal papillae. **What is the function of the epidermal ridges and dermal papillae?** Answer: Epidermal ridges and dermal papillae provide increased surface area for the epidermis and dermis to connect. Note the finer arrangement of collagen fibers in the papillary dermis **#112N papillary dermis** Webscope as opposed to that of the reticular dermis **#112N reticular dermis** Webscope (refer back to**#033 morphology and distribution of elastic fibers** Webscope in order to review the morphology and distribution of elastic fibers in the dermis). The fatty layer beneath the dermis, the subcutaneous connective tissue, is often called the hypodermis or superficial fascia. It is this layer that allows the skin to "move".

Thin Skin

- **105-1** *hair follicle H&E* Webscope Imagescope
- **105-2** *thin skin H&E* Webscope Imagescope
- **104-1** *thin skin H&E* Webscope Imagescope
- **104-2** *thin skin H&E* Webscope Imagescope

The epidermis in thin skin is much thinner and simpler in structure. Each stratum is thinner and the stratum granulosum may be absent.Melanocytes **#105-1 melanocytes** Webscope (derived from neural crest cells) capable of producing the pigment melanin are numerous in the deeper (toward the base) layers of the epidermis. They can be identified by the presence of a nucleus surrounded by a clear space. The cells with brownish pigments are actually keratinocytes that have received melanin granules from the melanocytes by pigment donation. The **slides 104-1**and **104-2** are skin samples from light and darker skinned individuals. It is not difficult to tell which sample is from which individual. Note the presence of portions of hair follicles and sebaceous glands in the dermis.

Peripheral Mechanosensory Receptors

Meissner's Corpuscles

- **UCSF 180** *finger tip H&E* Webscope Imagescope (virtual slide courtesy of the University of California, San Francisco)
- **112** *thick skin, sole of foot H&E* Webscope Imagescope (note, there's only one corpuscle apparent in this slide)

Meissner's corpuscles **#UCSF 180 meissner's corpuscles** Webscope are touch receptors that are responsive to low-frequency stimuli and are usually associated with hairless skin of the lips and palmar and plantar surfaces, particularly those of the fingers and toes. Generally, these receptors are tapered cylinders located in the undulating connective tissue just underneath the stratified epithelium of the skin. The long axis of the cylinder is perpendicular to that of the overlying epidermis and is usually about 150 um long and is usually tucked within extensions of the underlying connective tissue dermis (called "dermal papillae") that project into the underside of the epidermis. Within these receptors, one or two nonmyelinated endings of myelinated nerve fibers follow a spiral path through the corpuscle. The fibers are accompanied by ensheathing Schwann cells, the nuclei of which are flattened and stacked on top of each other giving the corpuscle its characteristic irregular, lamellar appearance.

Pacinian Corpuscles

- **108** *fetal fingar Masson* Webscope Imagescope
- **042** *mesentery H&E* Webscope Imagescope
- **095** *Small arteries and vein H&E* Webscope Imagescope
- **095M** *mesentary Masson* Webscope Imagescope

Pacinian corpuscles **#095M** Webscope (best seen in slide 108) are large, ovoid structures up to 1 mm in diameter found in the dermis and hypodermis of the skin and also in the connective tissue associated with bones,

joints, and internal organs. They respond primarily to pressure and vibration and are composed of a myelinated nerve ending surrounded by a capsule. The nerve enters the capsule at one pole (which might be out of the plane of section and therefore not visible) with its myelin sheath intact but then it is quickly lost. The unmyelinated portion of the axon extends toward the opposite pole from which it entered and its length is covered by flattened Schwann cell lamellae that form the inner core of the corpuscle. The remaining bulk of the capsule, or outer core, is comprised of a series of concentric, onionlike lamellae with each layer separated by an extracellular fluid similar to lymph. Each lamella is composed of flattened Schwann cells and endoneurial fibroblasts. In addition the fluid between each layer, delicate collagen fibers may be present as well as occasional capillaries. Displacement of the lamellae by pressure or vibrations effectively causes depolarization of the axon, which sends the signal to the central nervous system.

Scalp and Hair

- **107** *Scalp hair H&E* Webscope Imagescope

Underneath the thin epidermis, there are numerous circular to oblong structures with a hollow or yellow-brown center and surrounding cellular layers. These structures are hair follicles **#107** Webscope sectioned transversely or tangentially at different levels. The keratinized component of the hair occupies the central cavity of the follicle, and appears yellow-brown when present. However, the hair often falls out during tissue processing, in which case the central cavity will appear to be occupied by just empty space. The surrounding layers of clear cells form the external root sheath of the hair, which is a downgrowth of the epidermis. In fact, in cases where most of the epidermis is removed (such as severe abrasions or when taking skin graft), it is cells of the external root sheath that will divide and spread over the exposed surface to re-establish the epidermis. In some sections, you may also see an internal root sheath of darker staining cells right up against the hair follicle –this is the layer of cells that actually produce the keratinized hair shaft. Note also the presence of sebaceous glands **#107** Webscope and the arrector pili muscle **#107** Webscope near the hair follicle. In most instances, you will not find complete pilosebaceous units in a single section, so a bit of mental reconstruction will be required.

Sweat Glands

Eccrine Sweat Gland

- **106** *Thick skin, sole of foot (Homo)* Webscope ImageScope
- **112** *Thick skin (Homo)* Webscope ImageScope
- **112N** *Thick skin (Homo)* Webscope ImageScope
- **105-1** *Thin skin (Homo)* Webscope ImageScope

Numerous coiled eccrine sweat glands are located at the junction of dermis and hypodermis. The coiled morphology can be particularly appreciated in the example shown in **slide 112N**. Distinguish between the secretory portions of the gland (secretory cells and myoepithelial cells; the latter are best seen in the apocrine gland, see below, **slide 111** and **104-2**) and the stratified (two layers) cuboidal epithelial cell-lined duct. **Where do the ducts empty?**? Answer: Ducts of eccrine sweat glands empty onto the surface of the skin. Apocrine glands, however, empty into hair follicles in the axillary, areolar and perianal regions. **How does sweat get to the surface?** Answer: Eccrine sweat glands have ducts that lead to the surface of the skin. Eccrine sweat glands are a type of merocrine gland (a gland that releases its product by exocytosis). The secretory cells of the eccrine gland are surrounded by myoepithelial cells which can contract to propel its secretions to the surface. Apocrine sweat glands (apocrine being a misnomer, they are truly a merocrine gland, not an apocrine gland) function in the same way, however, their ducts lead to hair follicles, not directly to the skin surface.

Apocrine Glands

- **109-1** *Perianal region Masson* Webscope Imagescope
- **109-2** *Perianal region PAS/Pb hematoxylin* Webscope Imagescope
- **111** *axilla, subcutaneal region Masson* Webscope Imagescope
- **104-2** Webscope (this slide has both eccrine AND apocrine sweat glands; see if you can identify them)

Look in the deep dermis or hypodermis for secretory tubules with a wide lumen. The epithelium is cuboidal to columnar with distinct apical secretory granules. What should be apparent in your section is the apical "blebbing" of the secretory cells that was responsible for histologists originally designating these cells as "apocrine" secretory cells, although we now know the cells actually secrete in a MEROCRINE manner just like eccrine sweat glands. The "apocrine" sweat glands, present in the axillary, areolar, and anal regions, represent the second type of sweat glands. These glands produce a viscous secretion which acquires a distinctive odor as a result of bacterial decomposition.

In complete transverse sections of the glands (e.g. **slide #111**), look for oblong nuclei just inside the basement membrane. These are the nuclei of myoepithelial cells. In some planes of section, the nuclei may appear round. Now look for a tangential section of the gland. Look for regularly spaced, elongate strands of cytoplasm investing the outside of the secretory epithelium. With a bit more looking you should be able to see that these elongate bits of cytoplasm contain the above mentioned oblong nuclei. **Slide 104-2** is another good place to see myoepithelial cells **#104-2** Webscope ; look for eosinophilic strands of cytoplasm and small nuclei just peripheral to the secretory epithelial cells. In PAS stained slides (e.g. **#109-2**), densely staining granules are obvious in the apical cytoplasm the secretory cells, but the cytoplasm of myoepithelial cells is not well seen. Instead you see darker pink-stained basement membrane between the projections of myoepithelial cells. The relatively great number of these cells in sweat glands (and mammary glands) can only be appreciated by studying such tangential cuts.

Please also look for apocrine sweat gland ducts in these slides. They look similar to eccrine gland ducts described above (small diameter and small lumen with a stratified cuboidal epithelium). Similarly, they also lack lack myoepithelial cells. Make sure you can discriminate the ductal portion of apocrine sweat grlands from their secretory portion.

Electron Micrographs

- 65 Epidermis ***Skin*** Webscope Imagescope

Review the layering of the epidermis. Remember that there is a continuous process of cell migration and differentiation from the basal cell layer to the most superficial layer. Review the features of the epidermal-dermal junction.

- 67 Epidermis – Details of the Stratum Spinosum Webscope Imagescope

Observe the abundance of tonofibrils (= keratin intermediate filaments) and ribosomes and the small number of mitochondria. Note the absence of Golgi apparatus and granular endoplasmic reticulum. Epidermal cells do contain these organelles but in reduced amount, as the bulk of synthesis is for structural proteins, not exportable ones. What is the function of the numerous desmosomes? The function of the tonofibrils? (IN4)

- 69 Epidermis – Details of the Stratum Granulosum and Stratum Corneum WebscopeImagescope

Note the keratohyaline granules in the cells of the stratum granulosum. The keratinization process is completed in the cell layers above the stratum granulosum, indicated by the disappearance of nuclei and cell organelles. Note that the cornified cells are of variable appearance (some "dark" and some "light") a reflection of the tissue processing rather than of a functional difference.

Review Questions

1. What is the function of the numerous myoepithelial cells (in sweat glands)?

   ### Answer

   Myoepithelial cells are what propel the secretory contents of the glands to the surface of the body.
2. What is the function of the epidermal ridges and dermal papillae?

Answer

Epidermal ridges and dermal papillae provide increased surface area for the epidermis and dermis to connect.

3. Where do the ducts empty?

Answer

Ducts of eccrine sweat glands empty onto the surface of the skin. Apocrine glands, however, empty into hair follicles in the axillary, areolar and perianal regions.

4. How does sweat get to the surface?

Answer

Eccrine sweat glands have ducts that lead to the surface of the skin. Eccrine sweat glands are a type of merocrine gland (a gland that releases its product by exocytosis). The secretory cells of the eccrine gland are surrounded by myoepithelial cells which can contract to propel its secretions to the surface. Apocrine sweat glands (apocrine being a misnomer, they are truly a merocrine gland, not an apocrine gland) function in the same way, however, their ducts lead to hair follicles, not directly to the skin surface.

INTEGUMENTARY SYSTEM TUTORIAL

Interactive Link
http://www.innerbody.com/anatomy/integumentary

GLOSSARY: THE INTEGUMENTARY SYSTEM

acne: skin condition due to infected sebaceous glands

albinism: genetic disorder that affects the skin, in which there is no melanin production

anagen: active phase of the hair growth cycle

apocrine sweat gland: type of sweat gland that is associated with hair follicles in the armpits and genital regions

arrector pili: smooth muscle that is activated in response to external stimuli that pull on hair follicles and make the hair “stand up”

basal cell carcinoma: cancer that originates from basal cells in the epidermis of the skin

basal cell: type of stem cell found in the stratum basale and in the hair matrix that continually undergoes cell division, producing the keratinocytes of the epidermis

bedsore: sore on the skin that develops when regions of the body start necrotizing due to constant pressure and lack of blood supply; also called decubitis ulcers

callus: thickened area of skin that arises due to constant abrasion

catagen: transitional phase marking the end of the anagen phase of the hair growth cycle

corn: type of callus that is named for its shape and the elliptical motion of the abrasive force

cortex: in hair, the second or middle layer of keratinocytes originating from the hair matrix, as seen in a cross-section of the hair bulb

cuticle: in hair, the outermost layer of keratinocytes originating from the hair matrix, as seen in a cross-section of the hair bulb

dermal papilla: (plural = dermal papillae) extension of the papillary layer of the dermis that increases surface contact between the epidermis and dermis

dermis: layer of skin between the epidermis and hypodermis, composed mainly of connective tissue and containing blood vessels, hair follicles, sweat glands, and other structures

desmosome: structure that forms an impermeable junction between cells

eccrine sweat gland: type of sweat gland that is common throughout the skin surface; it produces a hypotonic sweat for thermoregulation

eczema: skin condition due to an allergic reaction, which resembles a rash

elastin fibers: fibers made of the protein elastin that increase the elasticity of the dermis

eleiden: clear protein-bound lipid found in the stratum lucidum that is derived from keratohyalin and helps to prevent water loss

epidermis: outermost tissue layer of the skin

eponychium: nail fold that meets the proximal end of the nail body, also called the cuticle

external root sheath: outer layer of the hair follicle that is an extension of the epidermis, which encloses the hair root

first-degree burn: superficial burn that injures only the epidermis

fourth-degree burn: burn in which full thickness of the skin and underlying muscle and bone is damaged

glassy membrane: layer of connective tissue that surrounds the base of the hair follicle, connecting it to the dermis

hair bulb: structure at the base of the hair root that surrounds the dermal papilla

hair follicle: cavity or sac from which hair originates

hair matrix: layer of basal cells from which a strand of hair grows

hair papilla: mass of connective tissue, blood capillaries, and nerve endings at the base of the hair follicle

hair root: part of hair that is below the epidermis anchored to the follicle

hair shaft: part of hair that is above the epidermis but is not anchored to the follicle

hair: keratinous filament growing out of the epidermis

hypodermis: connective tissue connecting the integument to the underlying bone and muscle

hyponychium: thickened layer of stratum corneum that lies below the free edge of the nail

integumentary system: skin and its accessory structures

internal root sheath: innermost layer of keratinocytes in the hair follicle that surround the hair root up to the hair shaft

keloid: type of scar that has layers raised above the skin surface

keratin: type of structural protein that gives skin, hair, and nails its hard, water-resistant properties

keratinocyte: cell that produces keratin and is the most predominant type of cell found in the epidermis

keratohyalin: granulated protein found in the stratum granulosum

Langerhans cell: specialized dendritic cell found in the stratum spinosum that functions as a macrophage

lunula: basal part of the nail body that consists of a crescent-shaped layer of thick epithelium

Meissner corpuscle: (also, tactile corpuscle) receptor in the skin that responds to light touch

Merkel cell: receptor cell in the stratum basale of the epidermis that responds to the sense of touch

medulla: in hair, the innermost layer of keratinocytes originating from the hair matrix

melanin: pigment that determines the color of hair and skin

melanocyte: cell found in the stratum basale of the epidermis that produces the pigment melanin

melanoma: type of skin cancer that originates from the melanocytes of the skin

melanosome: intercellular vesicle that transfers melanin from melanocytes into keratinocytes of the epidermis

metastasis: spread of cancer cells from a source to other parts of the body

nail bed: layer of epidermis upon which the nail body forms

nail body: main keratinous plate that forms the nail

nail cuticle: fold of epithelium that extends over the nail bed, also called the eponychium

nail fold: fold of epithelium at that extend over the sides of the nail body, holding it in place

nail root: part of the nail that is lodged deep in the epidermis from which the nail grows

Pacinian corpuscle: (also, lamellated corpuscle) receptor in the skin that responds to vibration

papillary layer: superficial layer of the dermis, made of loose, areolar connective tissue

reticular layer: deeper layer of the dermis; it has a reticulated appearance due to the presence of abundant collagen and elastin fibers

rickets: disease in children caused by vitamin D deficiency, which leads to the weakening of bones

scar: collagen-rich skin formed after the process of wound healing that is different from normal skin

sebaceous gland: type of oil gland found in the dermis all over the body and helps to lubricate and waterproof the skin and hair by secreting sebum

sebum: oily substance that is composed of a mixture of lipids that lubricates the skin and hair

second-degree burn: partial-thickness burn that injures the epidermis and a portion of the dermis

squamous cell carcinoma: type of skin cancer that originates from the stratum spinosum of the epidermis

stratum basale: deepest layer of the epidermis, made of epidermal stem cells

stratum corneum: most superficial layer of the epidermis

stratum granulosum: layer of the epidermis superficial to the stratum spinosum

stratum lucidum: layer of the epidermis between the stratum granulosum and stratum corneum, found only in thick skin covering the palms, soles of the feet, and digits

stratum spinosum: layer of the epidermis superficial to the stratum basale, characterized by the presence of desmosomes

stretch mark: mark formed on the skin due to a sudden growth spurt and expansion of the dermis beyond its elastic limits

sudoriferous gland: sweat gland

telogen: resting phase of the hair growth cycle initiated with catagen and terminated by the beginning of a new anagen phase of hair growth

third-degree burn: burn that penetrates and destroys the full thickness of the skin (epidermis and dermis)

vitamin D: compound that aids absorption of calcium and phosphates in the intestine to improve bone health

vitiligo: skin condition in which melanocytes in certain areas lose the ability to produce melanin, possibly due an autoimmune reaction that leads to loss of color in patches

PRACTICE TEST: THE INTEGUMENTARY SYSTEM

Review the material from this module by completing the practice in course online.

MODULE 7: BONE TISSUE AND THE SKELETAL SYSTEM

Learning Objectives

- List and describe the functions of bones
- Describe the classes of bones
- Discuss the process of bone formation and development
- Explain how bone repairs itself after a fracture
- Discuss the effect of exercise, nutrition, and hormones on bone tissue
- Describe how an imbalance of calcium can affect bone tissue

Bones make good fossils. While the soft tissue of a once living organism will decay and fall away over time, bone tissue will, under the right conditions, undergo a process of mineralization, effectively turning the bone to stone. A well-preserved fossil skeleton can give us a good sense of the size and shape of an organism, just as your skeleton helps to define your size and shape. Unlike a fossil skeleton, however, your skeleton is a structure of living tissue that grows, repairs, and renews itself. The bones within it are dynamic and complex organs that serve a number of important functions, including some necessary to maintain homeostasis.

Figure 1. Child Looking at Bones. *Bone is a living tissue. Unlike the bones of a fossil made inert by a process of mineralization, a child's bones will continue to grow and develop while contributing to the support and function of other body systems. (credit: James Emery)*

THE FUNCTIONS OF THE SKELETAL SYSTEM

Learning Objectives

- Define bone, cartilage, and the skeletal system
- List and describe the functions of the skeletal system

Bone, or **osseous tissue**, is a hard, dense connective tissue that forms most of the adult skeleton, the support structure of the body. In the areas of the skeleton where bones move (for example, the ribcage and joints), **cartilage**, a semi-rigid form of connective tissue, provides flexibility and smooth surfaces for movement. The **skeletal system** is the body system composed of bones and cartilage and performs the following critical functions for the human body:

- supports the body
- facilitates movement
- protects internal organs
- produces blood cells
- stores and releases minerals and fat

Support, Movement, and Protection

The most apparent functions of the skeletal system are the gross functions—those visible by observation. Simply by looking at a person, you can see how the bones support, facilitate movement, and protect the human body.

Figure 1. Bones Support Movement. *Bones act as levers when muscles span a joint and contract. (credit: Benjamin J. DeLong)*

Just as the steel beams of a building provide a scaffold to support its weight, the bones and cartilage of your skeletal system compose the scaffold that supports the rest of your body. Without the skeletal system, you would be a limp mass of organs, muscle, and skin.

Bones also facilitate movement by serving as points of attachment for your muscles. While some bones only serve as a support for the muscles, others also transmit the forces produced when your muscles contract. From a mechanical point of view, bones act as levers and joints serve as fulcrums (Figure 1).

Unless a muscle spans a joint and contracts, a bone is not going to move. For information on the interaction of the skeletal and muscular systems, that is, the musculoskeletal system, seek additional content.

Bones also protect internal organs from injury by covering or surrounding them. For example, your ribs protect your lungs and heart, the bones of your vertebral column (spine) protect your spinal cord, and the bones of your cranium (skull) protect your brain (Figure 2).

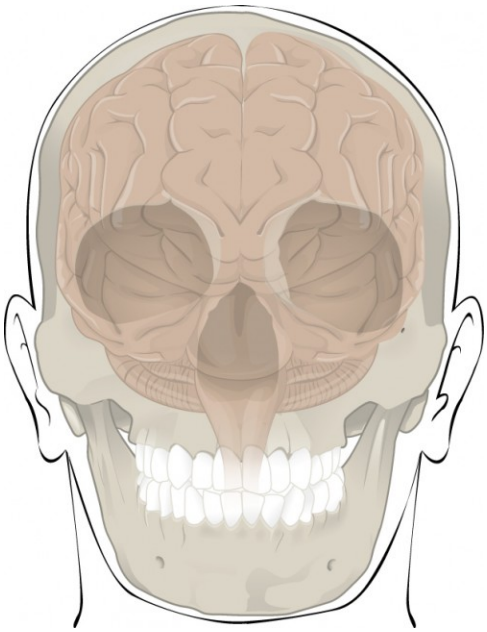


Figure 2. Bones Protect Brain. *The cranium completely surrounds and protects the brain from non-traumatic injury.*

Career Connection: Orthopedist

An **orthopedist** is a doctor who specializes in diagnosing and treating disorders and injuries related to the musculoskeletal system. Some orthopedic problems can be treated with medications, exercises, braces, and other devices, but others may be best treated with surgery (Figure 3).

While the origin of the word “orthopedics” (ortho- = “straight”; paed- = “child”), literally means “straightening of the child,” orthopedists can have patients who range from pediatric to geriatric. In recent years, orthopedists have even performed prenatal surgery to correct spina bifida, a congenital defect in which the neural canal in the spine of the fetus fails to close completely during embryologic development.

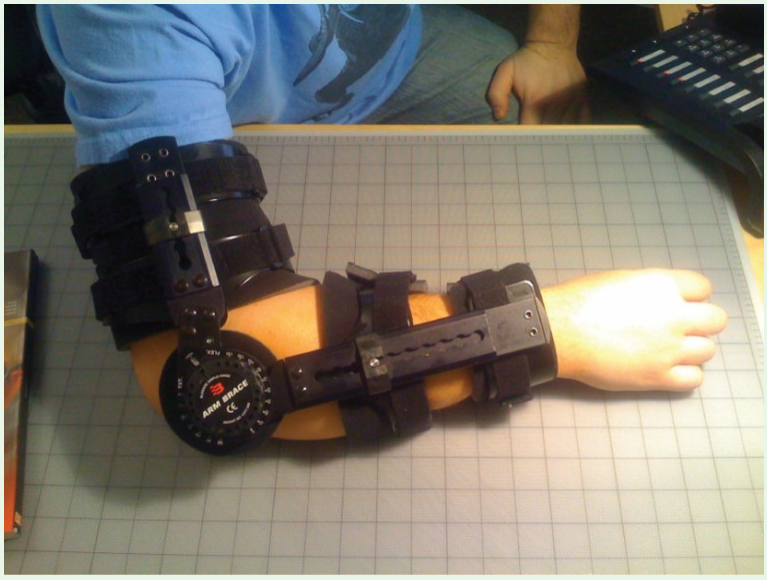


Figure 3. Arm Brace. *An orthopedist will sometimes prescribe the use of a brace that reinforces the underlying bone structure it is being used to support. (credit: Juhan Sonin)*

Orthopedists commonly treat bone and joint injuries but they also treat other bone conditions including curvature of the spine. Lateral curvatures (scoliosis) can be severe enough to slip under the shoulder blade (scapula) forcing it up as a hump. Spinal curvatures can also be excessive dorsoventrally (kyphosis) causing a hunch back and thoracic compression. These curvatures often appear in preteens as the result of poor posture, abnormal growth, or indeterminate causes. Mostly, they are readily treated by orthopedists. As people age, accumulated spinal column injuries and diseases like osteoporosis can also lead to curvatures of the spine, hence the stooping you sometimes see in the elderly.

Some orthopedists sub-specialize in sports medicine, which addresses both simple injuries, such as a sprained ankle, and complex injuries, such as a torn rotator cuff in the shoulder. Treatment can range from exercise to surgery.

Mineral Storage, Energy Storage, and Hematopoiesis

On a metabolic level, bone tissue performs several critical functions. For one, the bone matrix acts as a reservoir for a number of minerals important to the functioning of the body, especially calcium, and potassium. These minerals, incorporated into bone tissue, can be released back into the bloodstream to maintain levels needed to support physiological processes. Calcium ions, for example, are essential for muscle contractions and controlling the flow of other ions involved in the transmission of nerve impulses.

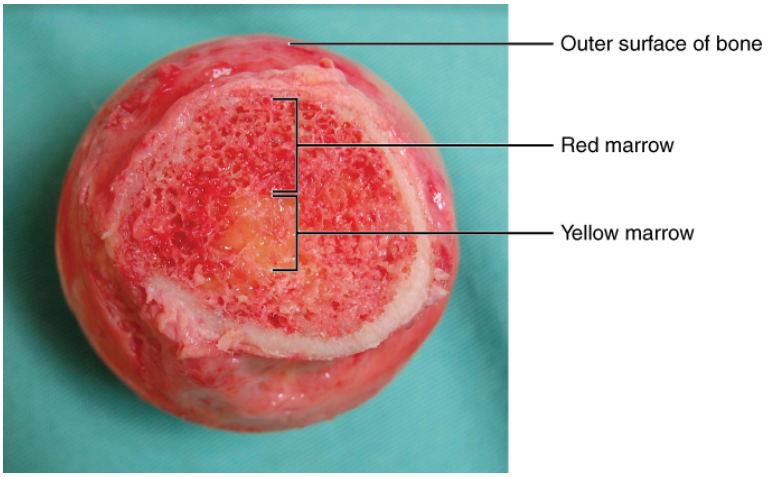


Figure 4. Head of Femur Showing Red and Yellow Marrow. *The head of the femur contains both yellow and red marrow. Yellow marrow stores fat. Red marrow is responsible for hematopoiesis. (credit: modification of work by "stevenfruitsmaak"/Wikimedia Commons)*

Bone also serves as a site for fat storage and blood cell production. The softer connective tissue that fills the interior of most bone is referred to as bone marrow (Figure 4). There are two types of bone marrow: yellow marrow and red marrow. **Yellow marrow** contains adipose tissue; the triglycerides stored in the adipocytes of the tissue can serve as a source of energy. **Red marrow** is where **hematopoiesis**—the production of blood cells—takes place. Red blood cells, white blood cells, and platelets are all produced in the red marrow.

BONE CLASSIFICATION

Learning Objectives

- Classify bones according to their shapes
- Describe the function of each category of bones

The 206 bones that compose the adult skeleton are divided into five categories based on their shapes (Figure 1). Their shapes and their functions are related such that each categorical shape of bone has a distinct function.

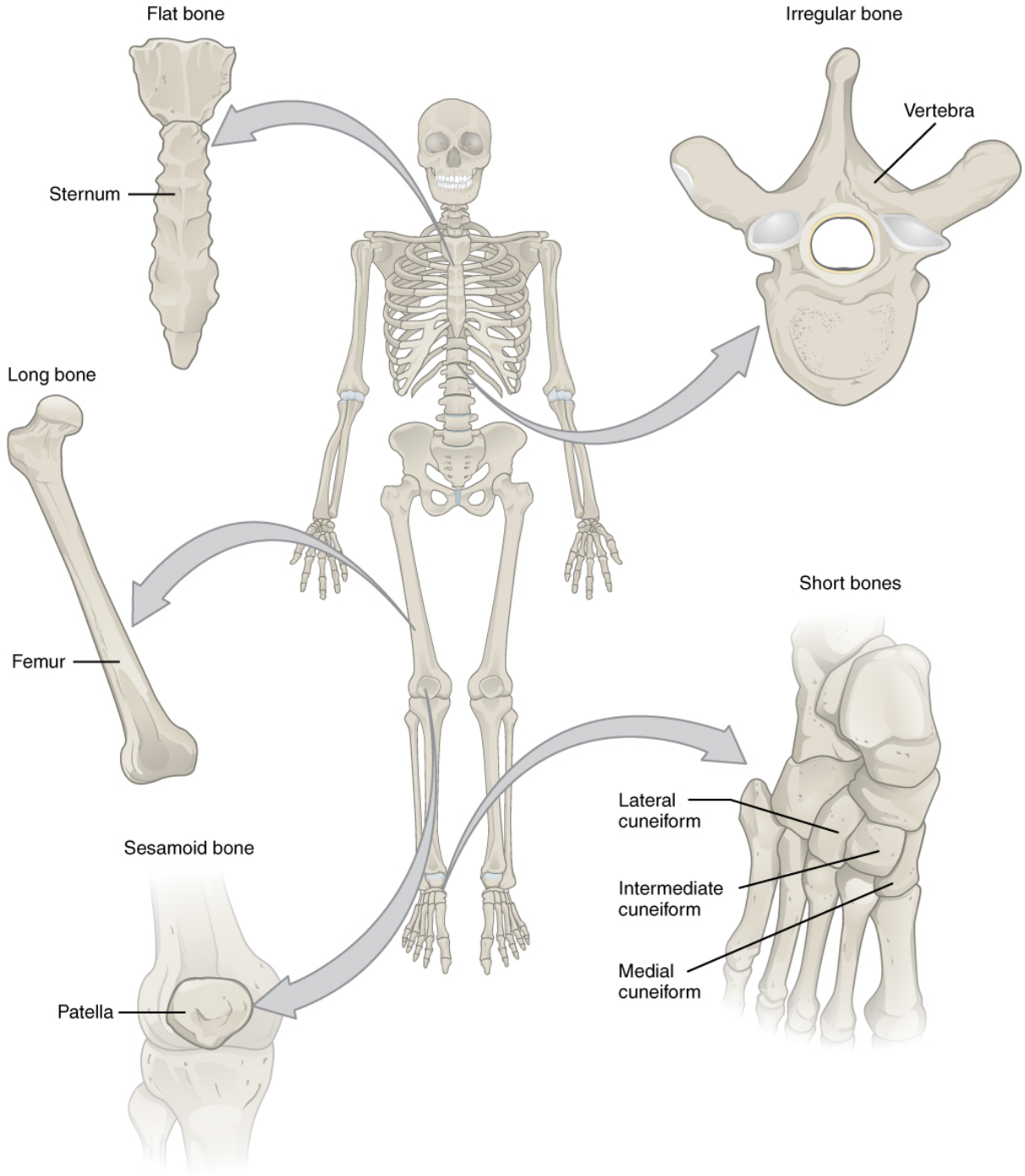


Figure 1. Classifications of Bones. *Bones are classified according to their shape.*

Long Bones

A long bone is one that is cylindrical in shape, being longer than it is wide. Keep in mind, however, that the term describes the shape of a bone, not its size. Long bones are found in the arms (humerus, ulna, radius) and legs (femur, tibia, fibula), as well as in the fingers (metacarpals, phalanges) and toes (metatarsals, phalanges). Long bones function as levers; they move when muscles contract.

Short Bones

A **short bone** is one that is cube-like in shape, being approximately equal in length, width, and thickness. The only short bones in the human skeleton are in the carpals of the wrists and the tarsals of the ankles. Short bones provide stability and support as well as some limited motion.

Flat Bones

The term ***flat bone*** is somewhat of a misnomer because, although a flat bone is typically thin, it is also often curved. Examples include the cranial (skull) bones, the scapulae (shoulder blades), the sternum (breastbone), and the ribs. Flat bones serve as points of attachment for muscles and often protect internal organs.

Irregular Bones

An **irregular bone** is one that does not have any easily characterized shape and therefore does not fit any other classification. These bones tend to have more complex shapes, like the vertebrae that support the spinal cord and protect it from compressive forces. Many facial bones, particularly the ones containing sinuses, are classified as irregular bones.

Sesamoid Bones

A **sesamoid bone** is a small, round bone that, as the name suggests, is shaped like a sesame seed. These bones form in tendons (the sheaths of tissue that connect bones to muscles) where a great deal of pressure is generated in a joint. The sesamoid bones protect tendons by helping them overcome compressive forces. Sesamoid bones vary in number and placement from person to person but are typically found in tendons associated with the feet, hands, and knees. The patellae (singular = patella) are the only sesamoid bones found in common with every person. Table 1 reviews bone classifications with their associated features, functions, and examples.

Table 1. Bone Classifications

Bone classification	Features	Function(s)	Examples
Long	Cylinder-like shape, longer than it is wide	Leverage	Femur, tibia, fibula, metatarsals, humerus, ulna, radius, metacarpals, phalanges
Short	Cube-like shape, approximately equal in length, width, and thickness	Provide stability, support, while allowing for some motion	Carpals, tarsals
Flat	Thin and curved	Points of attachment for muscles; protectors of internal organs	Sternum, ribs, scapulae, cranial bones
Irregular	Complex shape	Protect internal organs	Vertebrae, facial bones
Sesamoid	Small and round; embedded in tendons	Protect tendons from compressive forces	Patellae

Self-Check Questions

Visit your course online to take a quiz to check your understanding of Bone Classification:

BONE STRUCTURE

Learning Objectives

- Identify the anatomical features of a bone
- Define and list examples of bone markings
- Describe the histology of bone tissue
- Compare and contrast compact and spongy bone
- Identify the structures that compose compact and spongy bone
- Describe how bones are nourished and innervated

Bone tissue (osseous tissue) differs greatly from other tissues in the body. Bone is hard and many of its functions depend on that characteristic hardness. Later discussions in this chapter will show that bone is also dynamic in that its shape adjusts to accommodate stresses. This section will examine the gross anatomy of bone first and then move on to its histology.

Gross Anatomy of Bone

The structure of a long bone allows for the best visualization of all of the parts of a bone (Figure 1). A long bone has two parts: the **diaphysis** and the **epiphysis**. The diaphysis is the tubular shaft that runs between the proximal and distal ends of the bone. The hollow region in the diaphysis is called the **medullary cavity**, which is filled with yellow marrow. The walls of the diaphysis are composed of dense and hard **compact bone**.

The wider section at each end of the bone is called the *epiphysis* (plural = *epiphyses*), which is filled with spongy bone. Red marrow fills the spaces in the spongy bone. Each epiphysis meets the diaphysis at the metaphysis, the narrow area that contains the **epiphyseal plate** (growth plate), a layer of hyaline (transparent) cartilage in a growing bone. When the bone stops growing in early adulthood (approximately 18–21 years), the cartilage is replaced by osseous tissue and the epiphyseal plate becomes an epiphyseal line.

The medullary cavity has a delicate membranous lining called the **endosteum** (*end–* = "inside"; *oste–* = "bone"), where bone growth, repair, and remodeling occur. The outer surface of the bone is covered with a fibrous membrane called the **periosteum** (*peri–* = "around" or "surrounding"). The periosteum contains blood vessels, nerves, and lymphatic vessels that nourish compact bone. Tendons and ligaments also attach to bones at the periosteum. The periosteum covers the entire outer surface except where the epiphyses meet other bones to form joints (Figure 2). In this region, the epiphyses are covered with **articular cartilage**, a thin layer of cartilage that reduces friction and acts as a shock absorber.

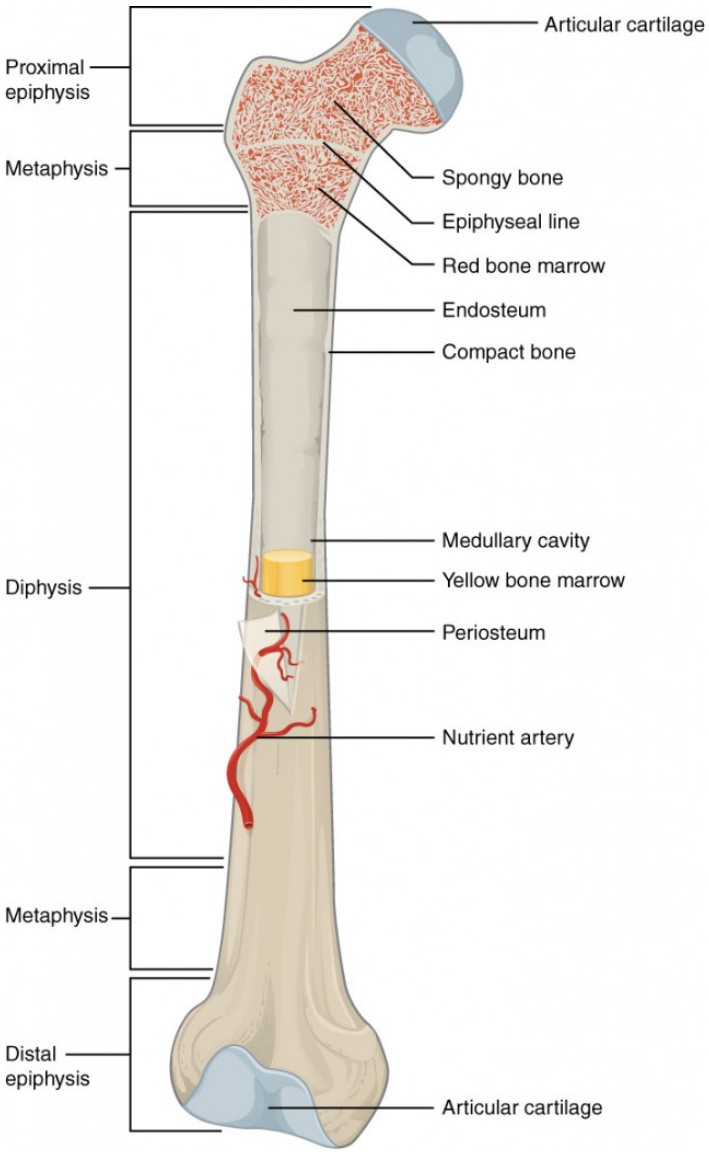


Figure 1. Anatomy of a Long Bone. *A typical long bone shows the gross anatomical characteristics of bone.*

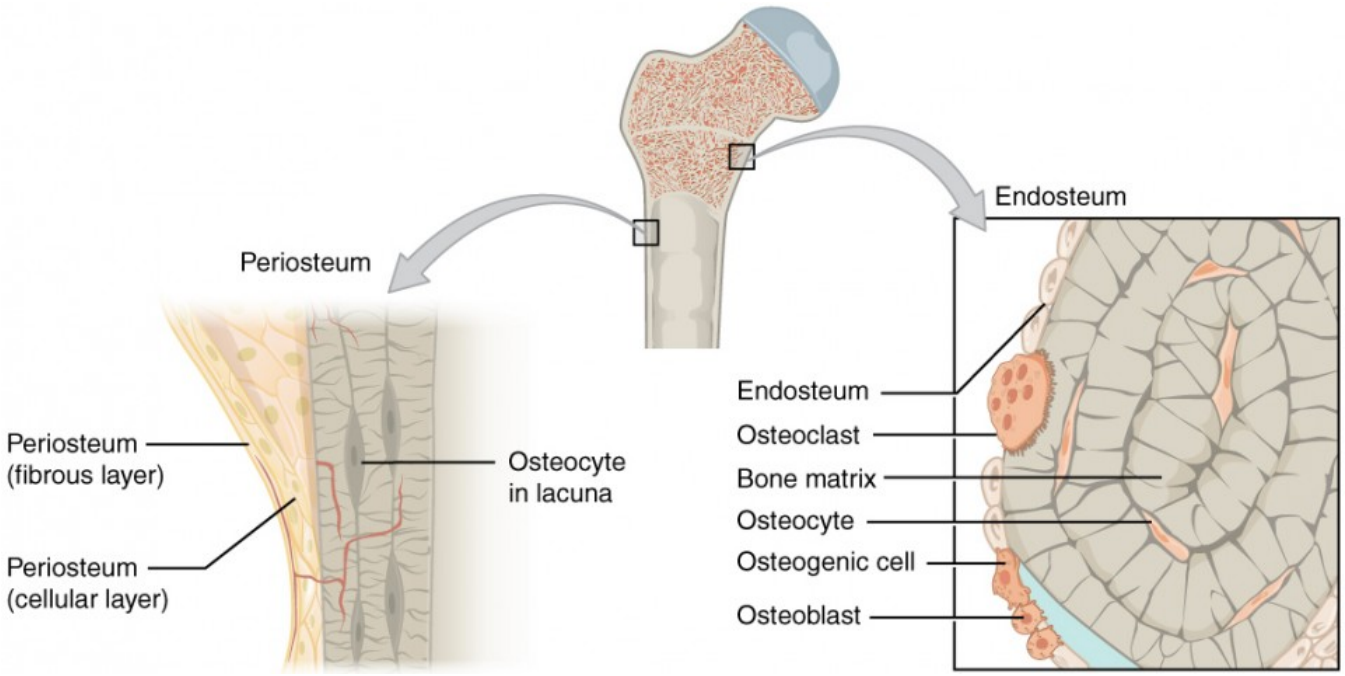


Figure 2. Periosteum and Endosteum. The periosteum forms the outer surface of bone, and the endosteum lines the medullary cavity.

Flat bones, like those of the cranium, consist of a layer of **diploë** (spongy bone), lined on either side by a layer of compact bone (Figure 3). The two layers of compact bone and the interior spongy bone work together to protect the internal organs. If the outer layer of a cranial bone fractures, the brain is still protected by the intact inner layer.

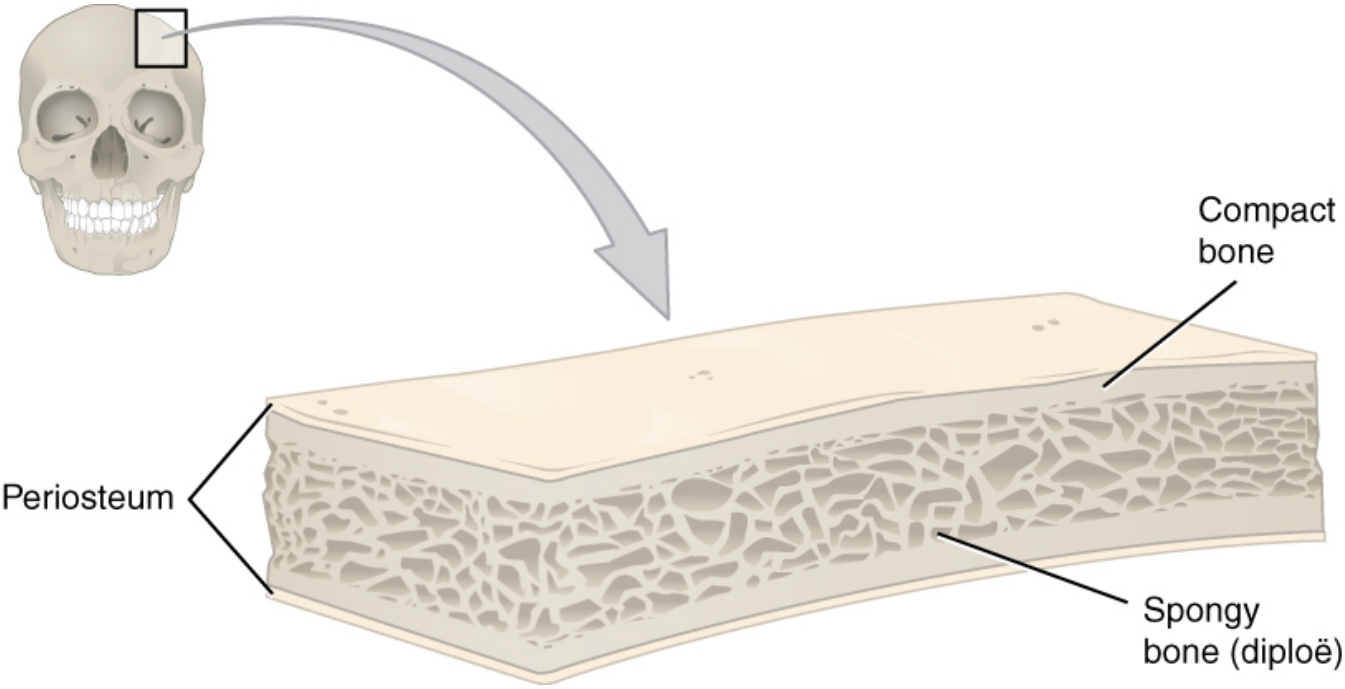


Figure 3. Anatomy of a Flat Bone. This cross-section of a flat bone shows the spongy bone (diploë) lined on either side by a layer of compact bone.

Bone Markings

The surface features of bones vary considerably, depending on the function and location in the body. Table 1 describes the bone markings, which are illustrated in (Figure 4). There are three general classes of bone markings: (1) articulations, (2) projections, and (3) holes. As the name implies, an **articulation** is where two bone surfaces come together (articulus = "joint"). These surfaces tend to conform to one another, such as one being rounded and the other cupped, to facilitate the function of the articulation. A **projection** is an area of a bone that projects above the surface of the bone. These are the attachment points for tendons and ligaments. In general, their size and shape is an indication of the forces exerted through the attachment to the bone. A **hole** is an opening or groove in the bone that allows blood vessels and nerves to enter the bone. As with the other markings, their size and shape reflect the size of the vessels and nerves that penetrate the bone at these points.

Table 1. Bone Markings

Marking	Description	Example
Articulations	Where two bones meet	Knee joint
Head	Prominent rounded surface	Head of femur
Facet	Flat surface	Vertebrae
Condyle	Rounded surface	Occipital condyles
Projections	Raised markings	Spinous process of the vertebrae
Protuberance	Protruding	Chin
Process	Prominence feature	Transverse process of vertebra
Spine	Sharp process	Ischial spine
Tubercle	Small, rounded process	Tubercle of humerus
Tuberosity	Rough surface	Deltoid tuberosity
Line	Slight, elongated ridge	Temporal lines of the parietal bones
Crest	Ridge	Iliac crest
Holes	Holes and depressions	Foramen (holes through which blood vessels can pass through)
Fossa	Elongated basin	Mandibular fossa
Fovea	Small pit	Fovea capitis on the head of the femur
Sulcus	Groove	Sigmoid sulcus of the temporal bones
Canal	Passage in bone	Auditory canal
Fissure	Slit through bone	Auricular fissure
Foramen	Hole through bone	Foramen magnum in the occipital bone
Meatus	Opening into canal	External auditory meatus

Table 1. Bone Markings		
Marking	Description	Example
Sinus	Air-filled space in bone	Nasal sinus

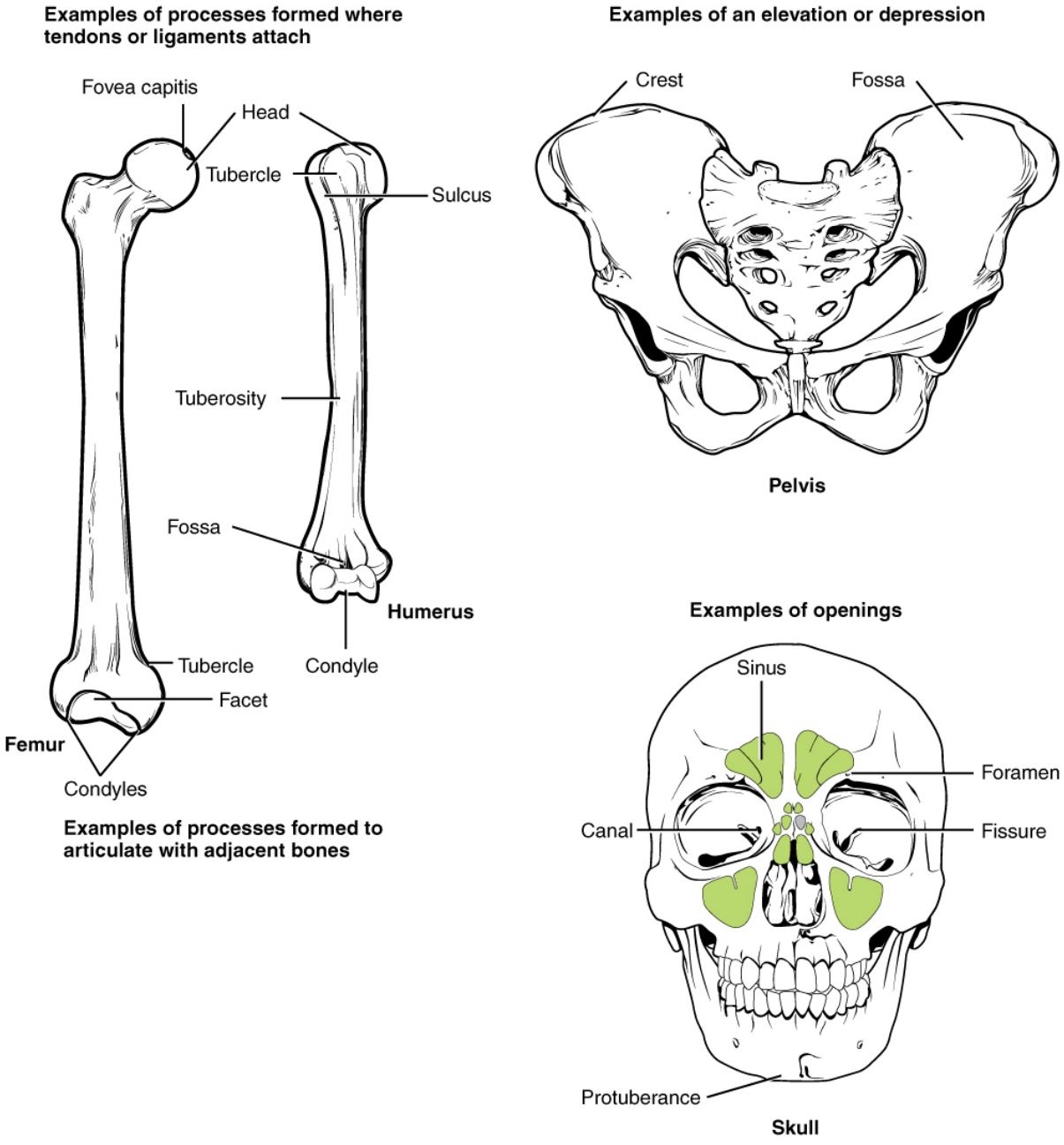


Figure 4. Bone Features. The surface features of bones depend on their function, location, attachment of ligaments and tendons, or the penetration of blood vessels and nerves.

Bone Cells and Tissue

Bone contains a relatively small number of cells entrenched in a matrix of collagen fibers that provide a surface for inorganic salt crystals to adhere. These salt crystals form when calcium phosphate and calcium carbonate combine to create hydroxyapatite, which incorporates other inorganic salts like magnesium hydroxide, fluoride,

and sulfate as it crystallizes, or calcifies, on the collagen fibers. The hydroxyapatite crystals give bones their hardness and strength, while the collagen fibers give them flexibility so that they are not brittle.

Although bone cells compose a small amount of the bone volume, they are crucial to the function of bones. Four types of cells are found within bone tissue: osteoblasts, osteocytes, osteogenic cells, and osteoclasts (Figure 5).

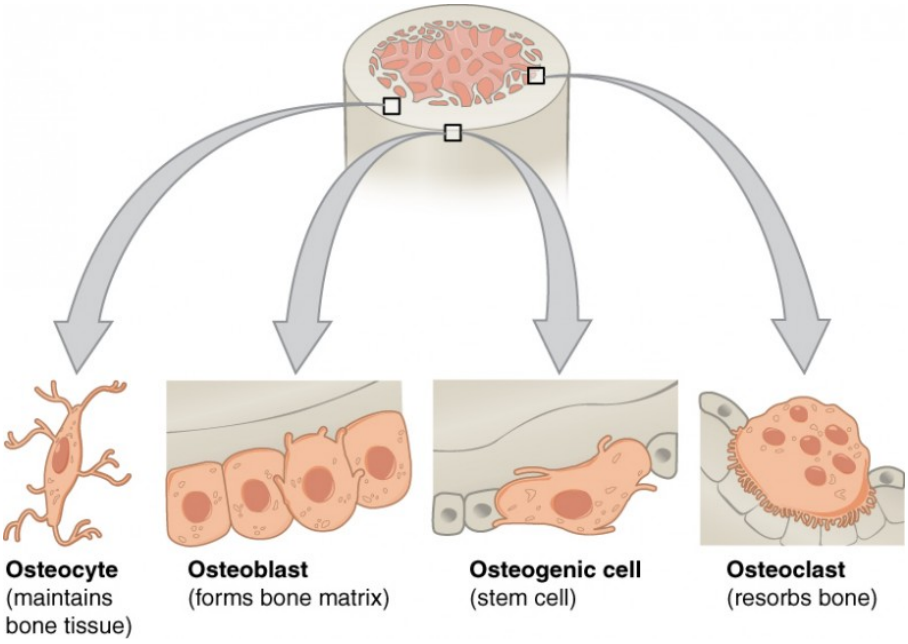


Figure 5. Bone Cells. Four types of cells are found within bone tissue. Osteogenic cells are undifferentiated and develop into osteoblasts. When osteoblasts get trapped within the calcified matrix, their structure and function changes, and they become osteocytes. Osteoclasts develop from monocytes and macrophages and differ in appearance from other bone cells.

The **osteoblast**. is the bone cell responsible for forming new bone and is found in the growing portions of bone, including the periosteum and endosteum. Osteoblasts, which do not divide, synthesize and secrete the collagen matrix and calcium salts. As the secreted matrix surrounding the osteoblast calcifies, the osteoblast become trapped within it; as a result, it changes in structure and becomes an **osteocyte**, the primary cell of mature bone and the most common type of bone cell. Each osteocyte is located in a space called a **lacuna** and is surrounded by bone tissue. Osteocytes maintain the mineral concentration of the matrix via the secretion of enzymes. Like osteoblasts, osteocytes lack mitotic activity. They can communicate with each other and receive nutrients via long cytoplasmic processes that extend through **canaliculi** (singular = *canaliculus*), channels within the bone matrix.

If osteoblasts and osteocytes are incapable of mitosis, then how are they replenished when old ones die? The answer lies in the properties of a third category of bone cells—the **osteogenic cell**. These osteogenic cells are undifferentiated with high mitotic activity and they are the only bone cells that divide. Immature osteogenic cells are found in the deep layers of the periosteum and the marrow. They differentiate and develop into osteoblasts.

The dynamic nature of bone means that new tissue is constantly formed, and old, injured, or unnecessary bone is dissolved for repair or for calcium release. The cell responsible for bone resorption, or breakdown, is the **osteoclast**. They are found on bone surfaces, are multinucleated, and originate from monocytes and macrophages, two types of white blood cells, not from osteogenic cells. Osteoclasts are continually breaking down old bone while osteoblasts are continually forming new bone. The ongoing balance between osteoblasts and osteoclasts is responsible for the constant but subtle reshaping of bone. Table 2 reviews the bone cells, their functions, and locations.

Table 2. Bone Cells

Cell type	Function	Location
Osteogenic cells	Develop into osteoblasts	Deep layers of the periosteum and the marrow
Osteoblasts	Bone formation	Growing portions of bone, including periosteum and endosteum

Table 2. Bone Cells		
Cell type	**Function**	**Location**
Osteocytes	Maintain mineral concentration of matrix	Entrapped in matrix
Osteoclasts	Bone resorption	Bone surfaces and at sites of old, injured, or unneeded bone

Compact and Spongy Bone

The differences between compact and spongy bone are best explored via their histology. Most bones contain compact and spongy osseous tissue, but their distribution and concentration vary based on the bone's overall function. Compact bone is dense so that it can withstand compressive forces, while spongy (cancellous) bone has open spaces and supports shifts in weight distribution.

Compact Bone

Compact bone is the denser, stronger of the two types of bone tissue (Figure 6). It can be found under the periosteum and in the diaphyses of long bones, where it provides support and protection.

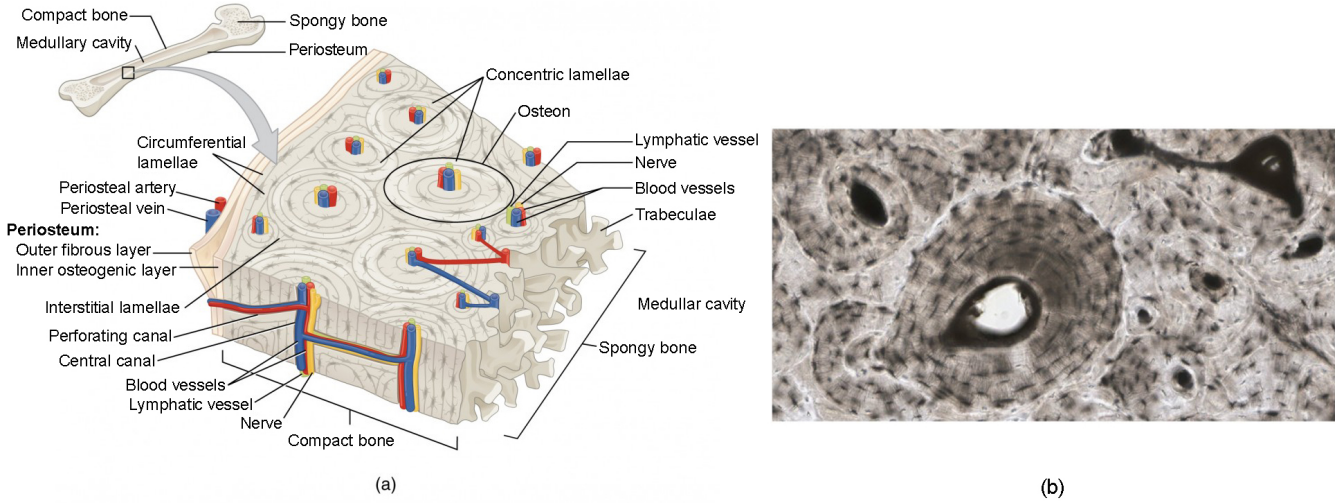


Figure 6. Diagram of Compact Bone. *(a) This cross-sectional view of compact bone shows the basic structural unit, the osteon. (b) In this micrograph of the osteon, you can clearly see the concentric lamellae and central canals. LM × 40. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

The microscopic structural unit of compact bone is called an **osteon**, or Haversian system. Each osteon is composed of concentric rings of calcified matrix called lamellae (singular = lamella). Running down the center of each osteon is the **central canal**, or Haversian canal, which contains blood vessels, nerves, and lymphatic vessels. These vessels and nerves branch off at right angles through a **perforating canal**, also known as Volkmann's canals, to extend to the periosteum and endosteum.

The osteocytes are located inside spaces called lacunae (singular = lacuna), found at the borders of adjacent lamellae. As described earlier, canaliculi connect with the canaliculi of other lacunae and eventually with the central canal. This system allows nutrients to be transported to the osteocytes and wastes to be removed from them.

Spongy (Cancellous) Bone

Like compact bone, **spongy bone**, also known as cancellous bone, contains osteocytes housed in lacunae, but they are not arranged in concentric circles. Instead, the lacunae and osteocytes are found in a lattice-like network of matrix spikes called **trabeculae** (singular = *trabecula*) (Figure 7). The trabeculae may appear to be a random network, but each trabecula forms along lines of stress to provide strength to the bone. The spaces of the trabeculated network provide balance to the dense and heavy compact bone by making bones lighter so that muscles can move them more easily. In addition, the spaces in some spongy bones contain red marrow, protected by the trabeculae, where hematopoiesis occurs.

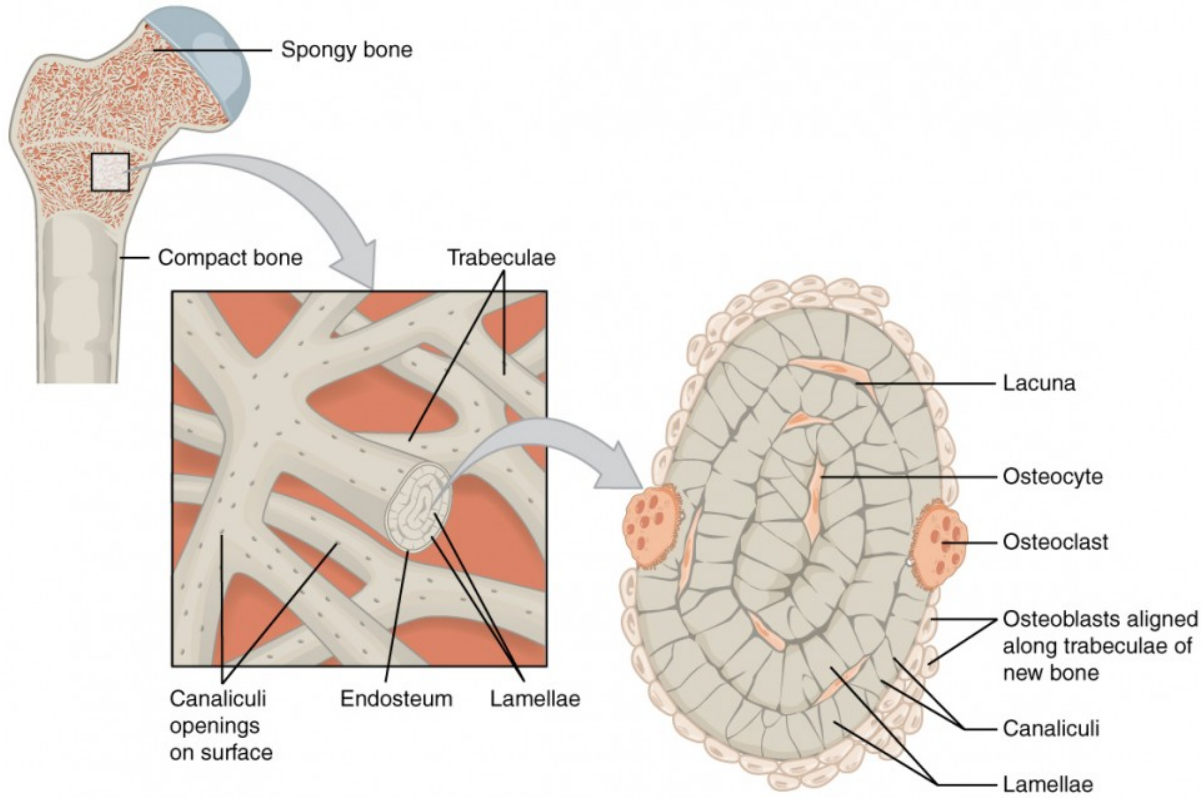


Figure 7. Diagram of Spongy Bone. *Spongy bone is composed of trabeculae that contain the osteocytes. Red marrow fills the spaces in some bones.*

Aging and the Skeletal System: Paget's Disease

Paget's disease usually occurs in adults over age 40. It is a disorder of the bone remodeling process that begins with overactive osteoclasts. This means more bone is resorbed than is laid down. The osteoblasts try to compensate but the new bone they lay down is weak and brittle and therefore prone to fracture.

While some people with Paget's disease have no symptoms, others experience pain, bone fractures, and bone deformities (Figure 8). Bones of the pelvis, skull, spine, and legs are the most commonly affected. When occurring in the skull, Paget's disease can cause headaches and hearing loss.

What causes the osteoclasts to become overactive? The answer is still unknown, but hereditary factors seem to play a role. Some scientists believe Paget's disease is due to an as-yet-unidentified virus.

Paget's disease is diagnosed via imaging studies and lab tests. X-rays may show bone deformities or areas of bone resorption. Bone scans are also useful. In these studies, a dye containing a radioactive ion is injected into the body. Areas of bone resorption have an affinity for the ion, so they will light up on the scan if the ions are absorbed. In addition, blood levels of an enzyme called alkaline phosphatase are typically elevated in people with Paget's disease.

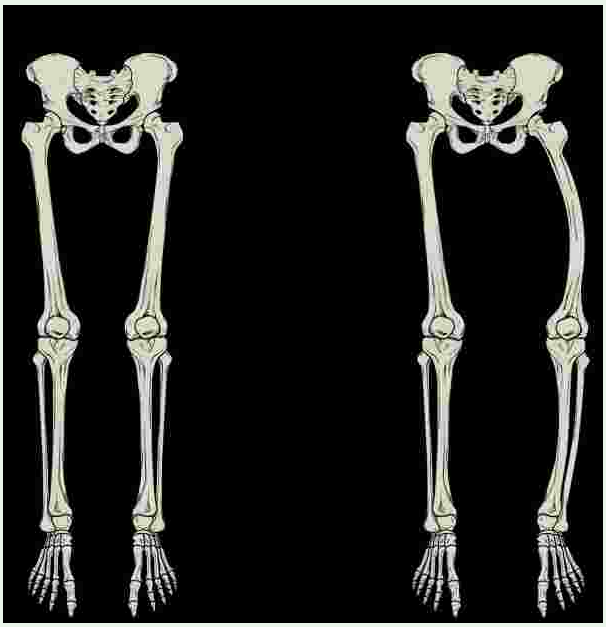


Figure 8. Paget's Disease. *Normal leg bones are relatively straight, but those affected by Paget's disease are porous and curved.*

Bisphosphonates, drugs that decrease the activity of osteoclasts, are often used in the treatment of Paget's disease. However, in a small percentage of cases, bisphosphonates themselves have been linked to an increased risk of fractures because the old bone that is left after bisphosphonates are administered becomes worn out and brittle. Still, most doctors feel that the benefits of bisphosphonates more than outweigh the risk; the medical professional has to weigh the benefits and risks on a case-by-case basis. Bisphosphonate treatment can reduce the overall risk of deformities or fractures, which in turn reduces the risk of surgical repair and its associated risks and complications.

Blood and Nerve Supply

The spongy bone and medullary cavity receive nourishment from arteries that pass through the compact bone. The arteries enter through the **nutrient foramen** (plural = *foramina*), small openings in the diaphysis (Figure 9). The osteocytes in spongy bone are nourished by blood vessels of the periosteum that penetrate spongy bone and blood that circulates in the marrow cavities. As the blood passes through the marrow cavities, it is collected by veins, which then pass out of the bone through the foramina.

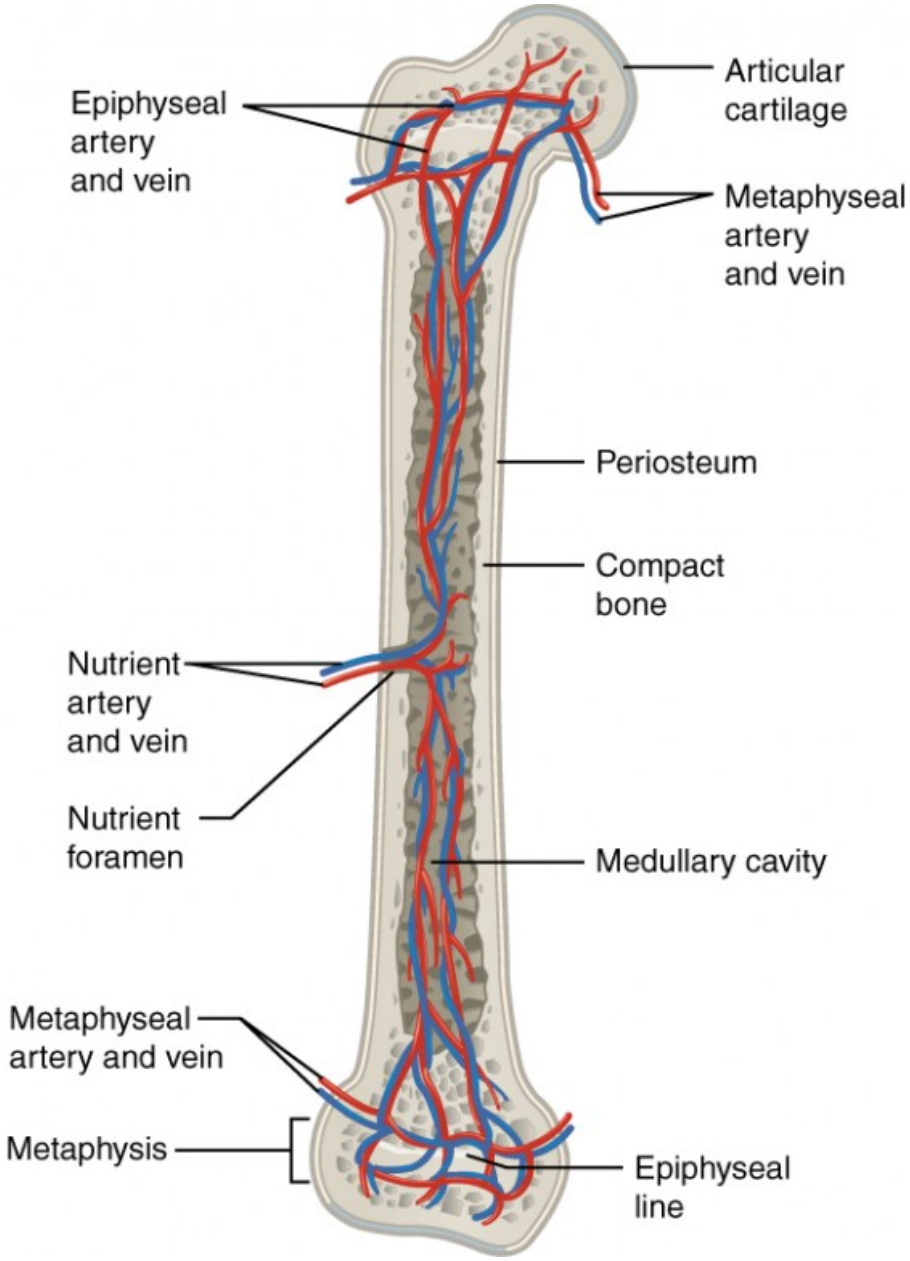


Figure 9. Diagram of Blood and Nerve Supply to Bone. *Blood vessels and nerves enter the bone through the nutrient foramen.*

In addition to the blood vessels, nerves follow the same paths into the bone where they tend to concentrate in the more metabolically active regions of the bone. The nerves sense pain, and it appears the nerves also play roles in regulating blood supplies and in bone growth, hence their concentrations in metabolically active sites of the bone.

Self-Check Questions

Visit your course online to take a quiz to check your understanding of Bone Structure:

BONE FORMATION AND DEVELOPMENT

Learning Objectives

- Explain the function of cartilage
- List the steps of intramembranous ossification
- List the steps of endochondral ossification
- Explain the growth activity at the epiphyseal plate
- Compare and contrast the processes of modeling and remodeling

In the early stages of embryonic development, the embryo's skeleton consists of fibrous membranes and hyaline cartilage. By the sixth or seventh week of embryonic life, the actual process of bone development, **ossification** (osteogenesis), begins. There are two osteogenic pathways—intramembranous ossification and endochondral ossification—but bone is the same regardless of the pathway that produces it.

Cartilage Templates

Bone is a replacement tissue; that is, it uses a model tissue on which to lay down its mineral matrix. For skeletal development, the most common template is cartilage. During fetal development, a framework is laid down that determines where bones will form. This framework is a flexible, semi-solid matrix produced by chondroblasts and consists of hyaluronic acid, chondroitin sulfate, collagen fibers, and water. As the matrix surrounds and isolates chondroblasts, they are called chondrocytes. Unlike most connective tissues, cartilage is avascular, meaning that it has no blood vessels supplying nutrients and removing metabolic wastes. All of these functions are carried on by diffusion through the matrix. This is why damaged cartilage does not repair itself as readily as most tissues do.

Throughout fetal development and into childhood growth and development, bone forms on the cartilaginous matrix. By the time a fetus is born, most of the cartilage has been replaced with bone. Some additional cartilage will be replaced throughout childhood, and some cartilage remains in the adult skeleton.

Intramembranous Ossification

During **intramembranous ossification**, compact and spongy bone develops directly from sheets of mesenchymal (undifferentiated) connective tissue. The flat bones of the face, most of the cranial bones, and the clavicles (collarbones) are formed via intramembranous ossification.

The process begins when mesenchymal cells in the embryonic skeleton gather together and begin to differentiate into specialized cells (Figure 1a). Some of these cells will differentiate into capillaries, while others will become osteogenic cells and then osteoblasts. Although they will ultimately be spread out by the formation of bone tissue, early osteoblasts appear in a cluster called an **ossification center**.

The osteoblasts secrete **osteoid**, uncalcified matrix, which calcifies (hardens) within a few days as mineral salts are deposited on it, thereby entrapping the osteoblasts within. Once entrapped, the osteoblasts become osteocytes (Figure 1b). As osteoblasts transform into osteocytes, osteogenic cells in the surrounding connective tissue differentiate into new osteoblasts.

Osteoid (unmineralized bone matrix) secreted around the capillaries results in a trabecular matrix, while osteoblasts on the surface of the spongy bone become the periosteum (Figure 1c). The periosteum then creates a protective layer of compact bone superficial to the trabecular bone. The trabecular bone crowds nearby blood vessels, which eventually condense into red marrow (Figure 1d).

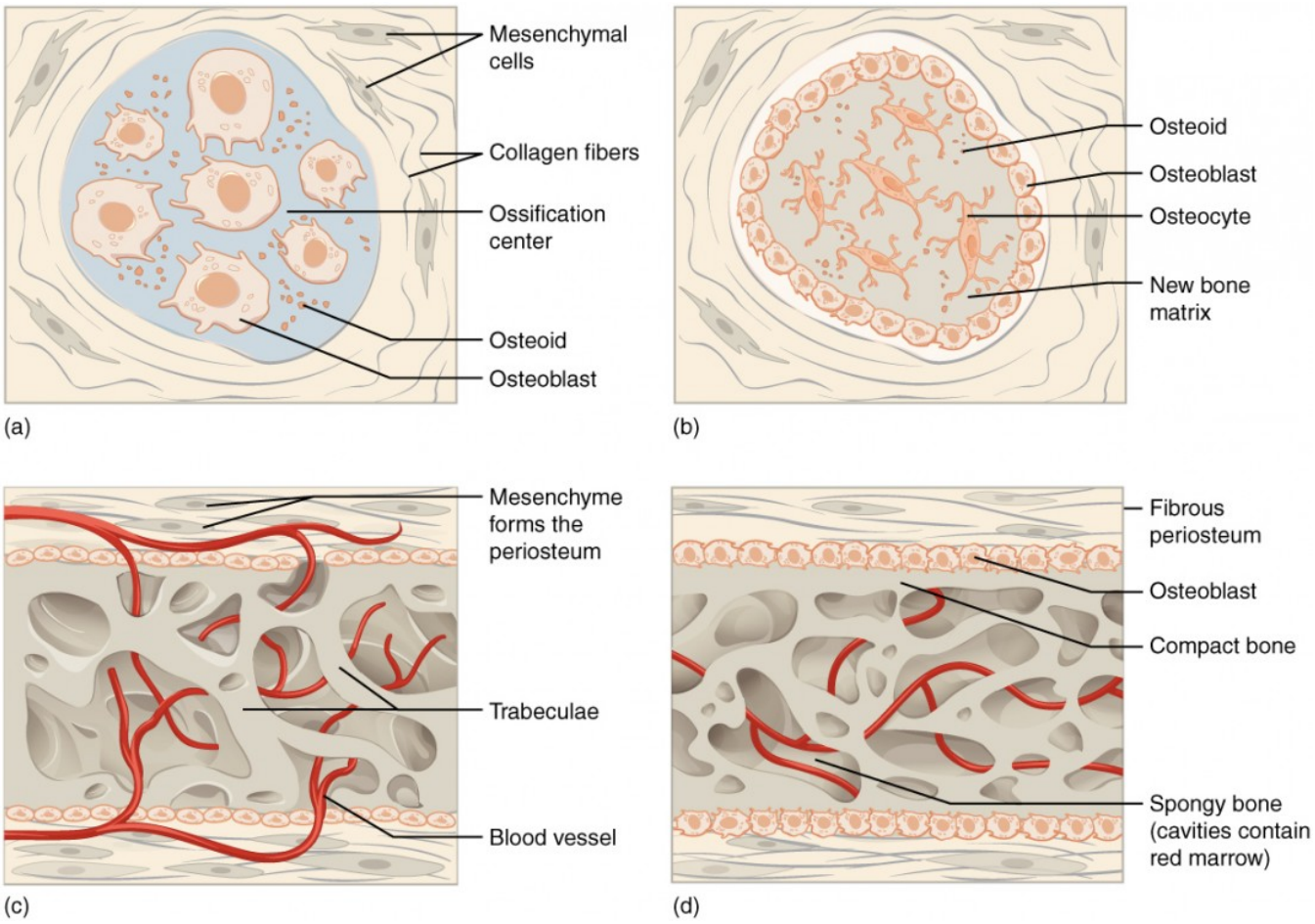


Figure 1. Intramembranous Ossification. *Intramembranous ossification follows four steps. (a) Mesenchymal cells group into clusters, and ossification centers form. (b) Secreted osteoid traps osteoblasts, which then become osteocytes. (c) Trabecular matrix and periosteum form. (d) Compact bone develops superficial to the trabecular bone, and crowded blood vessels condense into red marrow.*

Intramembranous ossification begins *in utero* during fetal development and continues on into adolescence. At birth, the skull and clavicles are not fully ossified nor are the sutures of the skull closed. This allows the skull and shoulders to deform during passage through the birth canal. The last bones to ossify via intramembranous ossification are the flat bones of the face, which reach their adult size at the end of the adolescent growth spurt.

Endochondral Ossification

In **endochondral ossification**, bone develops by *replacing* hyaline cartilage. Cartilage does not become bone. Instead, cartilage serves as a template to be completely replaced by new bone. Endochondral ossification takes much longer than intramembranous ossification. Bones at the base of the skull and long bones form via endochondral ossification.

In a long bone, for example, at about 6 to 8 weeks after conception, some of the mesenchymal cells differentiate into chondrocytes (cartilage cells) that form the cartilaginous skeletal precursor of the bones (Figure 2a). Soon after, the **perichondrium**, a membrane that covers the cartilage, appears Figure 2b).

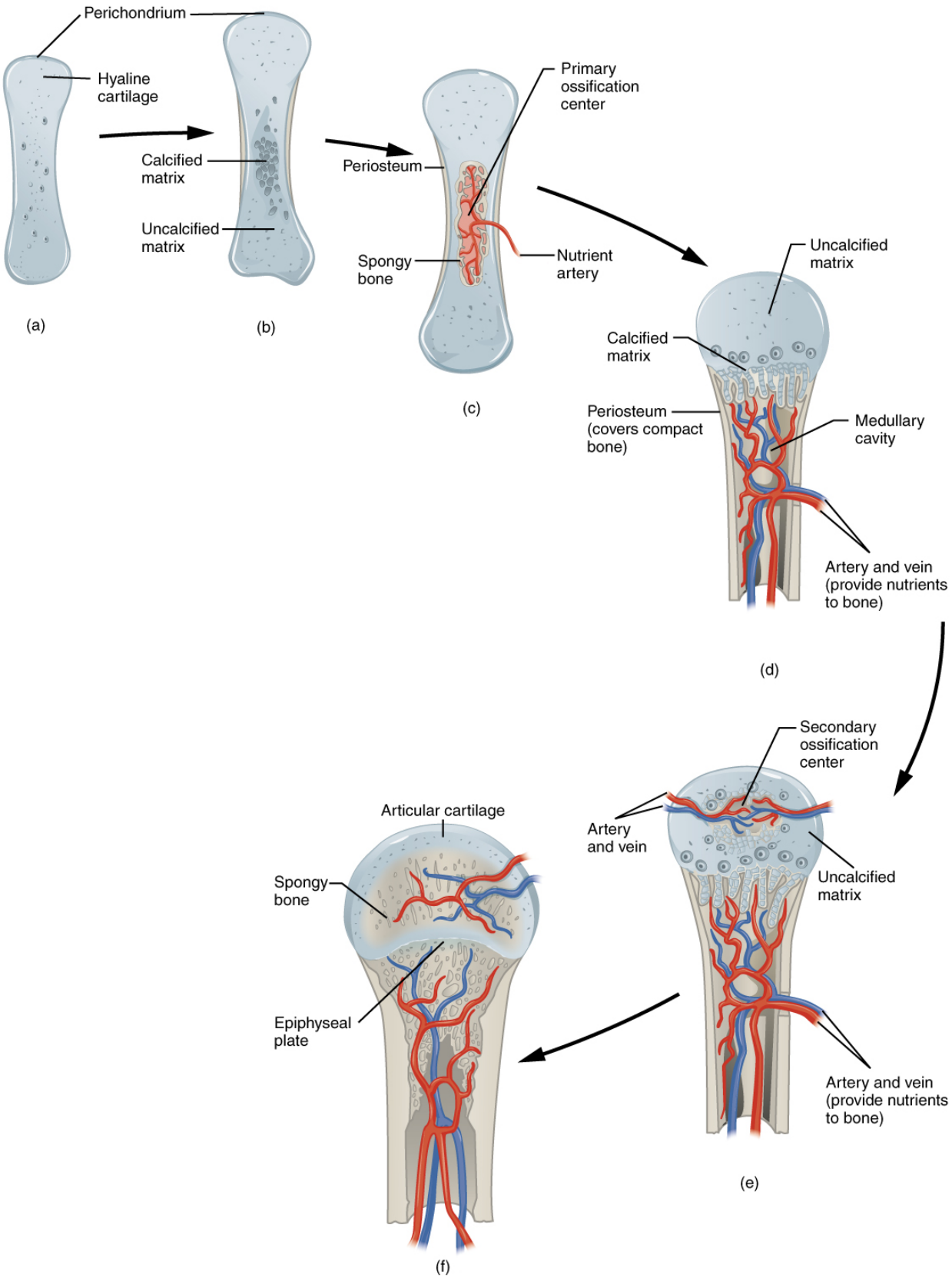


Figure 2. Endochondral Ossification. *Endochondral ossification follows five steps. (a) Mesenchymal cells differentiate into chondrocytes. (b) The cartilage model of the future bony skeleton and the perichondrium form. (c) Capillaries penetrate cartilage. Perichondrium transforms into periosteum. Periosteal collar develops. Primary ossification center develops. (d) Cartilage and*

chondrocytes continue to grow at ends of the bone. (e) Secondary ossification centers develop. (f) Cartilage remains at epiphyseal (growth) plate and at joint surface as articular cartilage.

As more matrix is produced, the chondrocytes in the center of the cartilaginous model grow in size. As the matrix calcifies, nutrients can no longer reach the chondrocytes. This results in their death and the disintegration of the surrounding cartilage. Blood vessels invade the resulting spaces, not only enlarging the cavities but also carrying osteogenic cells with them, many of which will become osteoblasts. These enlarging spaces eventually combine to become the medullary cavity.

As the cartilage grows, capillaries penetrate it. This penetration initiates the transformation of the perichondrium into the bone-producing periosteum. Here, the osteoblasts form a periosteal collar of compact bone around the cartilage of the diaphysis. By the second or third month of fetal life, bone cell development and ossification ramps up and creates the **primary ossification center**, a region deep in the periosteal collar where ossification begins (Figure 2c).

While these deep changes are occurring, chondrocytes and cartilage continue to grow at the ends of the bone (the future epiphyses), which increases the bone's length at the same time bone is replacing cartilage in the diaphyses. By the time the fetal skeleton is fully formed, cartilage only remains at the joint surface as articular cartilage and between the diaphysis and epiphysis as the epiphyseal plate, the latter of which is responsible for the longitudinal growth of bones. After birth, this same sequence of events (matrix mineralization, death of chondrocytes, invasion of blood vessels from the periosteum, and seeding with osteogenic cells that become osteoblasts) occurs in the epiphyseal regions, and each of these centers of activity is referred to as a **secondary ossification center** (Figure 2e).

How Bones Grow in Length

The epiphyseal plate is the area of growth in a long bone. It is a layer of hyaline cartilage where ossification occurs in immature bones. On the epiphyseal side of the epiphyseal plate, cartilage is formed. On the diaphyseal side, cartilage is ossified, and the diaphysis grows in length. The epiphyseal plate is composed of four zones of cells and activity (Figure 3). The **reserve zone** is the region closest to the epiphyseal end of the plate and contains small chondrocytes within the matrix. These chondrocytes do not participate in bone growth but secure the epiphyseal plate to the osseous tissue of the epiphysis.

The **proliferative zone** is the next layer toward the diaphysis and contains stacks of slightly larger chondrocytes. It makes new chondrocytes (via mitosis) to replace those that die at the diaphyseal end of the plate. Chondrocytes in the next layer, the **zone of maturation and hypertrophy**, are older and larger than those in the proliferative zone. The more mature cells are situated closer to the diaphyseal end of the plate. The longitudinal growth of bone is a result of cellular division in the proliferative zone and the maturation of cells in the zone of maturation and hypertrophy.

Most of the chondrocytes in the **zone of calcified matrix**, the zone closest to the diaphysis, are dead because the matrix around them has calcified. Capillaries and osteoblasts from the diaphysis penetrate this zone, and the osteoblasts secrete bone tissue on the remaining calcified cartilage. Thus, the zone of calcified matrix connects the epiphyseal plate to the diaphysis. A bone grows in length when osseous tissue is added to the diaphysis.

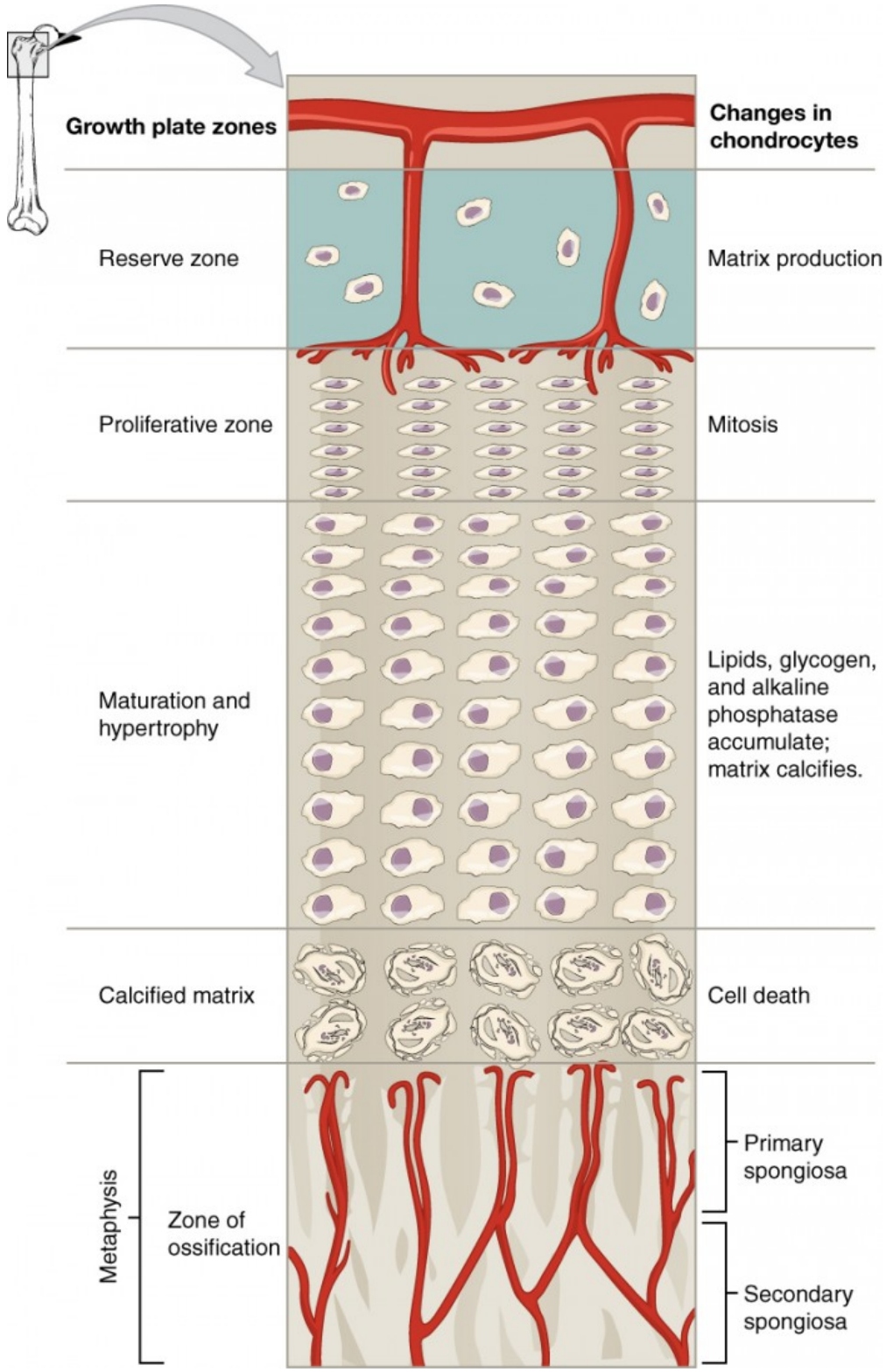


Figure 3. Longitudinal Bone Growth. *The epiphyseal plate is responsible for longitudinal bone growth.*

Bones continue to grow in length until early adulthood. The rate of growth is controlled by hormones, which will be discussed later. When the chondrocytes in the epiphyseal plate cease their proliferation and bone replaces the cartilage, longitudinal growth stops. All that remains of the epiphyseal plate is the **epiphyseal line** (Figure 4).

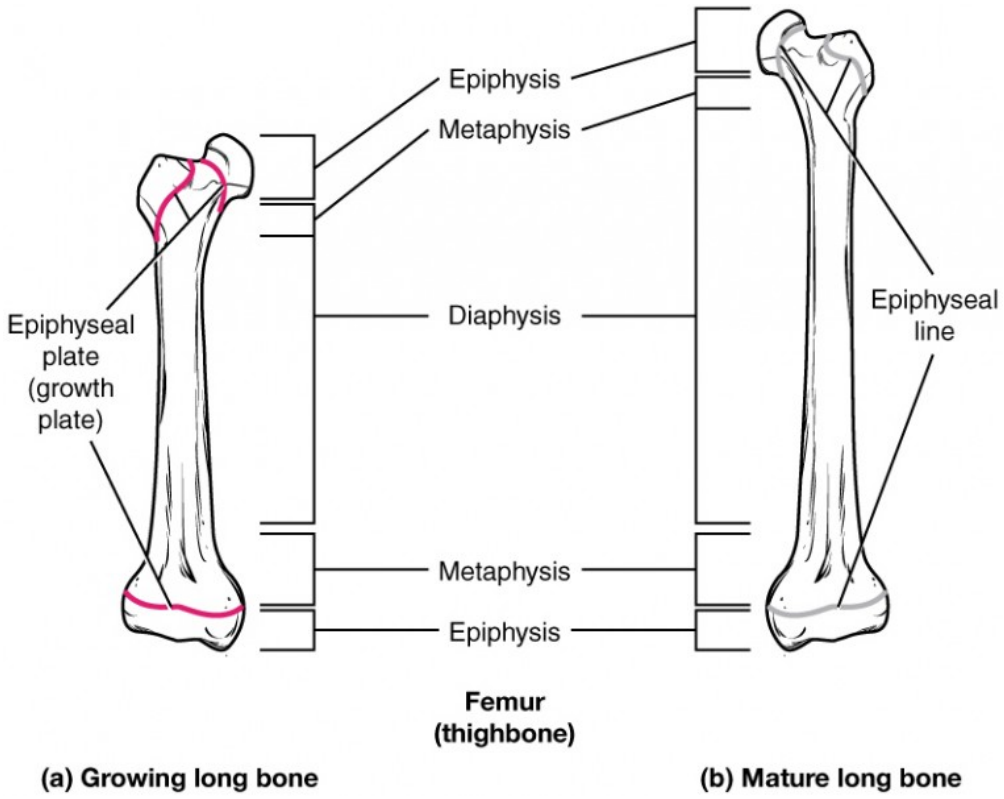


Figure 4. Progression from Epiphyseal Plate to Epiphyseal Line. *As a bone matures, the epiphyseal plate progresses to an epiphyseal line. (a) Epiphyseal plates are visible in a growing bone. (b) Epiphyseal lines are the remnants of epiphyseal plates in a mature bone.*

How Bones Grow in Diameter

While bones are increasing in length, they are also increasing in diameter; growth in diameter can continue even after longitudinal growth ceases. This is called appositional growth. Osteoclasts resorb old bone that lines the medullary cavity, while osteoblasts, via intramembranous ossification, produce new bone tissue beneath the periosteum. The erosion of old bone along the medullary cavity and the deposition of new bone beneath the periosteum not only increase the diameter of the diaphysis but also increase the diameter of the medullary cavity. This process is called **modeling**.

Bone Remodeling

The process in which matrix is resorbed on one surface of a bone and deposited on another is known as bone modeling. Modeling primarily takes place during a bone's growth. However, in adult life, bone undergoes **remodeling**, in which resorption of old or damaged bone takes place on the same surface where osteoblasts lay new bone to replace that which is resorbed. Injury, exercise, and other activities lead to remodeling. Those influences are discussed later in the chapter, but even without injury or exercise, about 5 to 10 percent of the skeleton is remodeled annually just by destroying old bone and renewing it with fresh bone.

Diseases of the Skeletal System

Osteogenesis imperfecta (OI) is a genetic disease in which bones do not form properly and therefore are fragile and break easily. It is also called brittle bone disease. The disease is present from birth and affects a person throughout life.

The genetic mutation that causes OI affects the body's production of collagen, one of the critical components of bone matrix. The severity of the disease can range from mild to severe. Those with the most severe forms of the disease sustain many more fractures than those with a mild form. Frequent and multiple fractures typically lead to bone deformities and short stature. Bowing of the long bones and curvature of the spine are also common in people afflicted with OI. Curvature of the spine makes breathing difficult because the lungs are compressed.

Because collagen is such an important structural protein in many parts of the body, people with OI may also experience fragile skin, weak muscles, loose joints, easy bruising, frequent nosebleeds, brittle teeth, blue sclera, and hearing loss. There is no known cure for OI. Treatment focuses on helping the person retain as much independence as possible while minimizing fractures and maximizing mobility. Toward that end, safe exercises, like swimming, in which the body is less likely to experience collisions or compressive forces, are recommended. Braces to support legs, ankles, knees, and wrists are used as needed. Canes, walkers, or wheelchairs can also help compensate for weaknesses.

When bones do break, casts, splints, or wraps are used. In some cases, metal rods may be surgically implanted into the long bones of the arms and legs. Research is currently being conducted on using bisphosphonates to treat OI. Smoking and being overweight are especially risky in people with OI, since smoking is known to weaken bones, and extra body weight puts additional stress on the bones.

Self-Check Questions

Visit your course online to take a quiz to check your understanding of Bone Formation and Development:

FRACTURES: BONE REPAIR

Learning Objectives

- Differentiate among the different types of fractures
- Describe the steps involved in bone repair

A **fracture** is a broken bone. It will heal whether or not a physician resets it in its anatomical position. If the bone is not reset correctly, the healing process will keep the bone in its deformed position.

When a broken bone is manipulated and set into its natural position without surgery, the procedure is called a **closed reduction**. **Open reduction** requires surgery to expose the fracture and reset the bone. While some fractures can be minor, others are quite severe and result in grave complications. For example, a fractured diaphysis of the femur has the potential to release fat globules into the bloodstream. These can become lodged in the capillary beds of the lungs, leading to respiratory distress and if not treated quickly, death.

Types of Fractures

Fractures are classified by their complexity, location, and other features (Figure 1). Table 1 outlines common types of fractures. Some fractures may be described using more than one term because it may have the features of more than one type (e.g., an open transverse fracture).

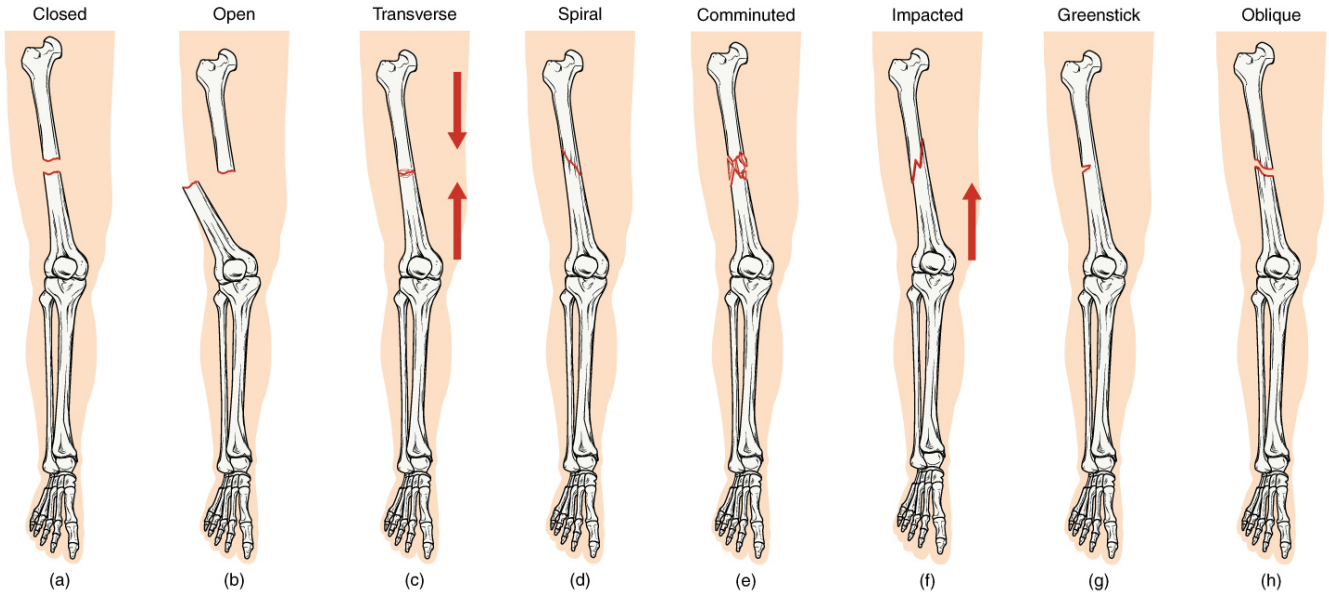


Figure 1. Types of Fractures. *Compare healthy bone with different types of fractures: (a) closed fracture, (b) open fracture, (c) transverse fracture, (d) spiral fracture, (e) comminuted fracture, (f) impacted fracture, (g) greenstick fracture, and (h) oblique fracture.*

Table 1. Types of Fractures	
Type of fracture	**Description**
Transverse	Occurs straight across the long axis of the bone
Oblique	Occurs at an angle that is not 90 degrees
Spiral	Bone segments are pulled apart as a result of a twisting motion
Comminuted	Several breaks result in many small pieces between two large segments
Impacted	One fragment is driven into the other, usually as a result of compression
Greenstick	A partial fracture in which only one side of the bone is broken
Open (or compound)	A fracture in which at least one end of the broken bone tears through the skin; carries a high risk of infection
Closed (or simple)	A fracture in which the skin remains intact

Bone Repair

When a bone breaks, blood flows from any vessel torn by the fracture. These vessels could be in the periosteum, osteons, and/or medullary cavity. The blood begins to clot, and about six to eight hours after the fracture, the clotting blood has formed a **fracture hematoma** (Figure 2). The disruption of blood flow to the bone results in the death of bone cells around the fracture.

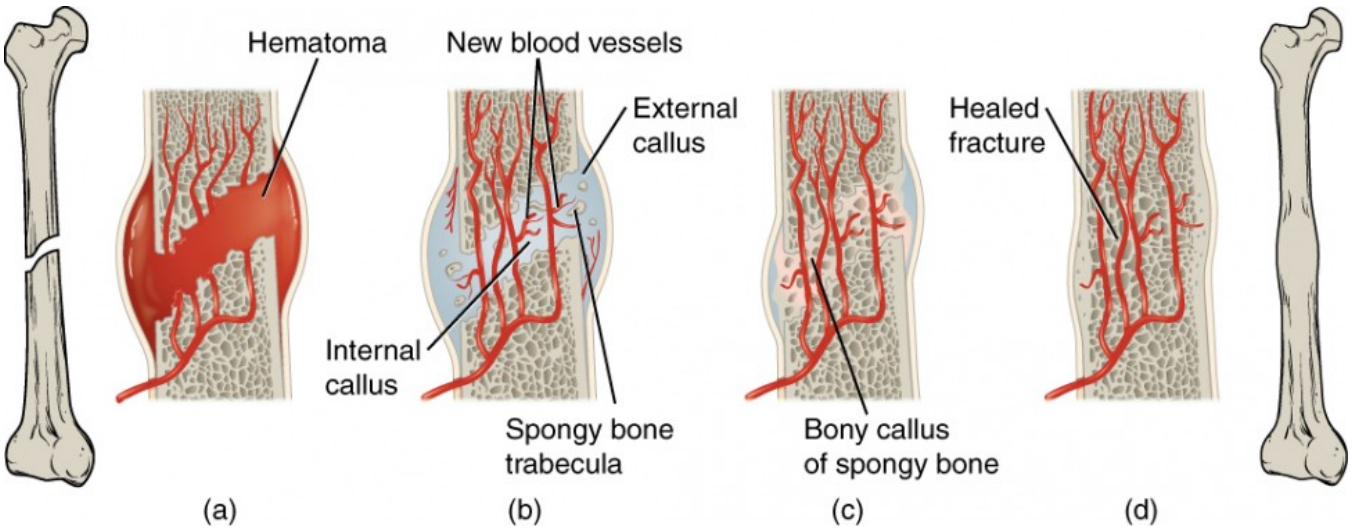


Figure 2 Stages in Fracture Repair. *The healing of a bone fracture follows a series of progressive steps: (a) A fracture hematoma forms. (b) Internal and external calli form. (c) Cartilage of the calli is replaced by trabecular bone. (d) Remodeling occurs.*

Within about 48 hours after the fracture, chondrocytes from the endosteum have created an **internal callus** (plural = *calli*) by secreting a fibrocartilaginous matrix between the two ends of the broken bone, while the periosteal chondrocytes and osteoblasts create an **external callus** of hyaline cartilage and bone, respectively, around the outside of the break (Figure 2b). This stabilizes the fracture.

Over the next several weeks, osteoclasts resorb the dead bone; osteogenic cells become active, divide, and differentiate into osteoblasts. The cartilage in the calli is replaced by trabecular bone via endochondral ossification (Figure 2c).

Eventually, the internal and external calli unite, compact bone replaces spongy bone at the outer margins of the fracture, and healing is complete. A slight swelling may remain on the outer surface of the bone, but quite often, that region undergoes remodeling (Figure 2d), and no external evidence of the fracture remains.

Visit this website to review different types of fractures and then take a short self-assessment quiz.

EXERCISE, NUTRITION, HORMONES, AND BONE TISSUE

Learning Objectives

- Describe the effect exercise has on bone tissue
- List the nutrients that affect bone health
- Discuss the role those nutrients play in bone health
- Describe the effects of hormones on bone tissue

All of the organ systems of your body are interdependent, and the skeletal system is no exception. The food you take in via your digestive system and the hormones secreted by your endocrine system affect your bones. Even using your muscles to engage in exercise has an impact on your bones.

Exercise and Bone Tissue

During long space missions, astronauts can lose approximately 1 to 2 percent of their bone mass per month. This loss of bone mass is thought to be caused by the lack of mechanical stress on astronauts' bones due to the low gravitational forces in space. Lack of mechanical stress causes bones to lose mineral salts and collagen fibers, and thus strength. Similarly, mechanical stress stimulates the deposition of mineral salts and collagen fibers. The internal and external structure of a bone will change as stress increases or decreases so that the bone is an ideal size and weight for the amount of activity it endures. That is why people who exercise regularly have thicker bones than people who are more sedentary. It is also why a broken bone in a cast atrophies while its contralateral mate maintains its concentration of mineral salts and collagen fibers. The bones undergo remodeling as a result of forces (or lack of forces) placed on them.

Numerous, controlled studies have demonstrated that people who exercise regularly have greater bone density than those who are more sedentary. Any type of exercise will stimulate the deposition of more bone tissue, but resistance training has a greater effect than cardiovascular activities. Resistance training is especially important to slow down the eventual bone loss due to aging and for preventing osteoporosis.

Nutrition and Bone Tissue

The vitamins and minerals contained in all of the food we consume are important for all of our organ systems. However, there are certain nutrients that affect bone health.

Calcium and Vitamin D

You already know that calcium is a critical component of bone, especially in the form of calcium phosphate and calcium carbonate. Since the body cannot make calcium, it must be obtained from the diet. However, calcium cannot be absorbed from the small intestine without vitamin D. Therefore, intake of vitamin D is also critical to bone health. In addition to vitamin D's role in calcium absorption, it also plays a role, though not as clearly understood, in bone remodeling.

Milk and other dairy foods are not the only sources of calcium. This important nutrient is also found in green leafy vegetables, broccoli, and intact salmon and canned sardines with their soft bones. Nuts, beans, seeds, and shellfish provide calcium in smaller quantities.

Except for fatty fish like salmon and tuna, or fortified milk or cereal, vitamin D is not found naturally in many foods. The action of sunlight on the skin triggers the body to produce its own vitamin D (Figure 1), but many people, especially those of darker complexion and those living in northern latitudes where the sun's rays are not as strong, are deficient in vitamin D. In cases of deficiency, a doctor can prescribe a vitamin D supplement.

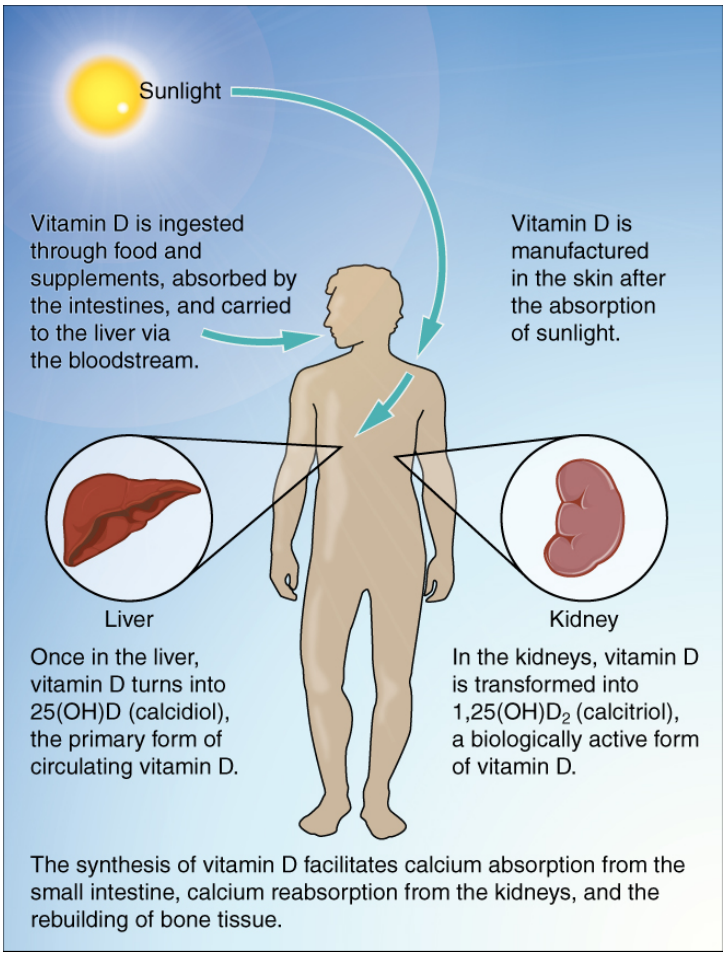


Figure 1. Synthesis of Vitamin D. *Sunlight is one source of vitamin D.*

Other Nutrients

Vitamin K also supports bone mineralization and may have a synergistic role with vitamin D in the regulation of bone growth. Green leafy vegetables are a good source of vitamin K.

The minerals magnesium and fluoride may also play a role in supporting bone health. While magnesium is only found in trace amounts in the human body, more than 60 percent of it is in the skeleton, suggesting it plays a role in the structure of bone. Fluoride can displace the hydroxyl group in bone's hydroxyapatite crystals and form fluorapatite. Similar to its effect on dental enamel, fluorapatite helps stabilize and strengthen bone mineral. Fluoride can also enter spaces within hydroxyapatite crystals, thus increasing their density.

Omega-3 fatty acids have long been known to reduce inflammation in various parts of the body. Inflammation can interfere with the function of osteoblasts, so consuming omega-3 fatty acids, in the diet or in supplements, may also help enhance production of new osseous tissue. Table 1 summarizes the role of nutrients in bone health.

Table 1. Nutrients and Bone Health

Nutrient	Role in bone health
Calcium	Needed to make calcium phosphate and calcium carbonate, which form the hydroxyapatite crystals that give bone its hardness
Vitamin D	Needed for calcium absorption
Vitamin K	Supports bone mineralization; may have synergistic effect with vitamin D
Magnesium	Structural component of bone
Fluoride	Structural component of bone
Omega-3 fatty acids	Reduces inflammation that may interfere with osteoblast function

Hormones and Bone Tissue

The endocrine system produces and secretes hormones, many of which interact with the skeletal system. These hormones are involved in controlling bone growth, maintaining bone once it is formed, and remodeling it.

Hormones That Influence Osteoblasts and/or Maintain the Matrix

Several hormones are necessary for controlling bone growth and maintaining the bone matrix. The pituitary gland secretes growth hormone (GH), which, as its name implies, controls bone growth in several ways. It triggers chondrocyte proliferation in epiphyseal plates, resulting in the increasing length of long bones. GH also increases calcium retention, which enhances mineralization, and stimulates osteoblastic activity, which improves bone density.

GH is not alone in stimulating bone growth and maintaining osseous tissue. Thyroxine, a hormone secreted by the thyroid gland promotes osteoblastic activity and the synthesis of bone matrix. During puberty, the sex hormones (estrogen in girls, testosterone in boys) also come into play. They too promote osteoblastic activity and production of bone matrix, and in addition, are responsible for the growth spurt that often occurs during adolescence. They also promote the conversion of the epiphyseal plate to the epiphyseal line (i.e., cartilage to its bony remnant), thus bringing an end to the longitudinal growth of bones. Additionally, calcitriol, the active form of vitamin D, is produced by the kidneys and stimulates the absorption of calcium and phosphate from the digestive tract.

Aging and the Skeletal System

Osteoporosis is a disease characterized by a decrease in bone mass that occurs when the rate of bone resorption exceeds the rate of bone formation, a common occurrence as the body ages. Notice how this is different from Paget's disease. In Paget's disease, new bone is formed in an attempt to keep up with the resorption by the overactive osteoclasts, but that new bone is produced haphazardly. In fact, when a physician is evaluating a patient with thinning bone, he or she will test for osteoporosis and Paget's disease (as well as other diseases). Osteoporosis does not have the elevated blood levels of alkaline phosphatase found in Paget's disease.

While osteoporosis can involve any bone, it most commonly affects the proximal ends of the femur, vertebrae, and wrist. As a result of the loss of bone density, the osseous tissue may not provide adequate support for everyday functions, and something as simple as a sneeze can cause a vertebral fracture. When an elderly person falls and breaks a hip (really, the femur), it is very likely the femur that broke first, which resulted in the fall. Histologically, osteoporosis is characterized by a reduction in the thickness of compact bone and the number and size of trabeculae in cancellous bone.

Figure 2 shows that women lose bone mass more quickly than men starting at about 50 years of age. This occurs because 50 is the approximate age at which women go through menopause. Not only do their menstrual periods lessen and eventually cease, but their ovaries reduce in size and then cease the production of estrogen, a hormone that promotes osteoblastic activity and production of bone matrix. Thus, osteoporosis is more common in women than in men, but men can develop it, too. Anyone with a family history of osteoporosis has a greater risk of developing the disease, so the best treatment is prevention, which should start with a childhood diet that includes adequate intake of calcium and vitamin D and a lifestyle that includes weight-bearing exercise. These actions, as discussed above, are important in building bone mass. Promoting proper nutrition and weight-bearing exercise early in life can maximize bone mass before the age of 30, thus reducing the risk of osteoporosis.

For many elderly people, a hip fracture can be life threatening. The fracture itself may not be serious, but the immobility that comes during the healing process can lead to the formation of blood clots that can lodge in the capillaries of the lungs, resulting in respiratory failure; pneumonia due to the lack of poor air exchange that accompanies immobility; pressure sores (bed sores) that allow pathogens to enter the body and cause infections; and urinary tract infections from catheterization.

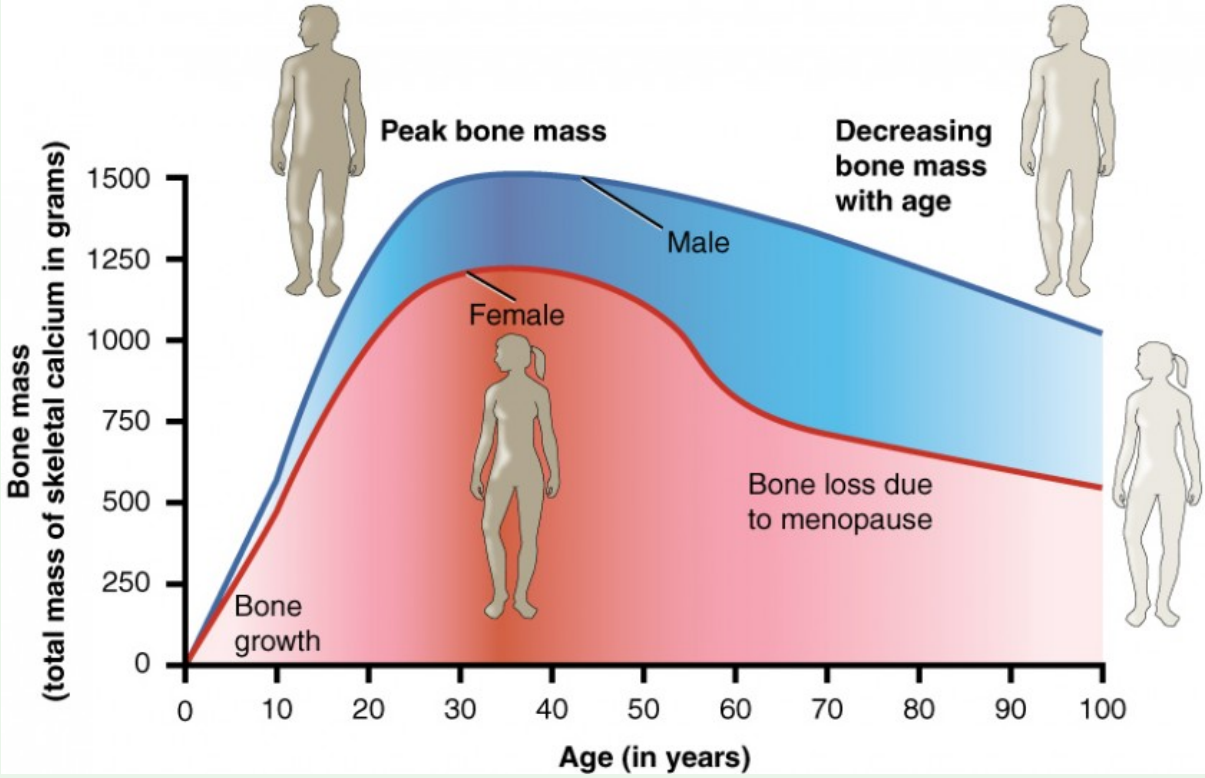


Figure 2. Graph Showing Relationship Between Age and Bone Mass. *Bone density peaks at about 30 years of age. Women lose bone mass more rapidly than men.*

Current treatments for managing osteoporosis include bisphosphonates (the same medications often used in Paget's disease), calcitonin, and estrogen (for women only). Minimizing the risk of falls, for example, by removing tripping hazards, is also an important step in managing the potential outcomes from the disease.

Hormones That Influence Osteoclasts

Bone modeling and remodeling require osteoclasts to resorb unneeded, damaged, or old bone, and osteoblasts to lay down new bone. Two hormones that affect the osteoclasts are parathyroid hormone (PTH) and calcitonin.

PTH stimulates osteoclast proliferation and activity. As a result, calcium is released from the bones into the circulation, thus increasing the calcium ion concentration in the blood. PTH also promotes the reabsorption of calcium by the kidney tubules, which can affect calcium homeostasis (see below).

The small intestine is also affected by PTH, albeit indirectly. Because another function of PTH is to stimulate the synthesis of vitamin D, and because vitamin D promotes intestinal absorption of calcium, PTH indirectly increases calcium uptake by the small intestine. Calcitonin, a hormone secreted by the thyroid gland, has some effects that counteract those of PTH. Calcitonin inhibits osteoclast activity and stimulates calcium uptake by the bones, thus reducing the concentration of calcium ions in the blood. As evidenced by their opposing functions in maintaining calcium homeostasis, PTH and calcitonin are generally *not* secreted at the same time. Table 2 summarizes the hormones that influence the skeletal system.

Table 2. Hormones That Affect the Skeletal System

Hormone	Role
Growth hormone	Increases length of long bones, enhances mineralization, and improves bone density

Table 2. Hormones That Affect the Skeletal System	
Hormone	**Role**
Thyroxine	Stimulates bone growth and promotes synthesis of bone matrix
Sex hormones	Promote osteoblastic activity and production of bone matrix; responsible for adolescent growth spurt; promote conversion of epiphyseal plate to epiphyseal line
Calcitriol	Stimulates absorption of calcium and phosphate from digestive tract
Parathyroid hormone	Stimulates osteoclast proliferation and resorption of bone by osteoclasts; promotes reabsorption of calcium by kidney tubules; indirectly increases calcium absorption by small intestine
Calcitonin	Inhibits osteoclast activity and stimulates calcium uptake by bones

CALCIUM HOMEOSTASIS: INTERACTIONS OF THE SKELETAL SYSTEM AND OTHER ORGAN SYSTEMS

Learning Objectives

- Describe the effect of too much or too little calcium on the body
- Explain the process of calcium homeostasis

Calcium is not only the most abundant mineral in bone, it is also the most abundant mineral in the human body. Calcium ions are needed not only for bone mineralization but for tooth health, regulation of the heart rate and strength of contraction, blood coagulation, contraction of smooth and skeletal muscle cells, and regulation of nerve impulse conduction. The normal level of calcium in the blood is about 10 mg/dL. When the body cannot maintain this level, a person will experience hypo- or hypercalcemia.

Hypocalcemia, a condition characterized by abnormally low levels of calcium, can have an adverse effect on a number of different body systems including circulation, muscles, nerves, and bone. Without adequate calcium, blood has difficulty coagulating, the heart may skip beats or stop beating altogether, muscles may have difficulty contracting, nerves may have difficulty functioning, and bones may become brittle. The causes of hypocalcemia can range from hormonal imbalances to an improper diet. Treatments vary according to the cause, but prognoses are generally good.

Conversely, in **hypercalcemia**, a condition characterized by abnormally high levels of calcium, the nervous system is underactive, which results in lethargy, sluggish reflexes, constipation and loss of appetite, confusion, and in severe cases, coma.

Obviously, calcium homeostasis is critical. The skeletal, endocrine, and digestive systems play a role in this, but the kidneys do, too. These body systems work together to maintain a normal calcium level in the blood (Figure 1).

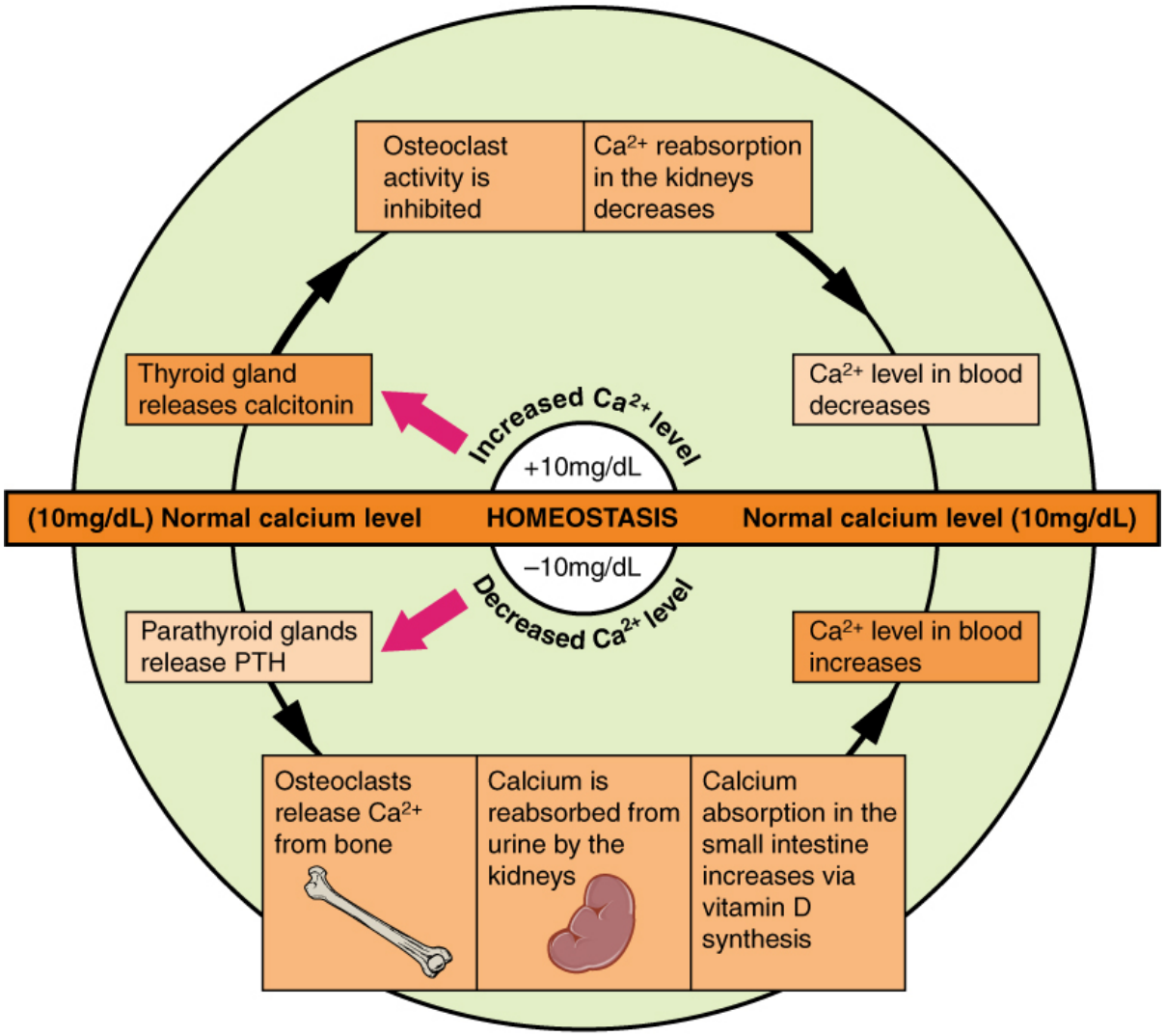


Figure 1. Pathways in Calcium Homeostasis. *The body regulates calcium homeostasis with two pathways; one is signaled to turn on when blood calcium levels drop below normal and one is the pathway that is signaled to turn on when blood calcium levels are elevated.*

Calcium is a chemical element that cannot be produced by any biological processes. The only way it can enter the body is through the diet. The bones act as a storage site for calcium: The body deposits calcium in the bones when blood levels get too high, and it releases calcium when blood levels drop too low. This process is regulated by PTH, vitamin D, and calcitonin.

Cells of the parathyroid gland have plasma membrane receptors for calcium. When calcium is not binding to these receptors, the cells release PTH, which stimulates osteoclast proliferation and resorption of bone by osteoclasts. This demineralization process releases calcium into the blood. PTH promotes reabsorption of calcium from the urine by the kidneys, so that the calcium returns to the blood. Finally, PTH stimulates the synthesis of vitamin D, which in turn, stimulates calcium absorption from any digested food in the small intestine.

When all these processes return blood calcium levels to normal, there is enough calcium to bind with the receptors on the surface of the cells of the parathyroid glands, and this cycle of events is turned off (Figure 1).

When blood levels of calcium get too high, the thyroid gland is stimulated to release calcitonin (Figure 1), which inhibits osteoclast activity and stimulates calcium uptake by the bones, but also decreases reabsorption of calcium by the kidneys. All of these actions lower blood levels of calcium. When blood calcium levels return to normal, the thyroid gland stops secreting calcitonin.

Self-Check Questions

Visit your course online to take a quiz to check your understanding of Calcium Homeostasis:

VIDEO: GENERAL SKELETON TUTORIAL

Watch this video online: https://youtu.be/floBoGSPkws

GLOSSARY: BONE TISSUE

articular cartilage: thin layer of cartilage covering an epiphysis; reduces friction and acts as a shock absorber

articulation: where two bone surfaces meet

bone: hard, dense connective tissue that forms the structural elements of the skeleton

canaliculi: (singular = canaliculus) channels within the bone matrix that house one of an osteocyte's many cytoplasmic extensions that it uses to communicate and receive nutrients

cartilage: semi-rigid connective tissue found on the skeleton in areas where flexibility and smooth surfaces support movement

central canal: longitudinal channel in the center of each osteon; contains blood vessels, nerves, and lymphatic vessels; also known as the Haversian canal

closed reduction: manual manipulation of a broken bone to set it into its natural position without surgery

compact bone: dense osseous tissue that can withstand compressive forces

diaphysis: tubular shaft that runs between the proximal and distal ends of a long bone

diploë: layer of spongy bone, that is sandwiched between two the layers of compact bone found in flat bones

endochondral ossification: process in which bone forms by replacing hyaline cartilage

endosteum: delicate membranous lining of a bone's medullary cavity

epiphyseal line: completely ossified remnant of the epiphyseal plate

epiphyseal plate: (also, growth plate) sheet of hyaline cartilage in the metaphysis of an immature bone; replaced by bone tissue as the organ grows in length

epiphysis: wide section at each end of a long bone; filled with spongy bone and red marrow

external callus: collar of hyaline cartilage and bone that forms around the outside of a fracture

flat bone: thin and curved bone; serves as a point of attachment for muscles and protects internal organs

fracture hematoma: blood clot that forms at the site of a broken bone

fracture: broken bone

hematopoiesis: production of blood cells, which occurs in the red marrow of the bones

hole: opening or depression in a bone

hypercalcemia: condition characterized by abnormally high levels of calcium

hypocalcemia: condition characterized by abnormally low levels of calcium

internal callus: fibrocartilaginous matrix, in the endosteal region, between the two ends of a broken bone

intramembranous ossification: process by which bone forms directly from mesenchymal tissue

irregular bone: bone of complex shape; protects internal organs from compressive forces

lacunae: (singular = lacuna) spaces in a bone that house an osteocyte

long bone: cylinder-shaped bone that is longer than it is wide; functions as a lever

medullary cavity: hollow region of the diaphysis; filled with yellow marrow

modeling: process, during bone growth, by which bone is resorbed on one surface of a bone and deposited on another

nutrient foramen: small opening in the middle of the external surface of the diaphysis, through which an artery enters the bone to provide nourishment

open reduction: surgical exposure of a bone to reset a fracture

orthopedist: doctor who specializes in diagnosing and treating musculoskeletal disorders and injuries

osseous tissue: bone tissue; a hard, dense connective tissue that forms the structural elements of the skeleton

ossification center: cluster of osteoblasts found in the early stages of intramembranous ossification

ossification: (also, osteogenesis) bone formation

osteoblast: cell responsible for forming new bone

osteoclast: cell responsible for resorbing bone

osteocyte: primary cell in mature bone; responsible for maintaining the matrix

osteogenic cell: undifferentiated cell with high mitotic activity; the only bone cells that divide; they differentiate and develop into osteoblasts

osteoid: uncalcified bone matrix secreted by osteoblasts

osteon: (also, Haversian system) basic structural unit of compact bone; made of concentric layers of calcified matrix

osteoporosis: disease characterized by a decrease in bone mass; occurs when the rate of bone resorption exceeds the rate of bone formation, a common occurrence as the body ages

perforating canal: (also, Volkmann's canal) channel that branches off from the central canal and houses vessels and nerves that extend to the periosteum and endosteum

perichondrium: membrane that covers cartilage

periosteum: fibrous membrane covering the outer surface of bone and continuous with ligaments

primary ossification center: region, deep in the periosteal collar, where bone development starts during endochondral ossification

projection: bone markings where part of the surface sticks out above the rest of the surface, where tendons and ligaments attach

proliferative zone: region of the epiphyseal plate that makes new chondrocytes to replace those that die at the diaphyseal end of the plate and contributes to longitudinal growth of the epiphyseal plate

red marrow: connective tissue in the interior cavity of a bone where hematopoiesis takes place

remodeling: process by which osteoclasts resorb old or damaged bone at the same time as and on the same surface where osteoblasts form new bone to replace that which is resorbed

reserve zone: region of the epiphyseal plate that anchors the plate to the osseous tissue of the epiphysis

secondary ossification center: region of bone development in the epiphyses

sesamoid bone: small, round bone embedded in a tendon; protects the tendon from compressive forces

short bone: cube-shaped bone that is approximately equal in length, width, and thickness; provides limited motion

skeletal system: organ system composed of bones and cartilage that provides for movement, support, and protection

spongy bone: (also, cancellous bone) trabeculated osseous tissue that supports shifts in weight distribution

trabeculae: (singular = trabecula) spikes or sections of the lattice-like matrix in spongy bone

yellow marrow: connective tissue in the interior cavity of a bone where fat is stored

zone of calcified matrix: region of the epiphyseal plate closest to the diaphyseal end; functions to connect the epiphyseal plate to the diaphysis

zone of maturation and hypertrophy: region of the epiphyseal plate where chondrocytes from the proliferative zone grow and mature and contribute to the longitudinal growth of the epiphyseal plate

PRACTICE TEST: BONE TISSUE AND THE SKELETAL SYSTEM

Review the material from this module by completing the practice in course online.

MODULE 8: AXIAL SKELETON

INTRODUCTION TO THE AXIAL SKELETON

Learning Objectives

- Describe the functions of the skeletal system and define its two major subdivisions
- Identify the bones and bony structures of the skull, the cranial suture lines, the cranial fossae, and the openings in the skull
- Discuss the vertebral column and regional variations in its bony components and curvatures
- Describe the components of the thoracic cage
- Discuss the embryonic development of the axial skeleton

The skeletal system forms the rigid internal framework of the body. It consists of the bones, cartilages, and ligaments. Bones support the weight of the body, allow for body movements, and protect internal organs. Cartilage provides flexible strength and support for body structures such as the thoracic cage, the external ear, and the trachea and larynx. At joints of the body, cartilage can also unite adjacent bones or provide cushioning between them. Ligaments are the strong connective tissue bands that hold the bones at a moveable joint together and serve to prevent excessive movements of the joint that would result in injury. Providing movement of the skeleton are the muscles of the body, which are firmly attached to the skeleton via connective tissue structures called tendons. As muscles contract, they pull on the bones to produce movements of the body. Thus, without a skeleton, you would not be able to stand, run, or even feed yourself!

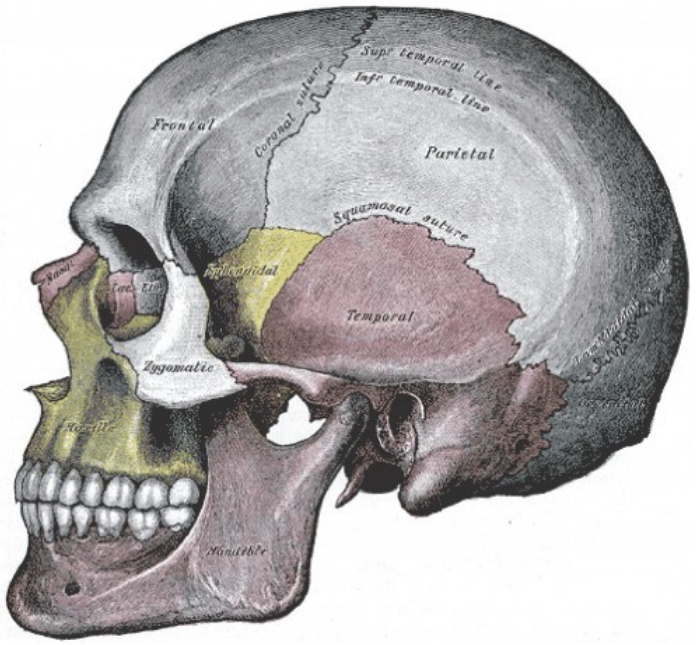


Figure 1. Lateral View of the Human Skull.

Each bone of the body serves a particular function, and therefore bones vary in size, shape, and strength based on these functions. For example, the bones of the lower back and lower limb are thick and strong to support your body weight. Similarly, the size of a bony landmark that serves as a muscle attachment site on an individual bone is related to the strength of this muscle. Muscles can apply very strong pulling forces to the bones of the skeleton. To resist these forces, bones have enlarged bony landmarks at sites where powerful muscles attach. This means that not only the size of a bone, but also its shape, is related to its function. For this reason, the identification of bony landmarks is important during your study of the skeletal system.

Bones are also dynamic organs that can modify their strength and thickness in response to changes in muscle strength or body weight. Thus, muscle attachment sites on bones will thicken if you begin a workout program that increases muscle strength. Similarly, the walls of weight-bearing bones will thicken if you gain body weight or begin pounding the pavement as part of a new running regimen. In contrast, a reduction in muscle strength or body weight will cause bones to become thinner. This may happen during a prolonged hospital stay, following limb immobilization in a cast, or going into the weightlessness of outer space. Even a change in diet, such as eating only soft food due to the loss of teeth, will result in a noticeable decrease in the size and thickness of the jaw bones.

DIVISIONS OF THE SKELETAL SYSTEM

Learning Objectives

- Discuss the functions of the skeletal system
- Distinguish between the axial skeleton and appendicular skeleton
- Define the axial skeleton and its components
- Define the appendicular skeleton and its components

The skeletal system includes all of the bones, cartilages, and ligaments of the body that support and give shape to the body and body structures. The **skeleton** consists of the bones of the body. For adults, there are 206 bones in the skeleton. Younger individuals have higher numbers of bones because some bones fuse together during childhood and adolescence to form an adult bone. The primary functions of the skeleton are to provide a rigid, internal structure that can support the weight of the body against the force of gravity, and to provide a structure upon which muscles can act to produce movements of the body. The lower portion of the skeleton is specialized for stability during walking or running. In contrast, the upper skeleton has greater mobility and ranges of motion, features that allow you to lift and carry objects or turn your head and trunk.

In addition to providing for support and movements of the body, the skeleton has protective and storage functions. It protects the internal organs, including the brain, spinal cord, heart, lungs, and pelvic organs. The bones of the skeleton serve as the primary storage site for important minerals such as calcium and phosphate. The bone marrow found within bones stores fat and houses the blood-cell producing tissue of the body.

The skeleton is subdivided into two major divisions—the axial and appendicular.

The Axial Skeleton

The skeleton is subdivided into two major divisions—the axial and appendicular. The **axial skeleton** forms the vertical, central axis of the body and includes all bones of the head, neck, chest, and back (Figure 1). It serves to protect the brain, spinal cord, heart, and lungs. It also serves as the attachment site for muscles that move the head, neck, and back, and for muscles that act across the shoulder and hip joints to move their corresponding limbs.

The axial skeleton of the adult consists of 80 bones, including the **skull**, the **vertebral column**, and the **thoracic cage**. The skull is formed by 22 bones. Also associated with the head are an additional seven bones, including the **hyoid bone** and the **ear ossicles** (three small bones found in each middle ear). The vertebral column consists of 24 bones, each called a **vertebra**, plus the **sacrum** and **coccyx**. The thoracic cage includes the 12 pairs of **ribs**, and the **sternum**, the flattened bone of the anterior chest.

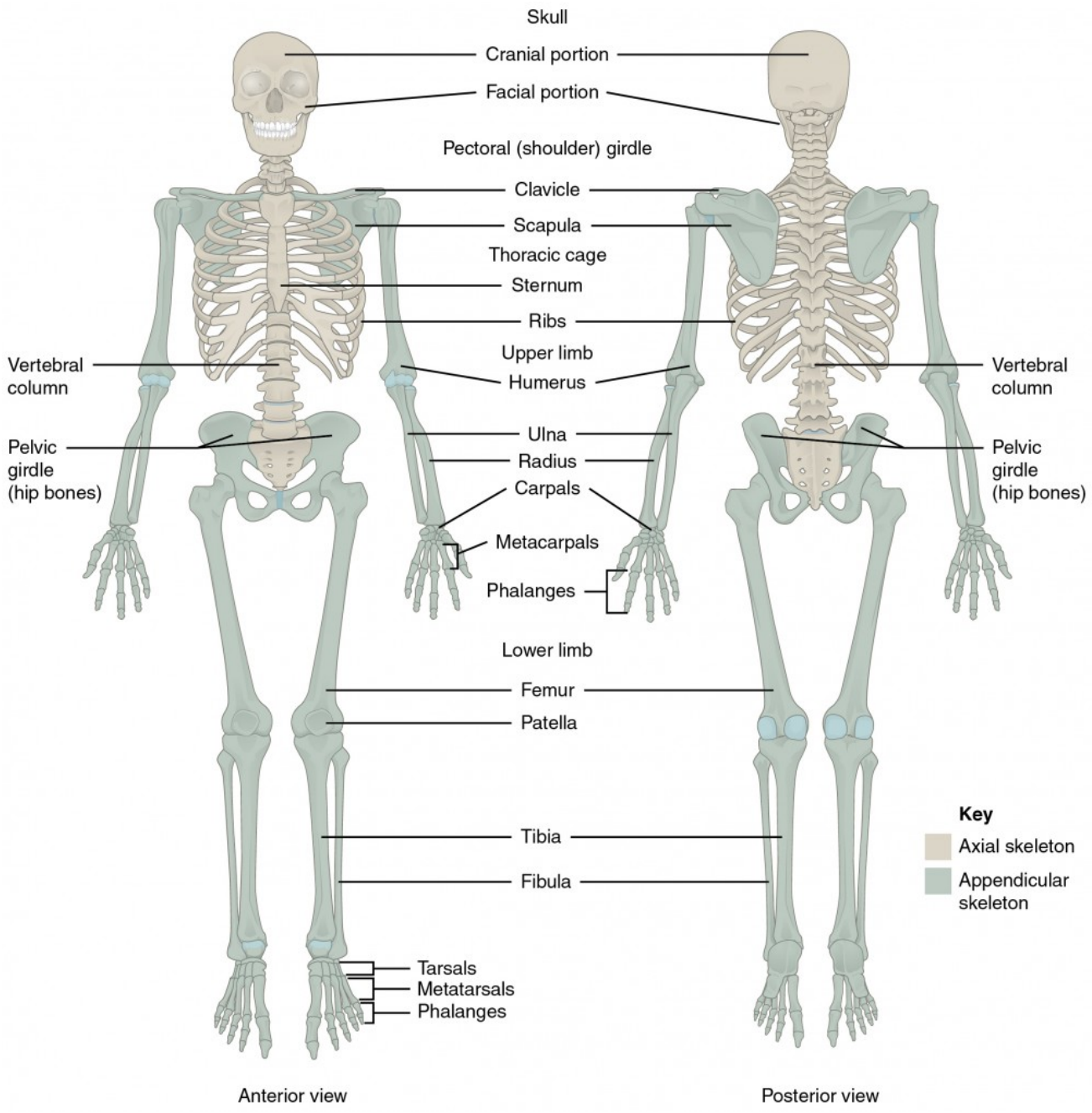


Figure 1. Axial and Appendicular Skeleton. *The axial skeleton supports the head, neck, back, and chest and thus forms the vertical axis of the body. It consists of the skull, vertebral column (including the sacrum and coccyx), and the thoracic cage, formed by the ribs and sternum. The appendicular skeleton is made up of all bones of the upper and lower limbs.*

The Appendicular Skeleton

The **appendicular skeleton** includes all bones of the upper and lower limbs, plus the bones that attach each limb to the axial skeleton. There are 126 bones in the appendicular skeleton of an adult. The bones of the appendicular skeleton are covered in a separate chapter.

THE SKULL

Learning Objectives

- List and identify the bones of the brain case and face
- Locate the major suture lines of the skull and name the bones associated with each
- Locate and define the boundaries of the anterior, middle, and posterior cranial fossae, the temporal fossa, and infratemporal fossa
- Define the paranasal sinuses and identify the location of each
- Name the bones that make up the walls of the orbit and identify the openings associated with the orbit
- Identify the bones and structures that form the nasal septum and nasal conchae, and locate the hyoid bone
- Identify the bony openings of the skull

The **cranium** (skull) is the skeletal structure of the head that supports the face and protects the brain. It is subdivided into the **facial bones** and the **brain case**, or cranial vault (Figure 1). The facial bones underlie the facial structures, form the nasal cavity, enclose the eyeballs, and support the teeth of the upper and lower jaws. The rounded brain case surrounds and protects the brain and houses the middle and inner ear structures.

In the adult, the skull consists of 22 individual bones, 21 of which are immobile and united into a single unit. The 22nd bone is the **mandible** (lower jaw), which is the only moveable bone of the skull.

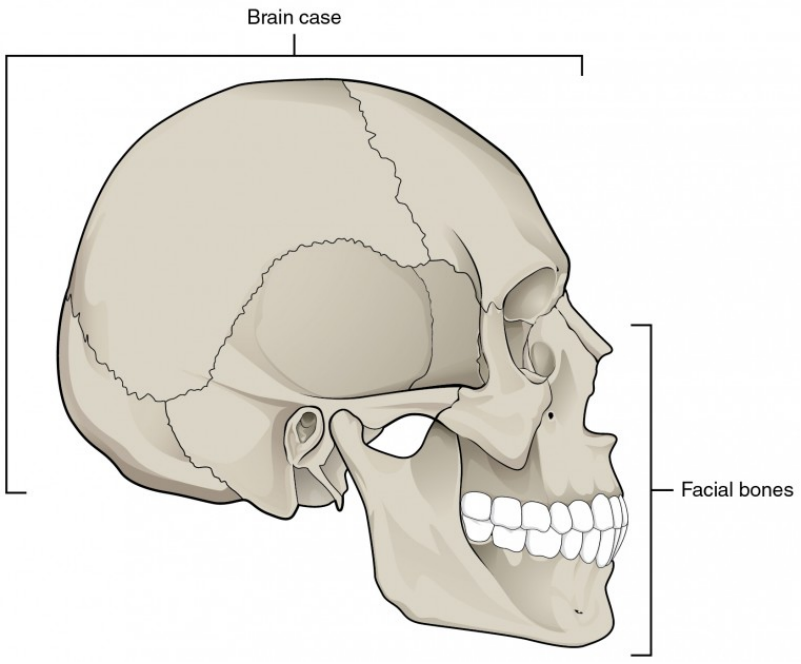


Figure 1. Parts of the Skull. *The skull consists of the rounded brain case that houses the brain and the facial bones that form the upper and lower jaws, nose, orbits, and other facial structures.*

Watch this video to view a rotating and exploded skull, with color-coded bones. Which bone (yellow) is centrally located and joins with most of the other bones of the skull?

Watch this video online: https://youtu.be/FrpVzSK23Q0

Anterior View of Skull

The anterior skull consists of the facial bones and provides the bony support for the eyes and structures of the face. This view of the skull is dominated by the openings of the orbits and the nasal cavity. Also seen are the upper and lower jaws, with their respective teeth (Figure 2).

The **orbit** is the bony socket that houses the eyeball and muscles that move the eyeball or open the upper eyelid. The upper margin of the anterior orbit is the **supraorbital margin**. Located near the midpoint of the supraorbital margin is a small opening called the **supraorbital foramen**. This provides for passage of a sensory nerve to the skin of the forehead. Below the orbit is the **infraorbital foramen**, which is the point of emergence for a sensory nerve that supplies the anterior face below the orbit.

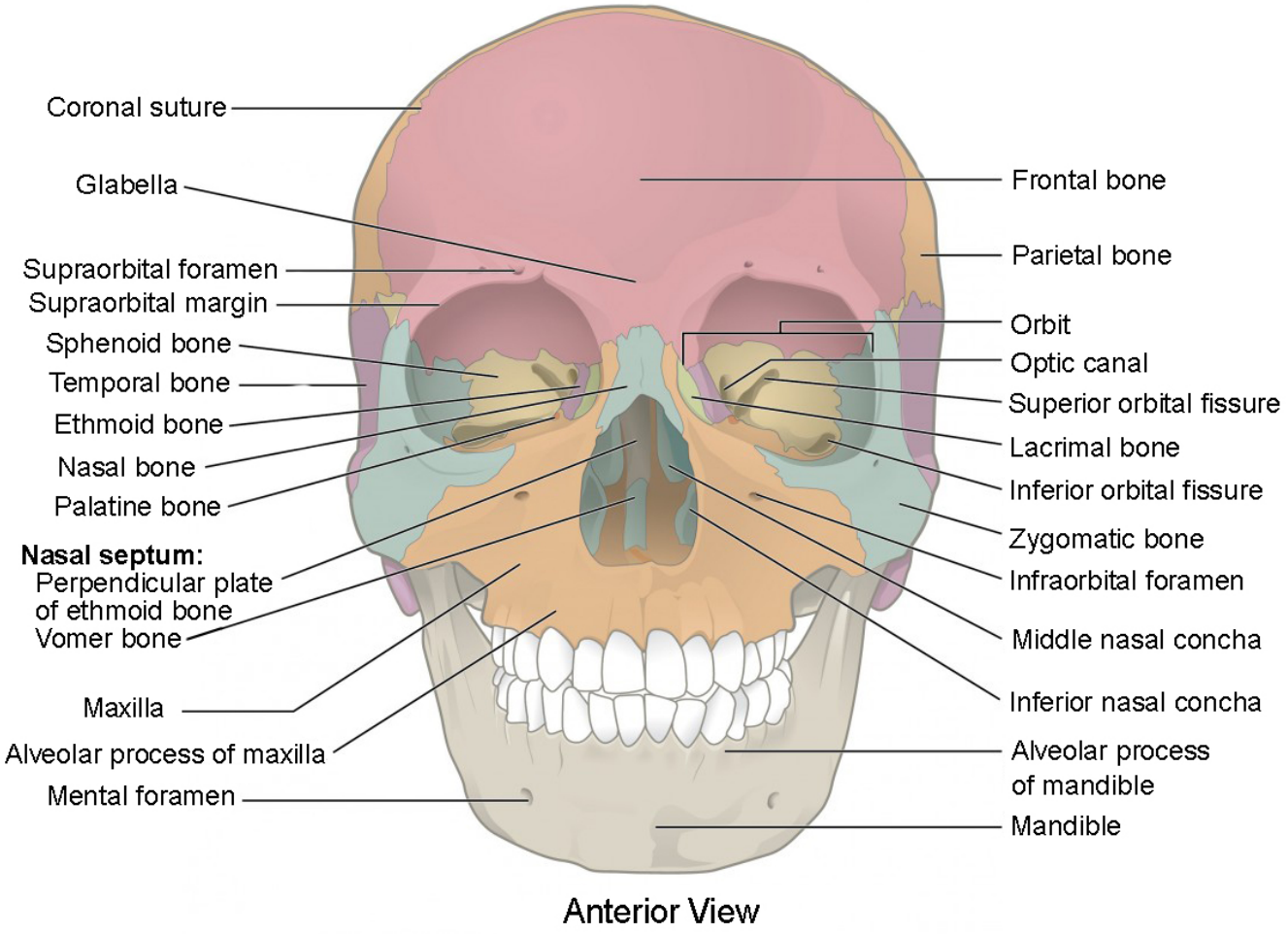


Figure 2. Anterior View of Skull. *An anterior view of the skull shows the bones that form the forehead, orbits (eye sockets), nasal cavity, nasal septum, and upper and lower jaws.*

Inside the nasal area of the skull, the **nasal cavity** is divided into halves by the **nasal septum**. The upper portion of the nasal septum is formed by the **perpendicular plate of the ethmoid bone** and the lower portion is the **vomer bone**. Each side of the nasal cavity is triangular in shape, with a broad inferior space that narrows superiorly. When looking into the nasal cavity from the front of the skull, two bony plates are seen projecting from each lateral wall. The larger of these is the **inferior nasal concha**, an independent bone of the skull. Located just above the inferior concha is the **middle nasal concha**, which is part of the ethmoid bone. A third bony plate, also part of the ethmoid bone, is the **superior nasal concha**. It is much smaller and out of sight, above the middle concha. The superior nasal concha is located just lateral to the perpendicular plate, in the upper nasal cavity.

Lateral View of Skull

A view of the lateral skull is dominated by the large, rounded brain case above and the upper and lower jaws with their teeth below (Figure 3). Separating these areas is the bridge of bone called the zygomatic arch.
The **zygomatic arch** is the bony arch on the side of skull that spans from the area of the cheek to just above the ear canal. It is formed by the junction of two bony processes: a short anterior component, the **temporal process of the zygomatic bone** (the cheekbone) and a longer posterior portion, the **zygomatic process of the temporal bone**, extending forward from the temporal bone. Thus the temporal process (anteriorly) and the zygomatic process (posteriorly) join together, like the two ends of a drawbridge, to form the zygomatic arch. One of the major muscles that pulls the mandible upward during biting and chewing arises from the zygomatic arch.

On the lateral side of the brain case, above the level of the zygomatic arch, is a shallow space called the **temporal fossa**. Below the level of the zygomatic arch and deep to the vertical portion of the mandible is another space called the ***infratemporal fossa***. Both the temporal fossa and infratemporal fossa contain muscles that act on the mandible during chewing.

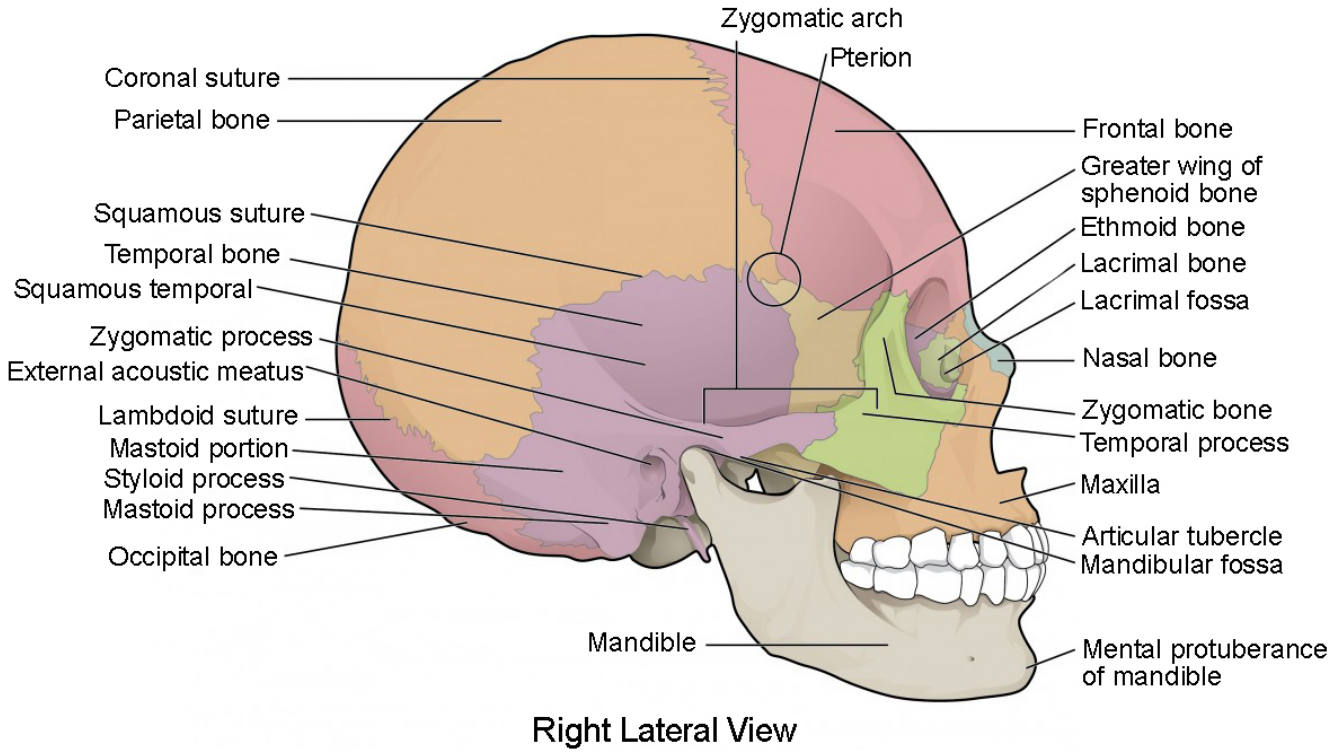


Figure 3. Lateral View of Skull. *The lateral skull shows the large rounded brain case, zygomatic arch, and the upper and lower jaws. The zygomatic arch is formed jointly by the zygomatic process of the temporal bone and the temporal process of the zygomatic bone. The shallow space above the zygomatic arch is the temporal fossa. The space inferior to the zygomatic arch and deep to the posterior mandible is the infratemporal fossa.*

Bones of the Brain Case

The brain case contains and protects the brain. The interior space that is almost completely occupied by the brain is called the **cranial cavity**. This cavity is bounded superiorly by the rounded top of the skull, which is called the **calvaria** (skullcap), and the lateral and posterior sides of the skull. The bones that form the top and sides of the brain case are usually referred to as the “flat” bones of the skull.

The floor of the brain case is referred to as the base of the skull. This is a complex area that varies in depth and has numerous openings for the passage of cranial nerves, blood vessels, and the spinal cord. Inside the skull, the base is subdivided into three large spaces, called the **anterior cranial fossa**, **middle cranial fossa**, and **posterior cranial fossa** (fossa = “trench or ditch”) (Figure 4). From anterior to posterior, the fossae increase in depth. The

shape and depth of each fossa corresponds to the shape and size of the brain region that each houses. The boundaries and openings of the cranial fossae (singular = *fossa*) will be described in a later section.

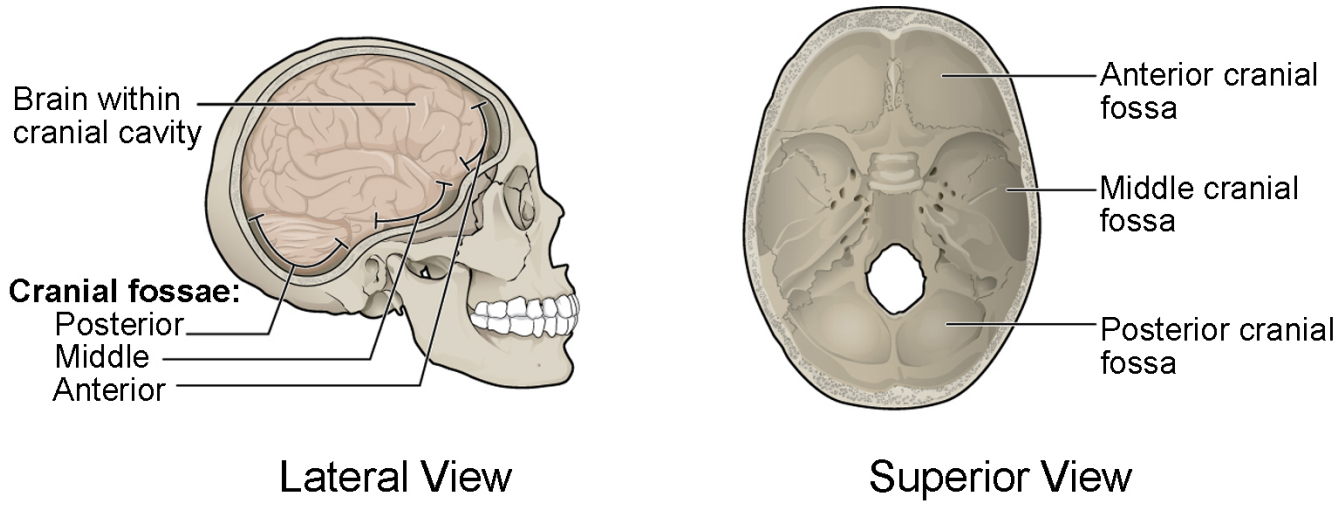


Figure 4. Cranial Fossae. *The bones of the brain case surround and protect the brain, which occupies the cranial cavity. The base of the brain case, which forms the floor of cranial cavity, is subdivided into the shallow anterior cranial fossa, the middle cranial fossa, and the deep posterior cranial fossa.*

The brain case consists of eight bones. These include the paired parietal and temporal bones, plus the unpaired frontal, occipital, sphenoid, and ethmoid bones.

Parietal Bone

The **parietal bone** forms most of the upper lateral side of the skull (see Figure 3). These are paired bones, with the right and left parietal bones joining together at the top of the skull. Each parietal bone is also bounded anteriorly by the frontal bone, inferiorly by the temporal bone, and posteriorly by the occipital bone.

Temporal Bone

The **temporal bone** forms the lower lateral side of the skull (see Figure 3). Common wisdom has it that the temporal bone (temporal = “time”) is so named because this area of the head (the temple) is where hair typically first turns gray, indicating the passage of time.

The temporal bone is subdivided into several regions (Figure 5). The flattened, upper portion is the squamous portion of the temporal bone. Below this area and projecting anteriorly is the zygomatic process of the temporal bone, which forms the posterior portion of the zygomatic arch. Posteriorly is the mastoid portion of the temporal bone. Projecting inferiorly from this region is a large prominence, the **mastoid process**, which serves as a muscle attachment site. The mastoid process can easily be felt on the side of the head just behind your earlobe. On the interior of the skull, the petrous portion of each temporal bone forms the prominent, diagonally oriented **petrous ridge** in the floor of the cranial cavity. Located inside each petrous ridge are small cavities that house the structures of the middle and inner ears.

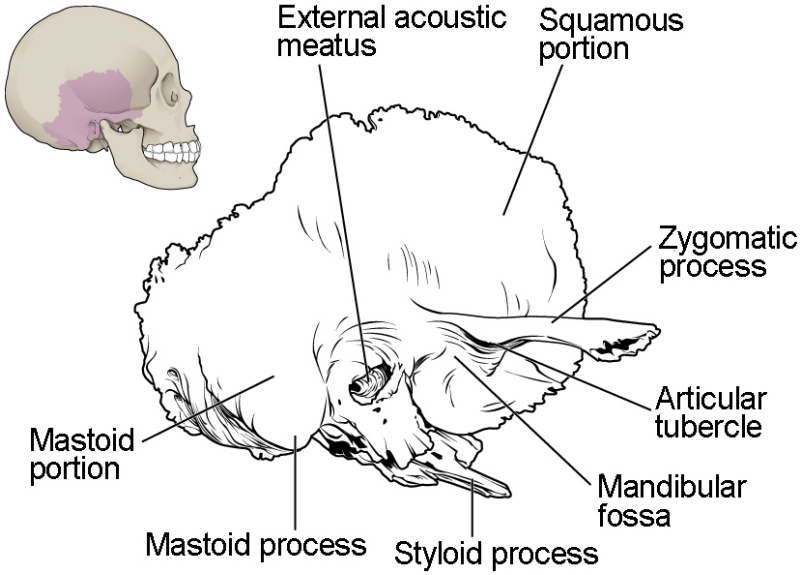


Figure 5. Temporal Bone. *A lateral view of the isolated temporal bone shows the squamous, mastoid, and zygomatic portions of the temporal bone.*

Important landmarks of the temporal bone, as shown in Figure 6, include the following:

- **External acoustic meatus** (ear canal)—This is the large opening on the lateral side of the skull that is associated with the ear.
- **Internal acoustic meatus**—This opening is located inside the cranial cavity, on the medial side of the petrous ridge. It connects to the middle and inner ear cavities of the temporal bone.
- **Mandibular fossa**—This is the deep, oval-shaped depression located on the external base of the skull, just in front of the external acoustic meatus. The mandible (lower jaw) joins with the skull at this site as part of the temporomandibular joint, which allows for movements of the mandible during opening and closing of the mouth.
- **Articular tubercle**—The smooth ridge located immediately anterior to the mandibular fossa. Both the articular tubercle and mandibular fossa contribute to the temporomandibular joint, the joint that provides for movements between the temporal bone of the skull and the mandible.
- **Styloid process**—Posterior to the mandibular fossa on the external base of the skull is an elongated, downward bony projection called the styloid process, so named because of its resemblance to a stylus (a pen or writing tool). This structure serves as an attachment site for several small muscles and for a ligament that supports the hyoid bone of the neck. (See also Figure 5.)
- **Stylomastoid foramen**—This small opening is located between the styloid process and mastoid process. This is the point of exit for the cranial nerve that supplies the facial muscles.
- **Carotid canal**—The carotid canal is a zig-zag shaped tunnel that provides passage through the base of the skull for one of the major arteries that supplies the brain. Its entrance is located on the outside base of the skull, anteromedial to the styloid process. The canal then runs anteromedially within the bony base of the skull, and then turns upward to its exit in the floor of the middle cranial cavity, above the foramen lacerum.

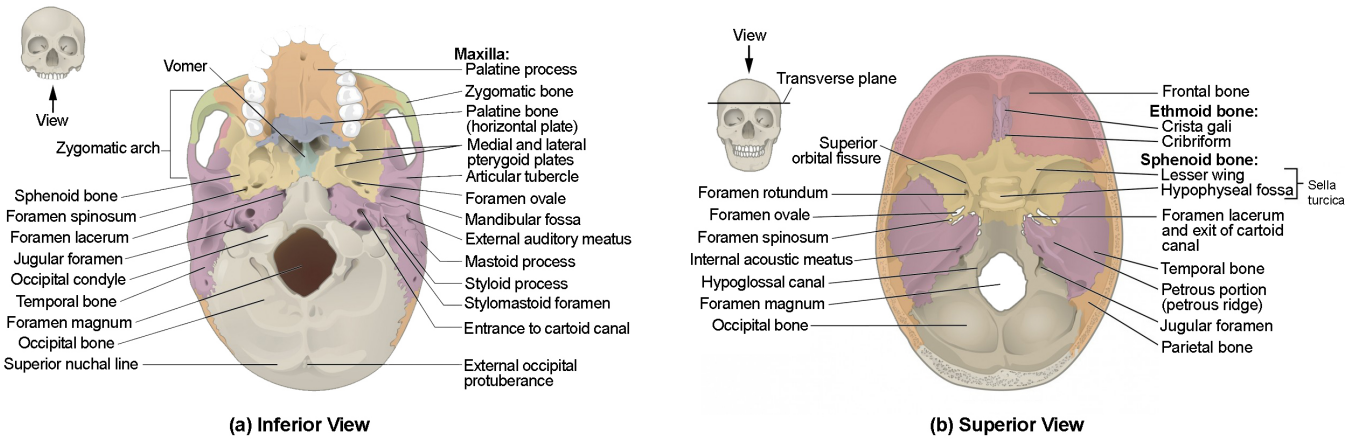


Figure 6. External and Internal Views of Base of Skull. *Click for a larger image. (a) The hard palate is formed anteriorly by the palatine processes of the maxilla bones and posteriorly by the horizontal plate of the palatine bones. (b) The complex floor of the cranial cavity is formed by the frontal, ethmoid, sphenoid, temporal, and occipital bones. The lesser wing of the sphenoid bone separates the anterior and middle cranial fossae. The petrous ridge (petrous portion of temporal bone) separates the middle and posterior cranial fossae.*

Frontal Bone

The **frontal bone** is the single bone that forms the forehead. At its anterior midline, between the eyebrows, there is a slight depression called the **glabella** (see Figure 3). The frontal bone also forms the supraorbital margin of the orbit. Near the middle of this margin, is the supraorbital foramen, the opening that provides passage for a sensory nerve to the forehead. The frontal bone is thickened just above each supraorbital margin, forming rounded brow ridges. These are located just behind your eyebrows and vary in size among individuals, although they are generally larger in males. Inside the cranial cavity, the frontal bone extends posteriorly. This flattened region forms both the roof of the orbit below and the floor of the anterior cranial cavity above (see Figure 6b).

Occipital Bone

The **occipital bone** is the single bone that forms the posterior skull and posterior base of the cranial cavity (Figure 7; see also Figure 6). On its outside surface, at the posterior midline, is a small protrusion called the **external occipital protuberance**, which serves as an attachment site for a ligament of the posterior neck. Lateral to either side of this bump is a **superior nuchal line** (nuchal = “nape” or “posterior neck”). The nuchal lines represent the most superior point at which muscles of the neck attach to the skull, with only the scalp covering the skull above these lines. On the base of the skull, the occipital bone contains the large opening of the **foramen magnum**, which allows for passage of the spinal cord as it exits the skull. On either side of the foramen magnum is an oval-shaped **occipital condyle**. These condyles form joints with the first cervical vertebra and thus support the skull on top of the vertebral column.

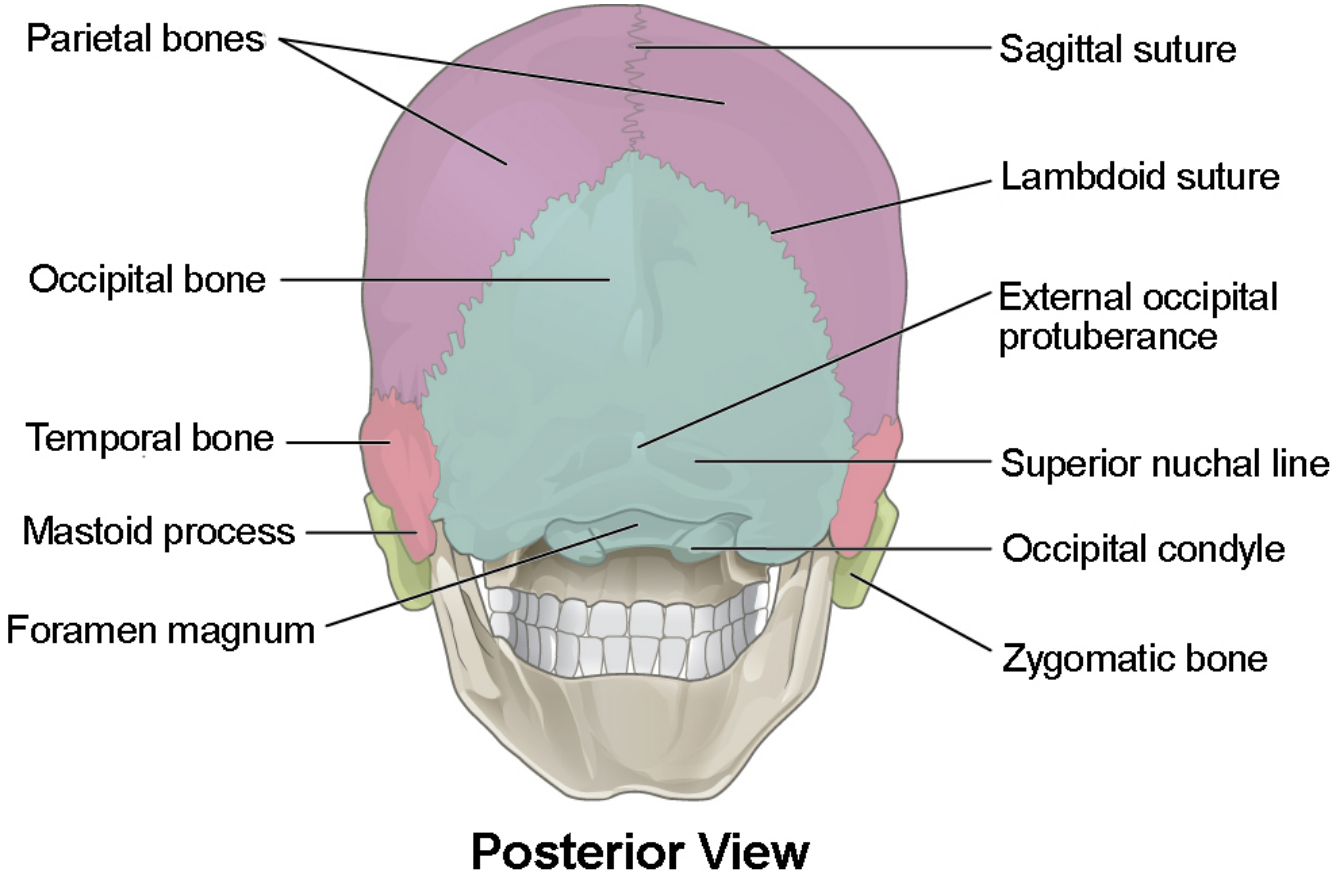


Figure 7. Posterior View of Skull. *This view of the posterior skull shows attachment sites for muscles and joints that support the skull.*

Sphenoid Bone

The **sphenoid bone** is a single, complex bone of the central skull (Figure 8). It serves as a "keystone" bone, because it joins with almost every other bone of the skull. The sphenoid forms much of the base of the central skull (see Figure 6) and also extends laterally to contribute to the sides of the skull (see Figure 3). Inside the cranial cavity, the right and left **lesser wings of the sphenoid bone**, which resemble the wings of a flying bird, form the lip of a prominent ridge that marks the boundary between the anterior and middle cranial fossae. The **sella turcica** ("Turkish saddle") is located at the midline of the middle cranial fossa. This bony region of the sphenoid bone is named for its resemblance to the horse saddles used by the Ottoman Turks, with a high back and a tall front. The rounded depression in the floor of the sella turcica is the ***hypophyseal (pituitary) fossa***, which houses the pea-sized pituitary (hypophyseal) gland. The **greater wings of the sphenoid bone** extend laterally to either side away from the sella turcica, where they form the anterior floor of the middle cranial fossa. The greater wing is best seen on the outside of the lateral skull, where it forms a rectangular area immediately anterior to the squamous portion of the temporal bone.

On the inferior aspect of the skull, each half of the sphenoid bone forms two thin, vertically oriented bony plates. These are the **medial pterygoid plate** and **lateral pterygoid plate** (pterygoid = "wing-shaped"). The right and left medial pterygoid plates form the posterior, lateral walls of the nasal cavity. The somewhat larger lateral pterygoid plates serve as attachment sites for chewing muscles that fill the infratemporal space and act on the mandible.

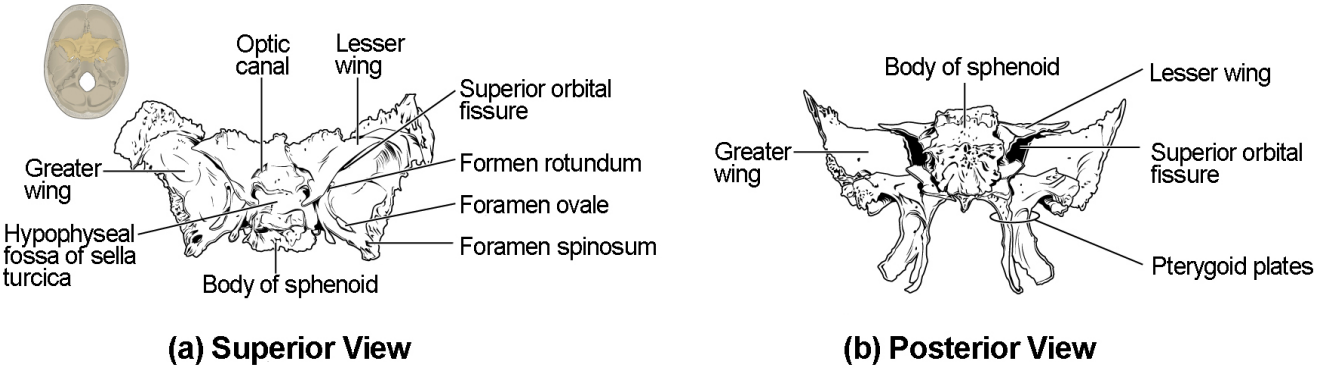


Figure 8. Sphenoid Bone. *Shown in isolation in (a) superior and (b) posterior views, the sphenoid bone is a single midline bone that forms the anterior walls and floor of the middle cranial fossa. It has a pair of lesser wings and a pair of greater wings. The sella turcica surrounds the hypophyseal fossa. Projecting downward are the medial and lateral pterygoid plates. The sphenoid has multiple openings for the passage of nerves and blood vessels, including the optic canal, superior orbital fissure, foramen rotundum, foramen ovale, and foramen spinosum.*

Ethmoid Bone

The **ethmoid bone** is a single, midline bone that forms the roof and lateral walls of the upper nasal cavity, the upper portion of the nasal septum, and contributes to the medial wall of the orbit (Figure 9 and Figure 10). On the interior of the skull, the ethmoid also forms a portion of the floor of the anterior cranial cavity (see Figure 6b).

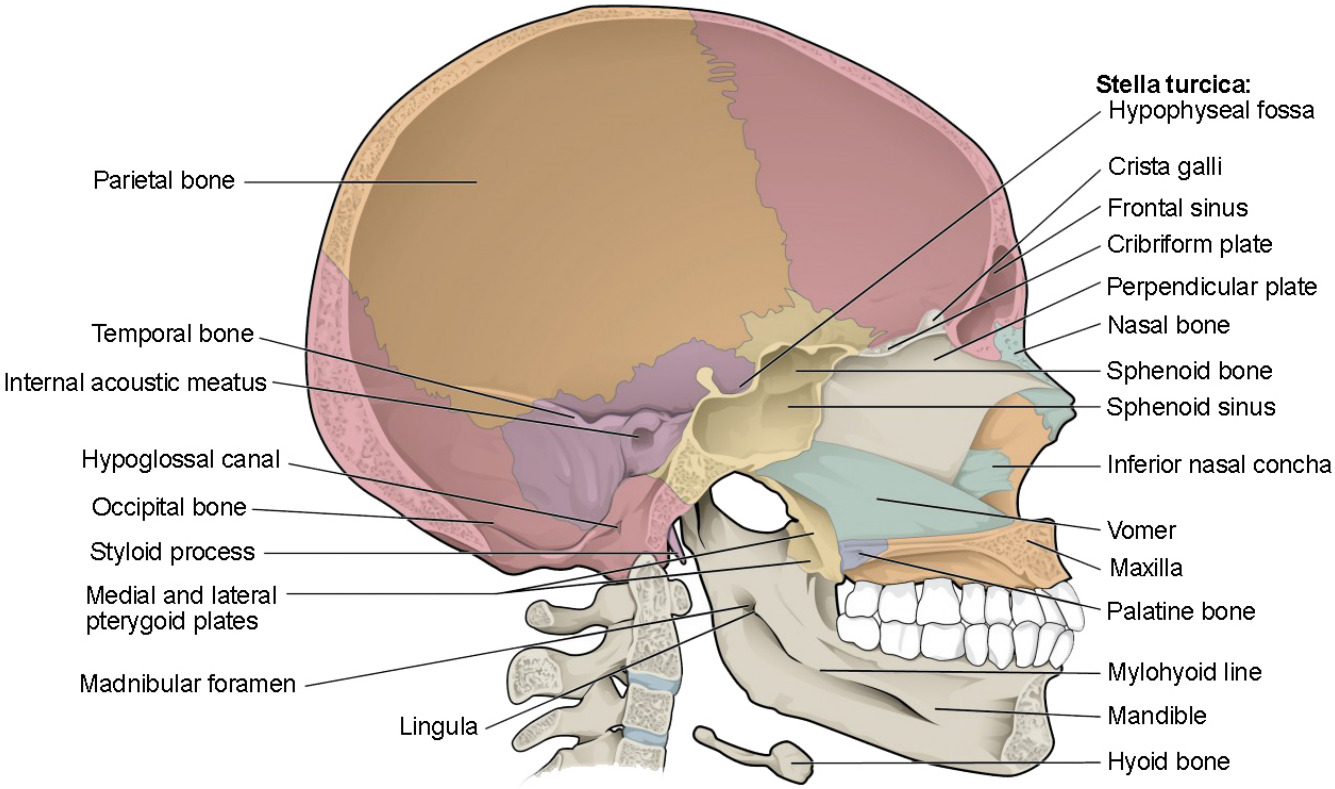


Figure 9. Sagittal Section of Skull. *This midline view of the sagittally sectioned skull shows the nasal septum.*

Within the nasal cavity, the perpendicular plate of the ethmoid bone forms the upper portion of the nasal septum. The ethmoid bone also forms the lateral walls of the upper nasal cavity. Extending from each lateral wall are the superior nasal concha and middle nasal concha, which are thin, curved projections that extend into the nasal cavity (Figure 11).

In the cranial cavity, the ethmoid bone forms a small area at the midline in the floor of the anterior cranial fossa. This region also forms the narrow roof of the underlying nasal cavity. This portion of the ethmoid bone consists of two parts, the crista galli and cribriform plates. The **crista galli** ("rooster's comb or crest") is a small upward bony projection located at the midline. It functions as an anterior attachment point for one of the covering layers of the brain. To either side of the crista galli is the **cribriform plate** (cribrum = "sieve"), a small, flattened area with numerous small openings termed olfactory foramina. Small nerve branches from the olfactory areas of the nasal cavity pass through these openings to enter the brain.

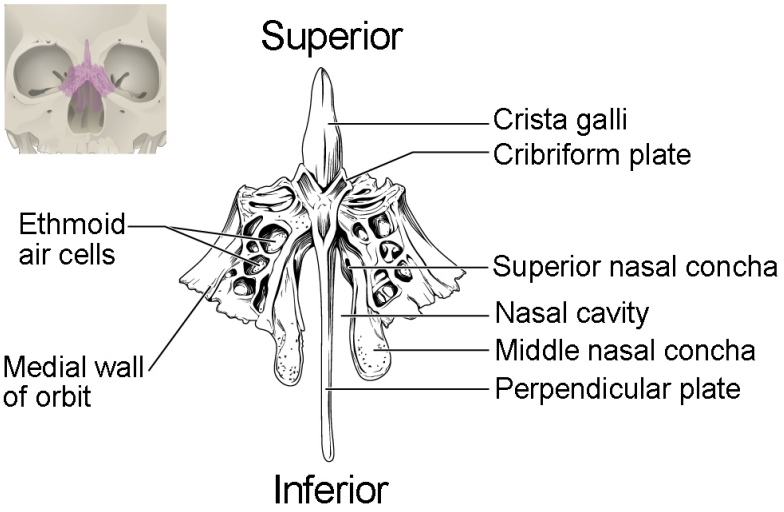


Figure 10. Ethmoid Bone. *The unpaired ethmoid bone is located at the midline within the central skull. It has an upward projection, the crista galli, and a downward projection, the perpendicular plate, which forms the upper nasal septum. The cribriform plates form both the roof of the nasal cavity and a portion of the anterior cranial fossa floor. The lateral sides of the ethmoid bone form the lateral walls of the upper nasal cavity, part of the medial orbit wall, and give rise to the superior and middle nasal conchae. The ethmoid bone also contains the ethmoid air cells.*

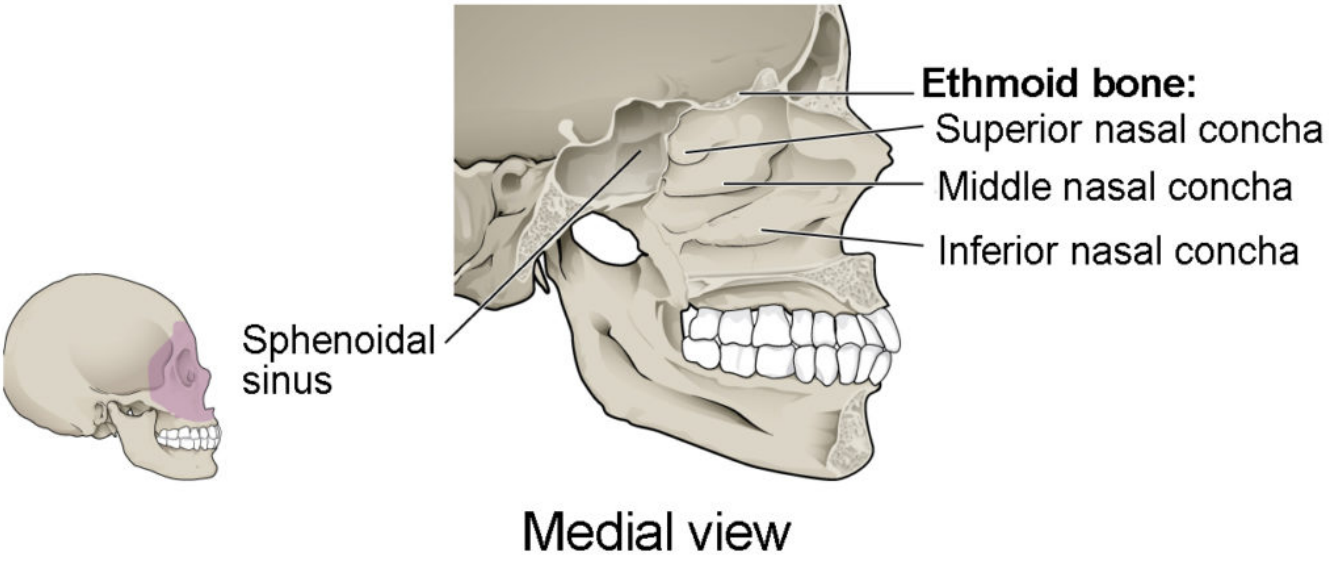


Figure 11. Lateral Wall of Nasal Cavity. *The three nasal conchae are curved bones that project from the lateral walls of the nasal cavity. The superior nasal concha and middle nasal concha are parts of the ethmoid bone. The inferior nasal concha is an independent bone of the skull.*

The lateral portions of the ethmoid bone are located between the orbit and upper nasal cavity, and thus form the lateral nasal cavity wall and a portion of the medial orbit wall. Located inside this portion of the ethmoid bone are several small, air-filled spaces that are part of the paranasal sinus system of the skull.

Sutures of the Skull

A **suture** is an immobile joint between adjacent bones of the skull. The narrow gap between the bones is filled with dense, fibrous connective tissue that unites the bones. The long sutures located between the bones of the brain case are not straight, but instead follow irregular, tightly twisting paths. These twisting lines serve to tightly interlock the adjacent bones, thus adding strength to the skull for brain protection.

The two suture lines seen on the top of the skull are the coronal and sagittal sutures. The **coronal suture** runs from side to side across the skull, within the coronal plane of section (see Figure 3). It joins the frontal bone to the right and left parietal bones. The **sagittal suture** extends posteriorly from the coronal suture, running along the midline at the top of the skull in the sagittal plane of section (see Figure 7). It unites the right and left parietal bones. On the posterior skull, the sagittal suture terminates by joining the lambdoid suture. The **lambdoid suture** extends downward and laterally to either side away from its junction with the sagittal suture. The lambdoid suture joins the occipital bone to the right and left parietal and temporal bones. This suture is named for its upside-down "V" shape, which resembles the capital letter version of the Greek letter lambda (Λ). The **squamous suture** is located on the lateral skull. It unites the squamous portion of the temporal bone with the parietal bone (see Figure 3). At the intersection of four bones is the **pterion**, a small, capital-H-shaped suture line region that unites the frontal bone, parietal bone, squamous portion of the temporal bone, and greater wing of the sphenoid bone. It is the weakest part of the skull. The pterion is located approximately two finger widths above the zygomatic arch and a thumb's width posterior to the upward portion of the zygomatic bone.

Disorders of the Skeletal System

Head and traumatic brain injuries are major causes of immediate death and disability, with bleeding and infections as possible additional complications. According to the Centers for Disease Control and Prevention (2010), approximately 30 percent of all injury-related deaths in the United States are caused by head injuries. The majority of head injuries involve falls. They are most common among young children (ages 0–4 years), adolescents (15–19 years), and the elderly (over 65 years). Additional causes vary, but prominent among these are automobile and motorcycle accidents.

Strong blows to the brain-case portion of the skull can produce fractures. These may result in bleeding inside the skull with subsequent injury to the brain. The most common is a linear skull fracture, in which fracture lines radiate from the point of impact. Other fracture types include a comminuted fracture, in which the bone is broken into several pieces at the point of impact, or a depressed fracture, in which the fractured bone is pushed inward. In a contrecoup (counterblow) fracture, the bone at the point of impact is not broken, but instead a fracture occurs on the opposite side of the skull. Fractures of the occipital bone at the base of the skull can occur in this manner, producing a basilar fracture that can damage the artery that passes through the carotid canal.

A blow to the lateral side of the head may fracture the bones of the pterion. The pterion is an important clinical landmark because located immediately deep to it on the inside of the skull is a major branch of an artery that supplies the skull and covering layers of the brain. A strong blow to this region can fracture the bones around the pterion. If the underlying artery is damaged, bleeding can cause the formation of a hematoma (collection of blood) between the brain and interior of the skull. As blood accumulates, it will put pressure on the brain. Symptoms associated with a hematoma may not be apparent immediately following the injury, but if untreated, blood accumulation will exert increasing pressure on the brain and can result in death within a few hours.

Facial Bones of the Skull

The facial bones of the skull form the upper and lower jaws, the nose, nasal cavity and nasal septum, and the orbit. The facial bones include 14 bones, with six paired bones and two unpaired bones. The paired bones are the maxilla, palatine, zygomatic, nasal, lacrimal, and inferior nasal conchae bones. The unpaired bones are the vomer and mandible bones. Although classified with the brain-case bones, the ethmoid bone also contributes to the nasal septum and the walls of the nasal cavity and orbit.

Maxillary Bone

The **maxillary bone**, often referred to simply as the maxilla (plural = maxillae), is one of a pair that together form the upper jaw, much of the hard palate, the medial floor of the orbit, and the lateral base of the nose (see Figure 2). The curved, inferior margin of the maxillary bone that forms the upper jaw and contains the upper teeth is the **alveolar process of the maxilla** (Figure 12). Each tooth is anchored into a deep socket called an alveolus. On the anterior maxilla, just below the orbit, is the infraorbital foramen. This is the point of exit for a sensory nerve that supplies the nose, upper lip, and anterior cheek. On the inferior skull, the **palatine process** from each maxillary bone can be seen joining together at the midline to form the anterior three-quarters of the hard palate (see Figure 6a). The **hard palate** is the bony plate that forms the roof of the mouth and floor of the nasal cavity, separating the oral and nasal cavities.

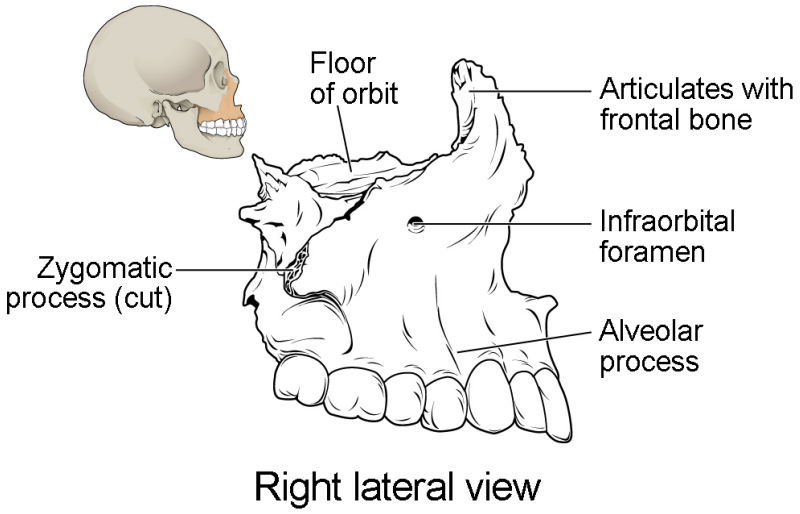


Figure 12. Maxillary Bone. *The maxillary bone forms the upper jaw and supports the upper teeth. Each maxilla also forms the lateral floor of each orbit and the majority of the hard palate.*

Palatine Bone

The **palatine bone** is one of a pair of irregularly shaped bones that contribute small areas to the lateral walls of the nasal cavity and the medial wall of each orbit. The largest region of each of the palatine bone is the **horizontal plate**. The plates from the right and left palatine bones join together at the midline to form the posterior quarter of the hard palate (see Figure 6a). Thus, the palatine bones are best seen in an inferior view of the skull and hard palate.

Homeostatic Imbalances: Cleft Lip and Cleft Palate

During embryonic development, the right and left maxilla bones come together at the midline to form the upper jaw. At the same time, the muscle and skin overlying these bones join together to form the upper lip. Inside the mouth, the palatine processes of the maxilla bones, along with the horizontal plates of the right and left palatine bones, join together to form the hard palate. If an error occurs in these developmental processes, a birth defect of cleft lip or cleft palate may result.

Cleft lip is a common development defect that affects approximately 1:1000 births, most of which are male. This defect involves a partial or complete failure of the right and left portions of the upper lip to fuse together, leaving a cleft (gap).

A more severe developmental defect is cleft palate, which affects the hard palate. The hard palate is the bony structure that separates the nasal cavity from the oral cavity. It is formed during embryonic development by the midline fusion of the horizontal plates from the right and left palatine bones and the palatine processes of the maxilla bones. Cleft palate affects approximately 1:2500 births and is more common in females. It results from a failure of the two halves of the hard palate to completely come together and fuse at the midline, thus leaving a gap between them. This gap allows for communication between the nasal and oral cavities. In severe cases, the bony gap continues into the anterior upper jaw where the alveolar processes of the maxilla bones also do not properly join together above the front teeth. If this occurs, a cleft lip will also be seen. Because of the communication between the oral and nasal cavities, a cleft palate makes it very difficult for an infant to generate the suckling needed for nursing, thus leaving the infant at risk for malnutrition. Surgical repair is required to correct cleft palate defects.

Zygomatic Bone

The **zygomatic bone** is also known as the cheekbone. Each of the paired zygomatic bones forms much of the lateral wall of the orbit and the lateral-inferior margins of the anterior orbital opening (see Figure 2). The short temporal process of the zygomatic bone projects posteriorly, where it forms the anterior portion of the zygomatic arch (see Figure 3).

Nasal Bone

The **nasal bone** is one of two small bones that articulate (join) with each other to form the bony base (bridge) of the nose. They also support the cartilages that form the lateral walls of the nose (see Figure 9). These are the bones that are damaged when the nose is broken.

Lacrimal Bone

Each **lacrimal bone** is a small, rectangular bone that forms the anterior, medial wall of the orbit (see Figure 2 and Figure 3). The anterior portion of the lacrimal bone forms a shallow depression called the **lacrimal fossa**, and extending inferiorly from this is the **nasolacrimal canal**. The lacrimal fluid (tears of the eye), which serves to maintain the moist surface of the eye, drains at the medial corner of the eye into the nasolacrimal canal. This duct then extends downward to open into the nasal cavity, behind the inferior nasal concha. In the nasal cavity, the lacrimal fluid normally drains posteriorly, but with an increased flow of tears due to crying or eye irritation, some fluid will also drain anteriorly, thus causing a runny nose.

Inferior Nasal Conchae

The right and left inferior nasal conchae form a curved bony plate that projects into the nasal cavity space from the lower lateral wall (see Figure 11). The inferior concha is the largest of the nasal conchae and can easily be seen when looking into the anterior opening of the nasal cavity.

Vomer Bone

The unpaired vomer bone, often referred to simply as the vomer, is triangular-shaped and forms the posterior-inferior part of the nasal septum (see Figure 9). The vomer is best seen when looking from behind into the posterior openings of the nasal cavity (see Figure 6a). In this view, the vomer is seen to form the entire height of the nasal septum. A much smaller portion of the vomer can also be seen when looking into the anterior opening of the nasal cavity.

Mandible

The **mandible** forms the lower jaw and is the only moveable bone of the skull. At the time of birth, the mandible consists of paired right and left bones, but these fuse together during the first year to form the single U-shaped mandible of the adult skull. Each side of the mandible consists of a horizontal body and posteriorly, a vertically oriented **ramus of the mandible** (ramus = "branch"). The outside margin of the mandible, where the body and ramus come together is called the **angle of the mandible** (Figure 13).

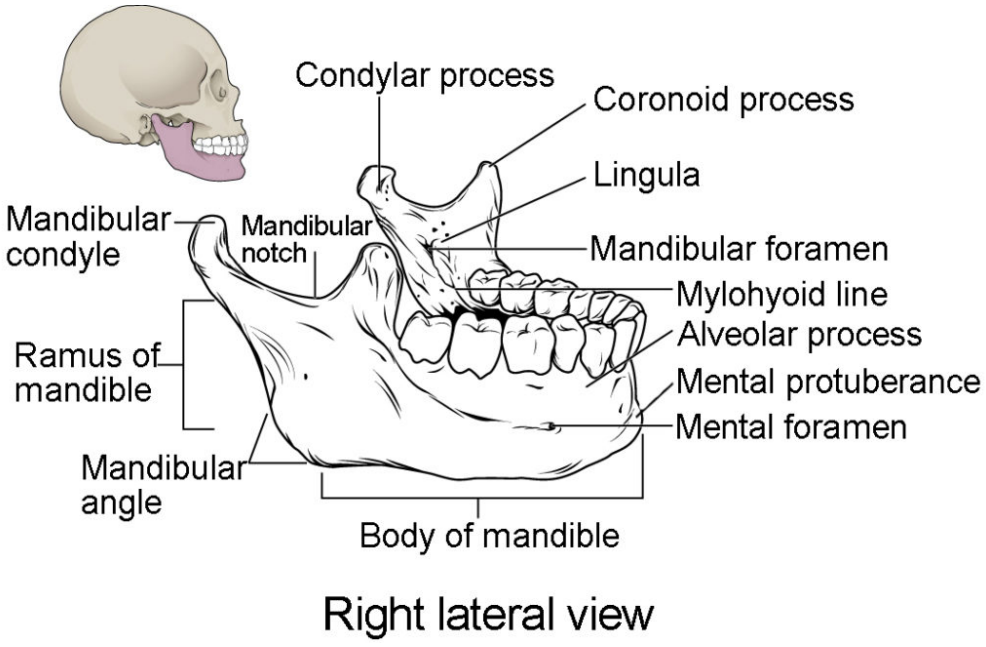


Figure 13. Isolated Mandible. *The mandible is the only moveable bone of the skull.*

The ramus on each side of the mandible has two upward-going bony projections. The more anterior projection is the flattened **coronoid process of the mandible**, which provides attachment for one of the biting muscles. The posterior projection is the **condylar process of the mandible**, which is topped by the oval-shaped **condyle**. The condyle of the mandible articulates (joins) with the mandibular fossa and articular tubercle of the temporal bone. Together these articulations form the temporomandibular joint, which allows for opening and closing of the mouth (see Figure 3). The broad U-shaped curve located between the coronoid and condylar processes is the **mandibular notch**.

Important landmarks for the mandible include the following:

- **Alveolar process of the mandible**—This is the upper border of the mandibular body and serves to anchor the lower teeth.
- **Mental protuberance**—The forward projection from the inferior margin of the anterior mandible that forms the chin (mental = "chin").
- **Mental foramen**—The opening located on each side of the anterior-lateral mandible, which is the exit site for a sensory nerve that supplies the chin.
- **Mylohyoid line**—This bony ridge extends along the inner aspect of the mandibular body (see Figure 9). The muscle that forms the floor of the oral cavity attaches to the mylohyoid lines on both sides of the mandible.
- **Mandibular foramen**—This opening is located on the medial side of the ramus of the mandible. The opening leads into a tunnel that runs down the length of the mandibular body. The sensory nerve and blood vessels that supply the lower teeth enter the mandibular foramen and then follow this tunnel. Thus, to numb the lower teeth prior to dental work, the dentist must inject anesthesia into the lateral wall of the oral cavity at a point prior to where this sensory nerve enters the mandibular foramen.
- **Lingula**—This small flap of bone is named for its shape (lingula = "little tongue"). It is located immediately next to the mandibular foramen, on the medial side of the ramus. A ligament that anchors the mandible during opening and closing of the mouth extends down from the base of the skull and attaches to the lingula.

The Orbit

The orbit is the bony socket that houses the eyeball and contains the muscles that move the eyeball or open the upper eyelid. Each orbit is cone-shaped, with a narrow posterior region that widens toward the large anterior opening. To help protect the eye, the bony margins of the anterior opening are thickened and somewhat

constricted. The medial walls of the two orbits are parallel to each other but each lateral wall diverges away from the midline at a 45° angle. This divergence provides greater lateral peripheral vision.

The walls of each orbit include contributions from seven skull bones (Figure 14). The frontal bone forms the roof and the zygomatic bone forms the lateral wall and lateral floor. The medial floor is primarily formed by the maxilla, with a small contribution from the palatine bone. The ethmoid bone and lacrimal bone make up much of the medial wall and the sphenoid bone forms the posterior orbit.

At the posterior apex of the orbit is the opening of the **optic canal**, which allows for passage of the optic nerve from the retina to the brain. Lateral to this is the elongated and irregularly shaped superior orbital fissure, which provides passage for the artery that supplies the eyeball, sensory nerves, and the nerves that supply the muscles involved in eye movements.

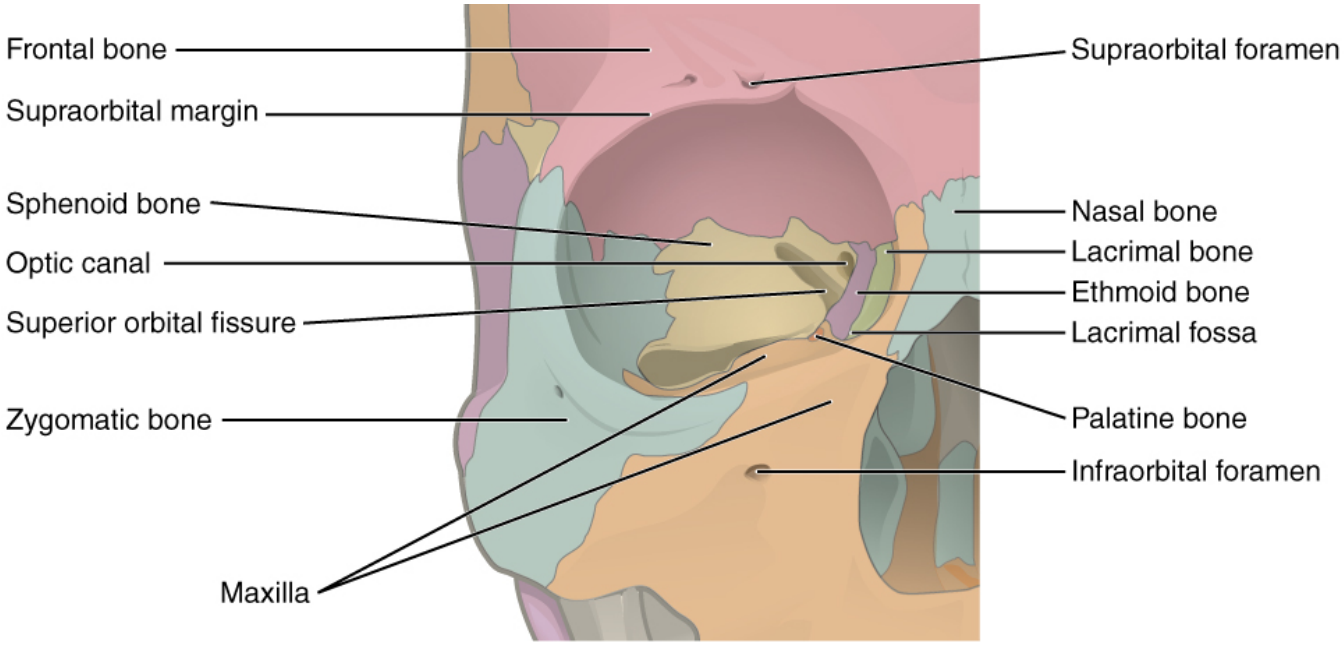


Figure 14. Bones of the Orbit. *Seven skull bones contribute to the walls of the orbit. Opening into the posterior orbit from the cranial cavity are the optic canal and superior orbital fissure.*

The Nasal Septum and Nasal Conchae

The **nasal septum** consists of both bone and cartilage components (Figure 15; see also Figure 9). The upper portion of the septum is formed by the perpendicular plate of the ethmoid bone. The lower and posterior parts of the septum are formed by the triangular-shaped vomer bone. In an anterior view of the skull, the perpendicular plate of the ethmoid bone is easily seen inside the nasal opening as the upper nasal septum, but only a small portion of the vomer is seen as the inferior septum. A better view of the vomer bone is seen when looking into the posterior nasal cavity with an inferior view of the skull, where the vomer forms the full height of the nasal septum. The anterior nasal septum is formed by the **septal cartilage**, a flexible plate that fills in the gap between the perpendicular plate of the ethmoid and vomer bones. This cartilage also extends outward into the nose where it separates the right and left nostrils. The septal cartilage is not found in the dry skull.

Attached to the lateral wall on each side of the nasal cavity are the superior, middle, and inferior *nasal conchae* (singular = concha), which are named for their positions (see Figure 11). These are bony plates that curve downward as they project into the space of the nasal cavity. They serve to swirl the incoming air, which helps to warm and moisturize it before the air moves into the delicate air sacs of the lungs. This also allows mucus, secreted by the tissue lining the nasal cavity, to trap incoming dust, pollen, bacteria, and viruses. The largest of the conchae is the inferior nasal concha, which is an independent bone of the skull. The middle concha and the superior conchae, which is the smallest, are both formed by the ethmoid bone. When looking into the anterior nasal opening of the skull, only the inferior and middle conchae can be seen. The small superior nasal concha is well hidden above and behind the middle concha.

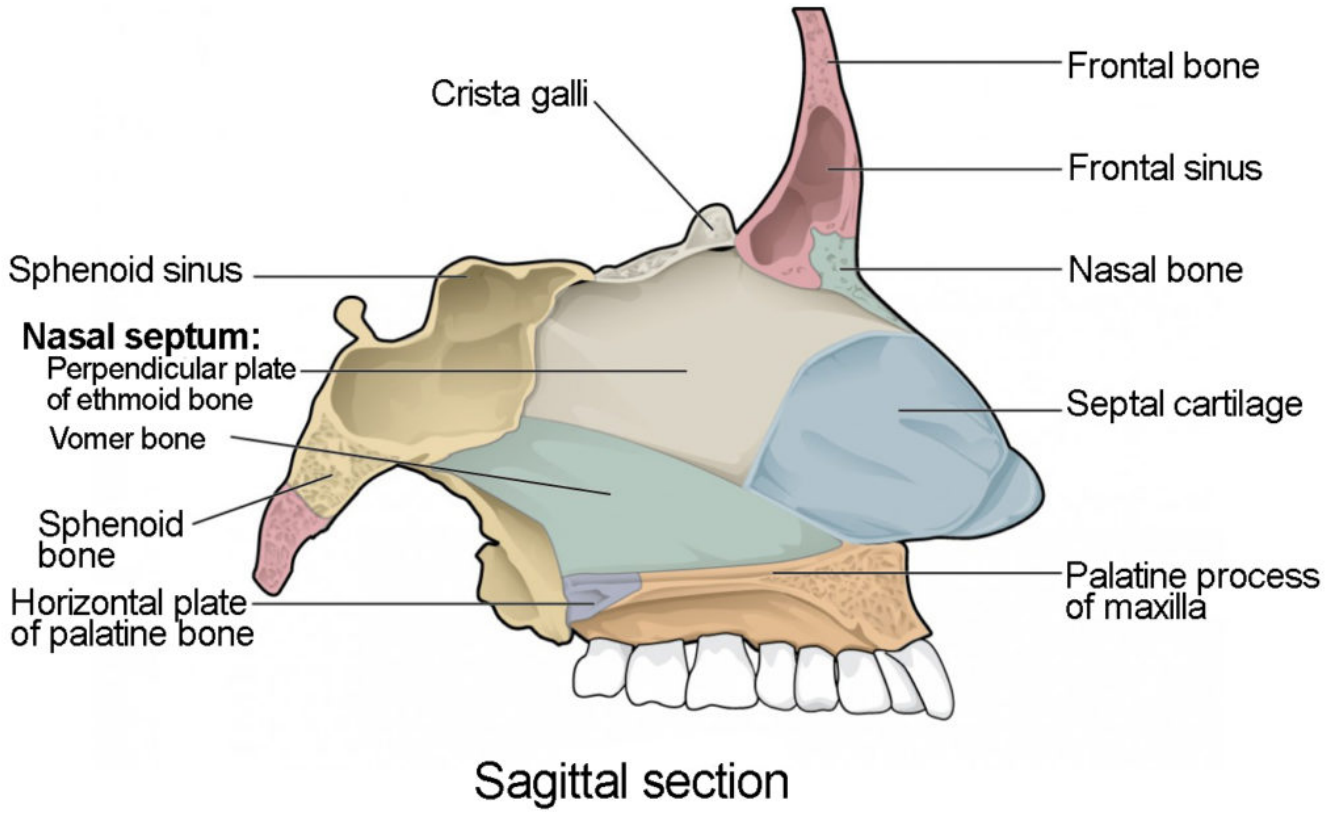


Figure 15. Nasal Septum. *The nasal septum is formed by the perpendicular plate of the ethmoid bone and the vomer bone. The septal cartilage fills the gap between these bones and extends into the nose.*

Cranial Fossae

Inside the skull, the floor of the cranial cavity is subdivided into three cranial fossae (spaces), which increase in depth from anterior to posterior (see Figure 4, Figure 6b, and Figure 9). Since the brain occupies these areas, the shape of each conforms to the shape of the brain regions that it contains. Each cranial fossa has anterior and posterior boundaries and is divided at the midline into right and left areas by a significant bony structure or opening.

Anterior Cranial Fossa

The anterior cranial fossa is the most anterior and the shallowest of the three cranial fossae. It overlies the orbits and contains the frontal lobes of the brain. Anteriorly, the anterior fossa is bounded by the frontal bone, which also forms the majority of the floor for this space. The lesser wings of the sphenoid bone form the prominent ledge that marks the boundary between the anterior and middle cranial fossae. Located in the floor of the anterior cranial fossa at the midline is a portion of the ethmoid bone, consisting of the upward projecting crista galli and to either side of this, the cribriform plates.

Middle Cranial Fossa

The middle cranial fossa is deeper and situated posterior to the anterior fossa. It extends from the lesser wings of the sphenoid bone anteriorly, to the petrous ridges (petrous portion of the temporal bones) posteriorly. The large, diagonally positioned petrous ridges give the middle cranial fossa a butterfly shape, making it narrow at the midline and broad laterally. The temporal lobes of the brain occupy this fossa. The middle cranial fossa is divided at the midline by the upward bony prominence of the sella turcica, a part of the sphenoid bone. The middle cranial fossa has several openings for the passage of blood vessels and cranial nerves (see Figure 6).

Openings in the middle cranial fossa are as follows:

- Optic canal—This opening is located at the anterior lateral corner of the sella turcica. It provides for passage of the optic nerve into the orbit.
- Superior orbital fissure—This large, irregular opening into the posterior orbit is located on the anterior wall of the middle cranial fossa, lateral to the optic canal and under the projecting margin of the lesser wing of the sphenoid bone. Nerves to the eyeball and associated muscles, and sensory nerves to the forehead pass through this opening.
- Foramen rotundum—This rounded opening (rotundum = "round") is located in the floor of the middle cranial fossa, just inferior to the superior orbital fissure. It is the exit point for a major sensory nerve that supplies the cheek, nose, and upper teeth.
- Foramen ovale of the middle cranial fossa—This large, oval-shaped opening in the floor of the middle cranial fossa provides passage for a major sensory nerve to the lateral head, cheek, chin, and lower teeth.
- Foramen spinosum—This small opening, located posterior-lateral to the foramen ovale, is the entry point for an important artery that supplies the covering layers surrounding the brain. The branching pattern of this artery forms readily visible grooves on the internal surface of the skull and these grooves can be traced back to their origin at the foramen spinosum.
- Carotid canal—This is the zig-zag passageway through which a major artery to the brain enters the skull. The entrance to the carotid canal is located on the inferior aspect of the skull, anteromedial to the styloid process (see Figure 6a). From here, the canal runs anteromedially within the bony base of the skull. Just above the foramen lacerum, the carotid canal opens into the middle cranial cavity, near the posterior-lateral base of the sella turcica.
- Foramen lacerum—This irregular opening is located in the base of the skull, immediately inferior to the exit of the carotid canal. This opening is an artifact of the dry skull, because in life it is completely filled with cartilage. All the openings of the skull that provide for passage of nerves or blood vessels have smooth margins; the word lacerum ("ragged" or "torn") tells us that this opening has ragged edges and thus nothing passes through it.

Posterior Cranial Fossa

The posterior cranial fossa is the most posterior and deepest portion of the cranial cavity. It contains the cerebellum of the brain. The posterior fossa is bounded anteriorly by the petrous ridges, while the occipital bone forms the floor and posterior wall. It is divided at the midline by the large foramen magnum ("great aperture"), the opening that provides for passage of the spinal cord.

Located on the medial wall of the petrous ridge in the posterior cranial fossa is the internal acoustic meatus (see Figure 9). This opening provides for passage of the nerve from the hearing and equilibrium organs of the inner ear, and the nerve that supplies the muscles of the face. Located at the anterior-lateral margin of the foramen magnum is the **hypoglossal canal**. These emerge on the inferior aspect of the skull at the base of the occipital condyle and provide passage for an important nerve to the tongue.

Immediately inferior to the internal acoustic meatus is the large, irregularly shaped **jugular foramen** (see Figure 6a). Several cranial nerves from the brain exit the skull via this opening. It is also the exit point through the base of the skull for all the venous return blood leaving the brain. The venous structures that carry blood inside the skull form large, curved grooves on the inner walls of the posterior cranial fossa, which terminate at each jugular foramen.

Paranasal Sinuses

The **paranasal sinuses** are hollow, air-filled spaces located within certain bones of the skull (Figure 16). All of the sinuses communicate with the nasal cavity (paranasal = "next to nasal cavity") and are lined with nasal mucosa. They serve to reduce bone mass and thus lighten the skull, and they also add resonance to the voice. This second feature is most obvious when you have a cold or sinus congestion. These produce swelling of the mucosa and excess mucus production, which can obstruct the narrow passageways between the sinuses and the nasal cavity, causing your voice to sound different to yourself and others. This blockage can also allow the sinuses to fill with fluid, with the resulting pressure producing pain and discomfort.

The paranasal sinuses are named for the skull bone that each occupies. The **frontal sinus** is located just above the eyebrows, within the frontal bone (see Figure 15). This irregular space may be divided at the midline into bilateral spaces, or these may be fused into a single sinus space. The frontal sinus is the most anterior of the paranasal sinuses. The largest sinus is the **maxillary sinus**. These are paired and located within the right and left maxillary bones, where they occupy the area just below the orbits. The maxillary sinuses are most commonly involved during sinus infections. Because their connection to the nasal cavity is located high on their medial wall, they are difficult to drain. The **sphenoid sinus** is a single, midline sinus. It is located within the body of the sphenoid bone, just anterior and inferior to the sella turcica, thus making it the most posterior of the paranasal sinuses. The lateral aspects of the ethmoid bone contain multiple small spaces separated by very thin bony walls. Each of these spaces is called an **ethmoid air cell**. These are located on both sides of the ethmoid bone, between the upper nasal cavity and medial orbit, just behind the superior nasal conchae.

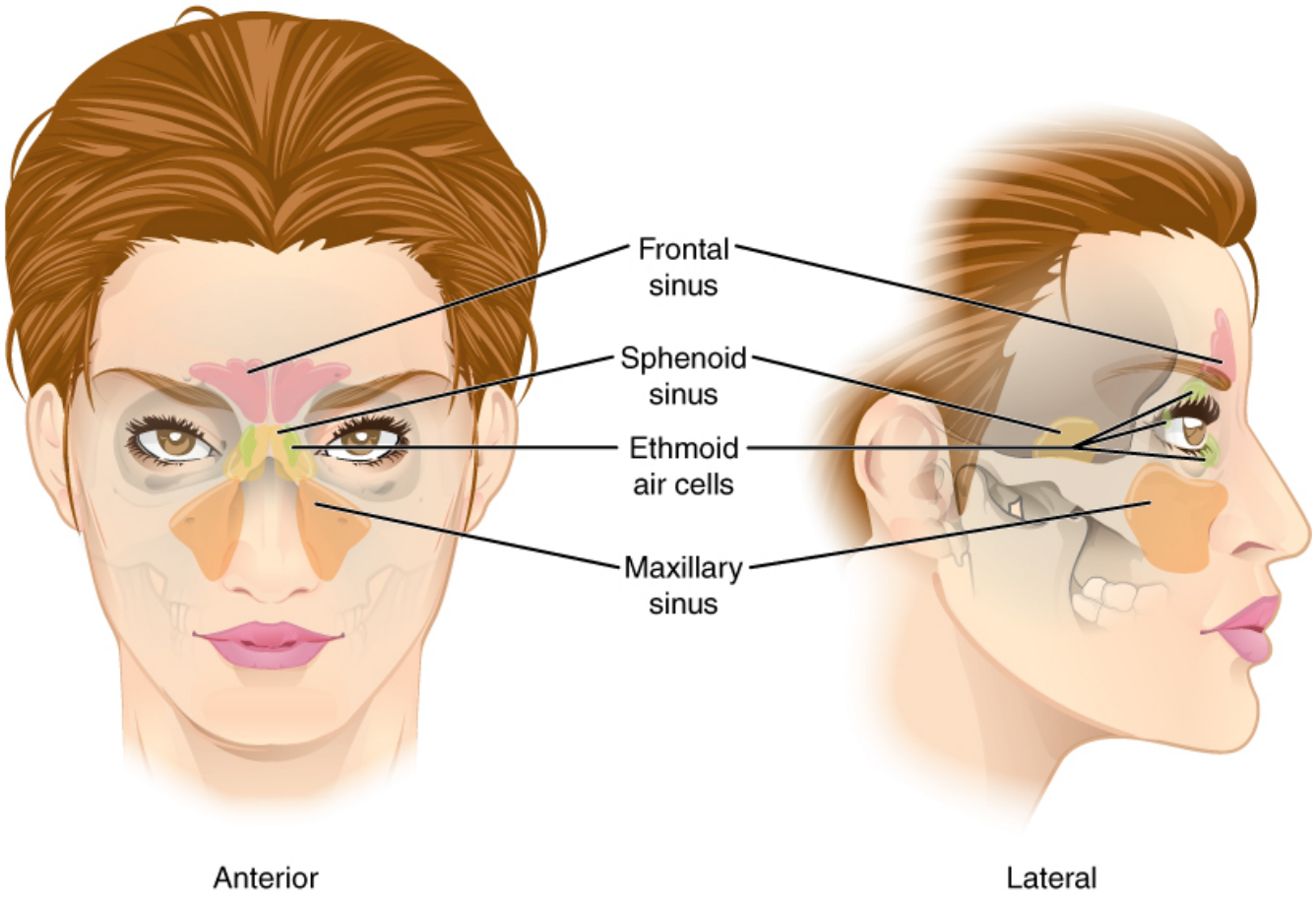


Figure 16. Paranasal Sinuses. *The paranasal sinuses are hollow, air-filled spaces named for the skull bone that each occupies. The most anterior is the frontal sinus, located in the frontal bone above the eyebrows. The largest are the maxillary sinuses, located in the right and left maxillary bones below the orbits. The most posterior is the sphenoid sinus, located in the body of the sphenoid bone, under the sella turcica. The ethmoid air cells are multiple small spaces located in the right and left sides of the ethmoid bone, between the medial wall of the orbit and lateral wall of the upper nasal cavity.*

Hyoid Bone

The hyoid bone is an independent bone that does not contact any other bone and thus is not part of the skull (Figure 17). It is a small U-shaped bone located in the upper neck near the level of the inferior mandible, with the tips of the “U” pointing posteriorly. The hyoid serves as the base for the tongue above, and is attached to the larynx below and the pharynx posteriorly. The hyoid is held in position by a series of small muscles that attach to it either from above or below. These muscles act to move the hyoid up/down or forward/back. Movements of the hyoid are coordinated with movements of the tongue, larynx, and pharynx during swallowing and speaking.

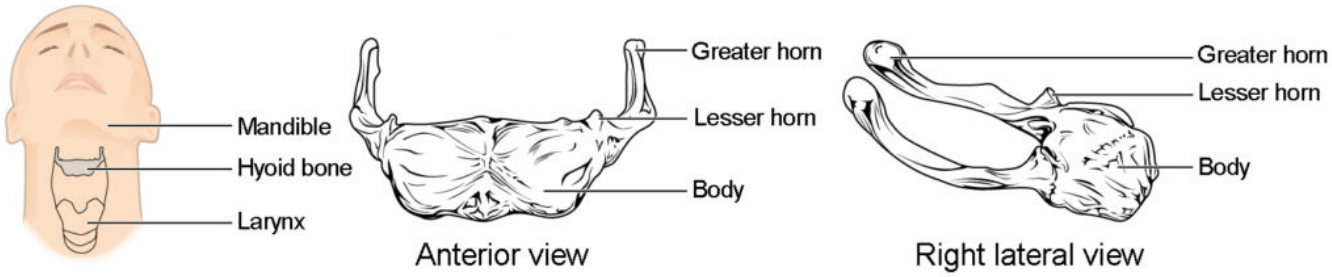


Figure 17. Hyoid Bone. *The hyoid bone is located in the upper neck and does not join with any other bone. It provides attachments for muscles that act on the tongue, larynx, and pharynx.*

THE VERTEBRAL COLUMN

Learning Objectives

- Describe each region of the vertebral column and the number of bones in each region
- Discuss the curves of the vertebral column and how these change after birth
- Describe a typical vertebra and determine the distinguishing characteristics for vertebrae in each vertebral region and features of the sacrum and the coccyx
- Define the structure of an intervertebral disc
- Determine the location of the ligaments that provide support for the vertebral column

The vertebral column is also known as the spinal column or spine (Figure 1). It consists of a sequence of vertebrae (singular = vertebra), each of which is separated and united by an **intervertebral disc**. Together, the vertebrae and intervertebral discs form the vertebral column. It is a flexible column that supports the head, neck, and body and allows for their movements. It also protects the spinal cord, which passes down the back through openings in the vertebrae.

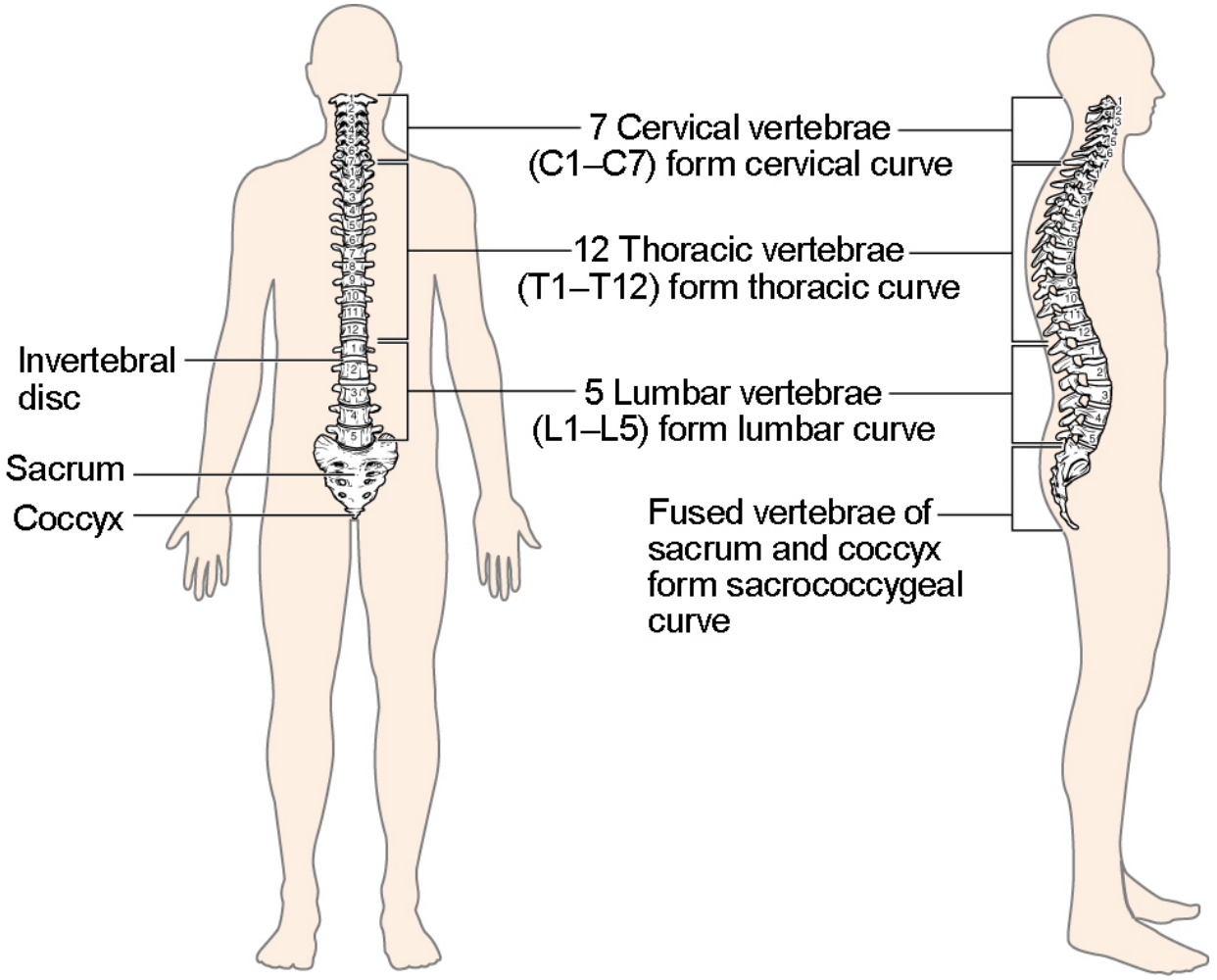


Figure 1. Vertebral Column. *The adult vertebral column consists of 24 vertebrae, plus the sacrum and coccyx. The vertebrae are divided into three regions: cervical C1–C7 vertebrae, thoracic T1–T12 vertebrae, and lumbar L1–L5 vertebrae. The vertebral column is curved, with two primary curvatures (thoracic and sacrococcygeal curves) and two secondary curvatures (cervical and lumbar curves).*

Regions of the Vertebral Column

The vertebral column originally develops as a series of 33 vertebrae, but this number is eventually reduced to 24 vertebrae, plus the sacrum and coccyx. The vertebral column is subdivided into five regions, with the vertebrae in each area named for that region and numbered in descending order. In the neck, there are seven cervical vertebrae, each designated with the letter “C” followed by its number. Superiorly, the C1 vertebra articulates (forms a joint) with the occipital condyles of the skull. Inferiorly, C1 articulates with the C2 vertebra, and so on. Below these are the 12 thoracic vertebrae, designated T1–T12. The lower back contains the L1–L5 lumbar vertebrae. The single sacrum, which is also part of the pelvis, is formed by the fusion of five sacral vertebrae. Similarly, the coccyx, or tailbone, results from the fusion of four small coccygeal vertebrae. However, the sacral and coccygeal fusions do not start until age 20 and are not completed until middle age.

An interesting anatomical fact is that almost all mammals have seven cervical vertebrae, regardless of body size. This means that there are large variations in the size of cervical vertebrae, ranging from the very small cervical vertebrae of a shrew to the greatly elongated vertebrae in the neck of a giraffe. In a full-grown giraffe, each cervical vertebra is 11 inches tall.

Curvatures of the Vertebral Column

The adult vertebral column does not form a straight line, but instead has four curvatures along its length (see Figure 1). These curves increase the vertebral column's strength, flexibility, and ability to absorb shock. When the load on the spine is increased, by carrying a heavy backpack for example, the curvatures increase in depth (become more curved) to accommodate the extra weight. They then spring back when the weight is removed. The four adult curvatures are classified as either primary or secondary curvatures. Primary curves are retained from the original fetal curvature, while secondary curvatures develop after birth.

During fetal development, the body is flexed anteriorly into the fetal position, giving the entire vertebral column a single curvature that is concave anteriorly. In the adult, this fetal curvature is retained in two regions of the vertebral column as the **thoracic curve**, which involves the thoracic vertebrae, and the **sacrococcygeal curve**, formed by the sacrum and coccyx. Each of these is thus called a **primary curve** because they are retained from the original fetal curvature of the vertebral column.

A **secondary curve** develops gradually after birth as the child learns to sit upright, stand, and walk. Secondary curves are concave posteriorly, opposite in direction to the original fetal curvature. The **cervical curve** of the neck region develops as the infant begins to hold their head upright when sitting. Later, as the child begins to stand and then to walk, the **lumbar curve** of the lower back develops. In adults, the lumbar curve is generally deeper in females.

Disorders associated with the curvature of the spine include **kyphosis** (an excessive posterior curvature of the thoracic region), **lordosis** (an excessive anterior curvature of the lumbar region), and **scoliosis** (an abnormal, lateral curvature, accompanied by twisting of the vertebral column).

Disorders of the Vertebral Column

Developmental anomalies, pathological changes, or obesity can enhance the normal vertebral column curves, resulting in the development of abnormal or excessive curvatures (Figure 2). Kyphosis, also referred to as humpback or hunchback, is an excessive posterior curvature of the thoracic region. This can develop when osteoporosis causes weakening and erosion of the anterior portions of the upper thoracic vertebrae, resulting in their gradual collapse (Figure 3). Lordosis, or swayback, is an excessive anterior curvature of the lumbar region and is most commonly associated with obesity or late pregnancy. The accumulation of body weight in the abdominal region results an anterior shift in the line of gravity that carries the weight of the body. This causes in an anterior tilt of the pelvis and a pronounced enhancement of the lumbar curve.

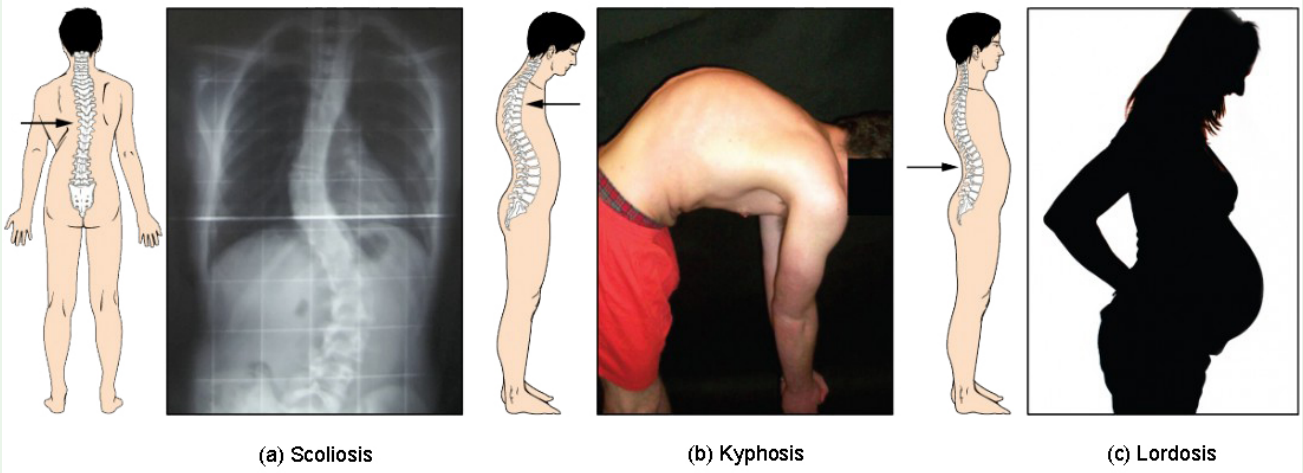


Figure 2. Abnormal Curvatures of the Vertebral Column. *(a) Scoliosis is an abnormal lateral bending of the vertebral column. (b) An excessive curvature of the upper thoracic vertebral column is called kyphosis. (c) Lordosis is an excessive curvature in the lumbar region of the vertebral column.*

Scoliosis is an abnormal, lateral curvature, accompanied by twisting of the vertebral column. Compensatory curves may also develop in other areas of the vertebral column to help maintain the head positioned over the feet. Scoliosis is the most common vertebral abnormality among girls. The cause is usually unknown, but it may result from weakness of the back muscles, defects such as differential growth rates in the right and left sides of the vertebral column, or differences in the length of the lower limbs. When present, scoliosis tends to get worse during adolescent growth spurts. Although most individuals do not require treatment, a back brace may be recommended for growing children. In extreme cases, surgery may be required.

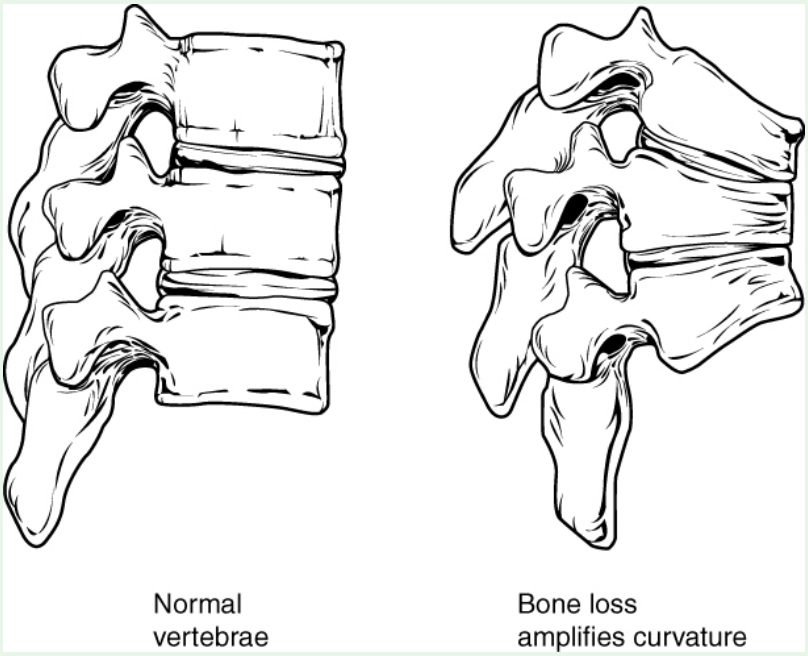


Figure 3. Osteoporosis. *Osteoporosis is an age-related disorder that causes the gradual loss of bone density and strength. When the thoracic vertebrae are affected, there can be a gradual collapse of the vertebrae. This results in kyphosis, an excessive curvature of the thoracic region.*

Excessive vertebral curves can be identified while an individual stands in the anatomical position. Observe the vertebral profile from the side and then from behind to check for kyphosis or lordosis. Then have the person bend forward. If scoliosis is present, an individual will have difficulty in bending directly forward, and the right and left sides of the back will not be level with each other in the bent position.

General Structure of a Vertebra

Within the different regions of the vertebral column, vertebrae vary in size and shape, but they all follow a similar structural pattern. A typical vertebra will consist of a body, a vertebral arch, and seven processes (Figure 4).

The body is the anterior portion of each vertebra and is the part that supports the body weight. Because of this, the vertebral bodies progressively increase in size and thickness going down the vertebral column. The bodies of adjacent vertebrae are separated and strongly united by an intervertebral disc.

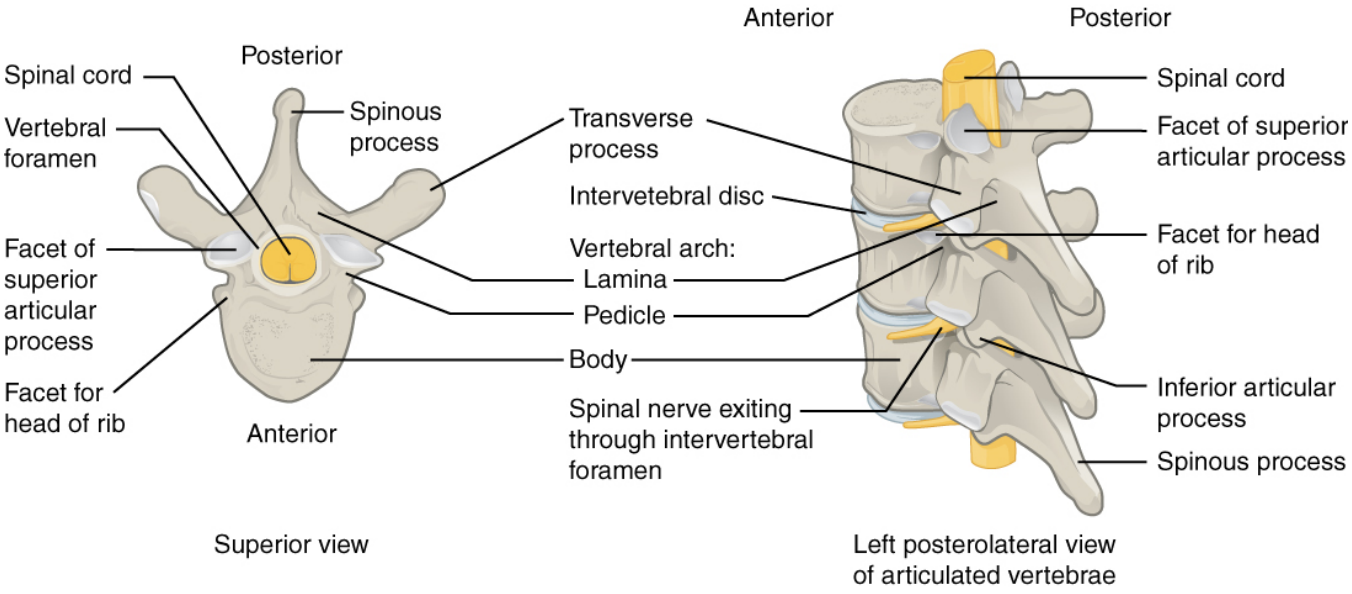


Figure 4. Parts of a Typical Vertebra. *A typical vertebra consists of a body and a vertebral arch. The arch is formed by the paired pedicles and paired laminae. Arising from the vertebral arch are the transverse, spinous, superior articular, and inferior articular processes. The vertebral foramen provides for passage of the spinal cord. Each spinal nerve exits through an intervertebral foramen, located between adjacent vertebrae. Intervertebral discs unite the bodies of adjacent vertebrae.*

The **vertebral arch** forms the posterior portion of each vertebra. It consists of four parts, the right and left pedicles and the right and left laminae. Each **pedicle** forms one of the lateral sides of the vertebral arch. The pedicles are anchored to the posterior side of the vertebral body. Each **lamina** forms part of the posterior roof of the vertebral arch. The large opening between the vertebral arch and body is the **vertebral foramen**, which contains the spinal cord. In the intact vertebral column, the vertebral foramina of all of the vertebrae align to form the **vertebral (spinal) canal**, which serves as the bony protection and passageway for the spinal cord down the back. When the vertebrae are aligned together in the vertebral column, notches in the margins of the pedicles of adjacent vertebrae together form an **intervertebral foramen**, the opening through which a spinal nerve exits from the vertebral column (Figure 5).

Seven processes arise from the vertebral arch. Each paired **transverse process** projects laterally and arises from the junction point between the pedicle and lamina. The single **spinous process** (vertebral spine) projects posteriorly at the midline of the back. The vertebral spines can easily be felt as a series of bumps just under the skin down the middle of the back. The transverse and spinous processes serve as important muscle attachment sites. A **superior articular process** extends or faces upward, and an **inferior articular process** faces or projects downward on each side of a vertebrae. The paired superior articular processes of one vertebra join with the corresponding paired inferior articular processes from the next higher vertebra. These junctions form slightly moveable joints between the adjacent vertebrae. The shape and orientation of the articular processes vary in different regions of the vertebral column and play a major role in determining the type and range of motion available in each region.

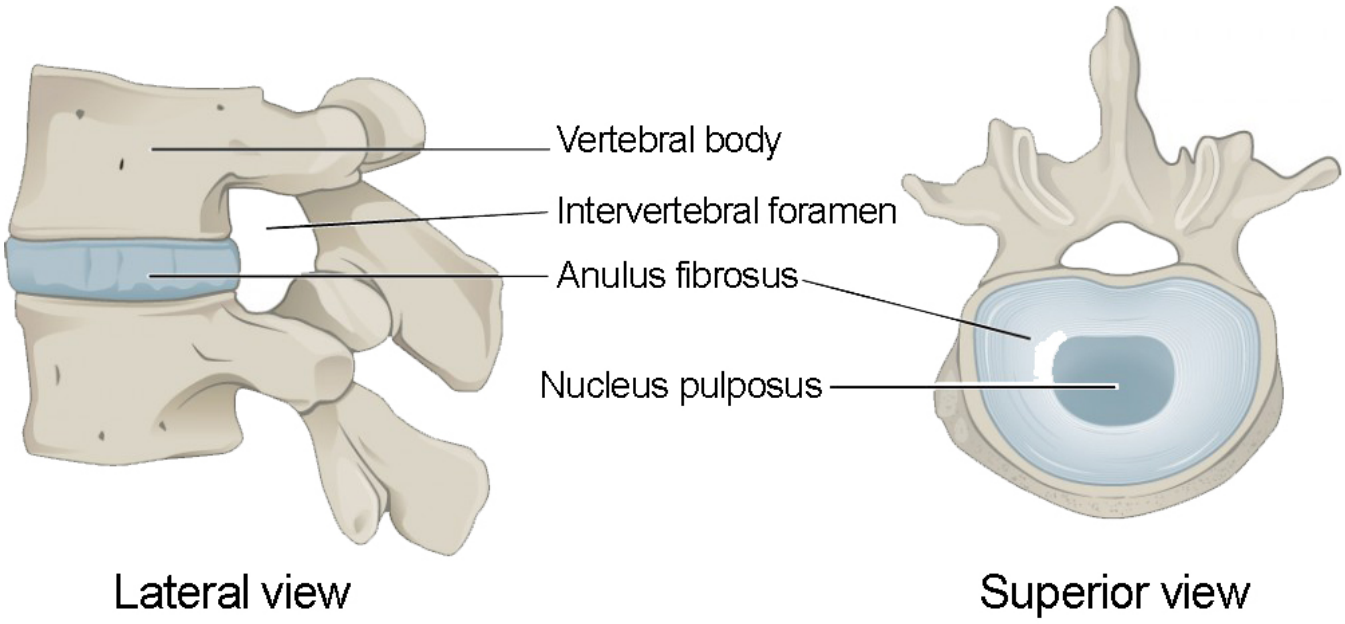


Figure 5. Intervertebral Disc. *The bodies of adjacent vertebrae are separated and united by an intervertebral disc, which provides padding and allows for movements between adjacent vertebrae. The disc consists of a fibrous outer layer called the anulus fibrosus and a gel-like center called the nucleus pulposus. The intervertebral foramen is the opening formed between adjacent vertebrae for the exit of a spinal nerve.*

Regional Modifications of Vertebrae

In addition to the general characteristics of a typical vertebra described above, vertebrae also display characteristic size and structural features that vary between the different vertebral column regions. Thus, cervical vertebrae are smaller than lumbar vertebrae due to differences in the proportion of body weight that each supports. Thoracic vertebrae have sites for rib attachment, and the vertebrae that give rise to the sacrum and coccyx have fused together into single bones.

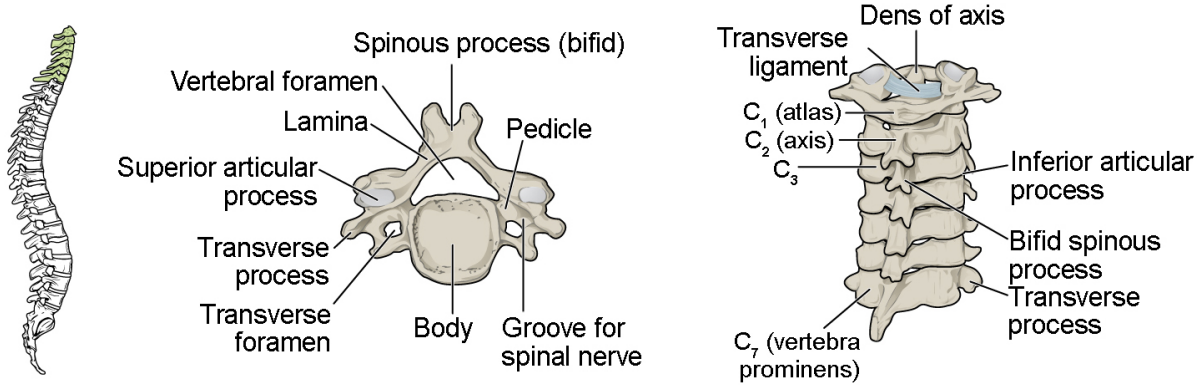
Cervical Vertebrae

Typical **cervical vertebrae**, such as C4 or C5, have several characteristic features that differentiate them from thoracic or lumbar vertebrae (Figure 6). Cervical vertebrae have a small body, reflecting the fact that they carry the least amount of body weight. Cervical vertebrae usually have a bifid (Y-shaped) spinous process. The spinous processes of the C3–C6 vertebrae are short, but the spine of C7 is much longer. You can find these vertebrae by running your finger down the midline of the posterior neck until you encounter the prominent C7 spine located at the base of the neck. The transverse processes of the cervical vertebrae are sharply curved (U-shaped) to allow for passage of the cervical spinal nerves. Each transverse process also has an opening called the **transverse foramen**. An important artery that supplies the brain ascends up the neck by passing through these openings. The superior and inferior articular processes of the cervical vertebrae are flattened and largely face upward or downward, respectively.

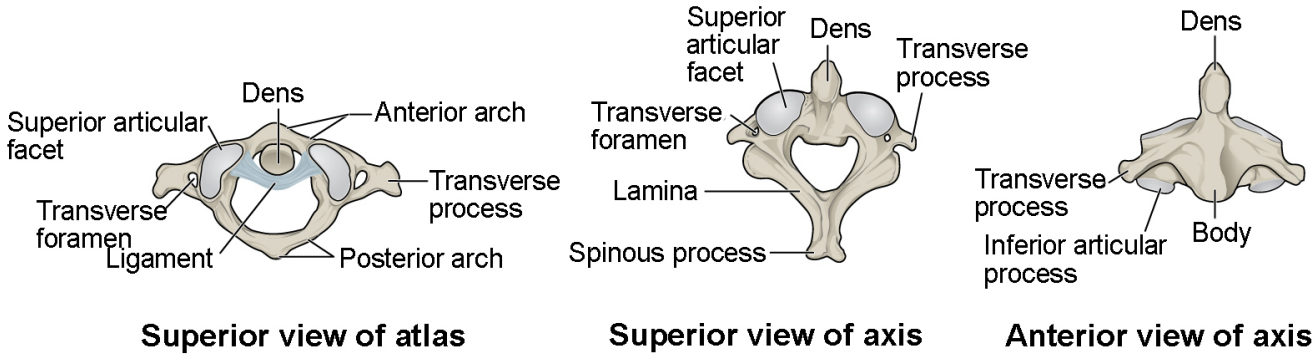
The first and second cervical vertebrae are further modified, giving each a distinctive appearance. The first cervical (C1) vertebra is also called the **atlas**, because this is the vertebra that supports the skull on top of the vertebral column (in Greek mythology, Atlas was the god who supported the heavens on his shoulders). The C1 vertebra does not have a body or spinous process. Instead, it is ring-shaped, consisting of an **anterior arch** and a **posterior arch**. The transverse processes of the atlas are longer and extend more laterally than do the transverse processes of any other cervical vertebrae. The superior articular processes face upward and are deeply curved for articulation with the occipital condyles on the base of the skull. The inferior articular processes are flat and face downward to join with the superior articular processes of the C2 vertebra.

The second cervical (C2) vertebra is called the **axis**, because it serves as the axis for rotation when turning the head toward the right or left. The axis resembles typical cervical vertebrae in most respects, but is easily

distinguished by the **dens** (odontoid process), a bony projection that extends upward from the vertebral body. The dens joins with the inner aspect of the anterior arch of the atlas, where it is held in place by transverse ligament.



Structure of a typical cervical vertebra



Superior view of atlas **Superior view of axis** **Anterior view of axis**

Figure 6. Cervical Vertebrae. *A typical cervical vertebra has a small body, a bifid spinous process, transverse processes that have a transverse foramen and are curved for spinal nerve passage. The atlas (C1 vertebra) does not have a body or spinous process. It consists of an anterior and a posterior arch and elongated transverse processes. The axis (C2 vertebra) has the upward projecting dens, which articulates with the anterior arch of the atlas.*

Thoracic Vertebrae

The bodies of the **thoracic vertebrae** are larger than those of cervical vertebrae (Figure 7). The characteristic feature for a typical midthoracic vertebra is the spinous process, which is long and has a pronounced downward angle that causes it to overlap the next inferior vertebra. The superior articular processes of thoracic vertebrae face anteriorly and the inferior processes face posteriorly. These orientations are important determinants for the type and range of movements available to the thoracic region of the vertebral column.

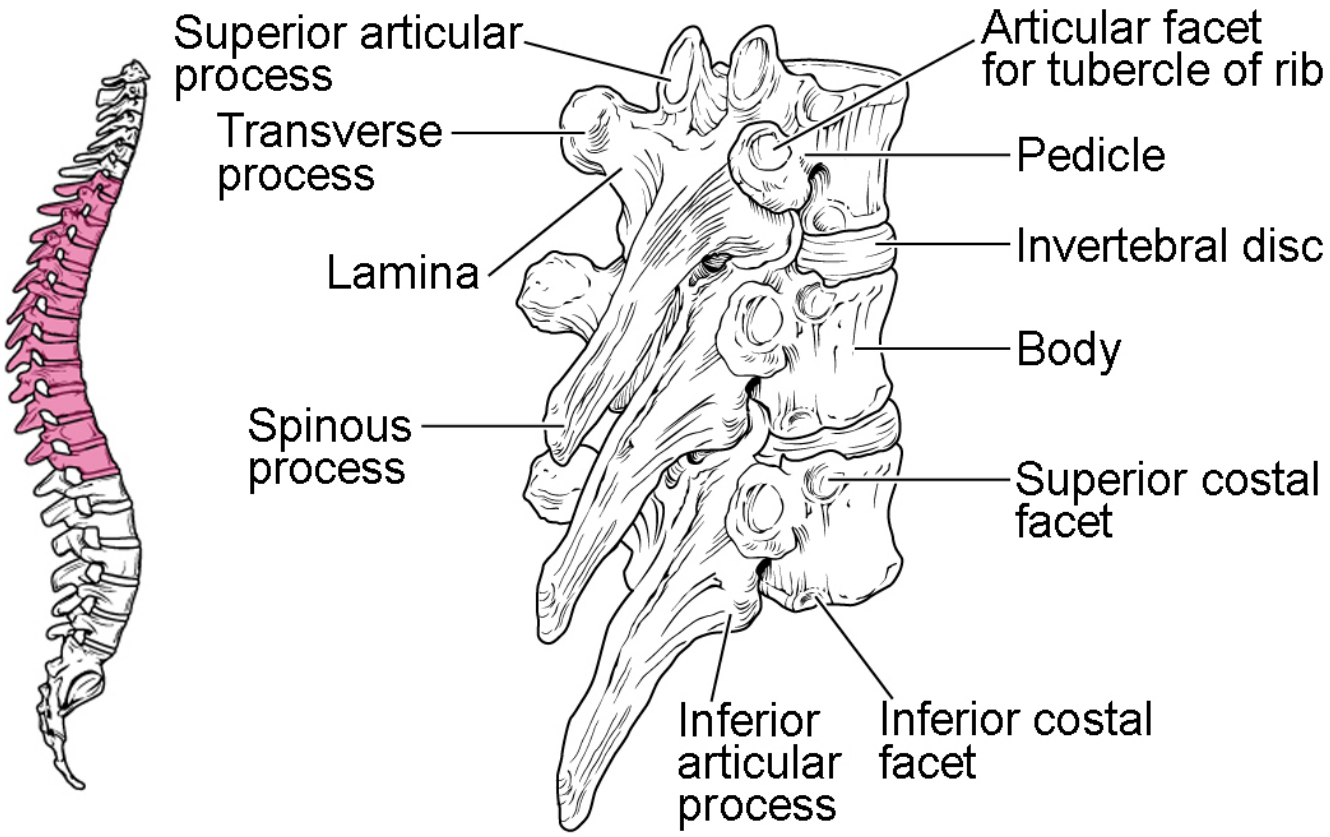


Figure 7. Thoracic Vertebrae. *A typical thoracic vertebra is distinguished by the spinous process, which is long and projects downward to overlap the next inferior vertebra. It also has articulation sites (facets) on the vertebral body and a transverse process for rib attachment.*

Thoracic vertebrae have several additional articulation sites, each of which is called a **facet**, where a rib is attached. Most thoracic vertebrae have two facets located on the lateral sides of the body, each of which is called a **costal facet** (costal = “rib”). These are for articulation with the head (end) of a rib. An additional facet is located on the transverse process for articulation with the tubercle of a rib.

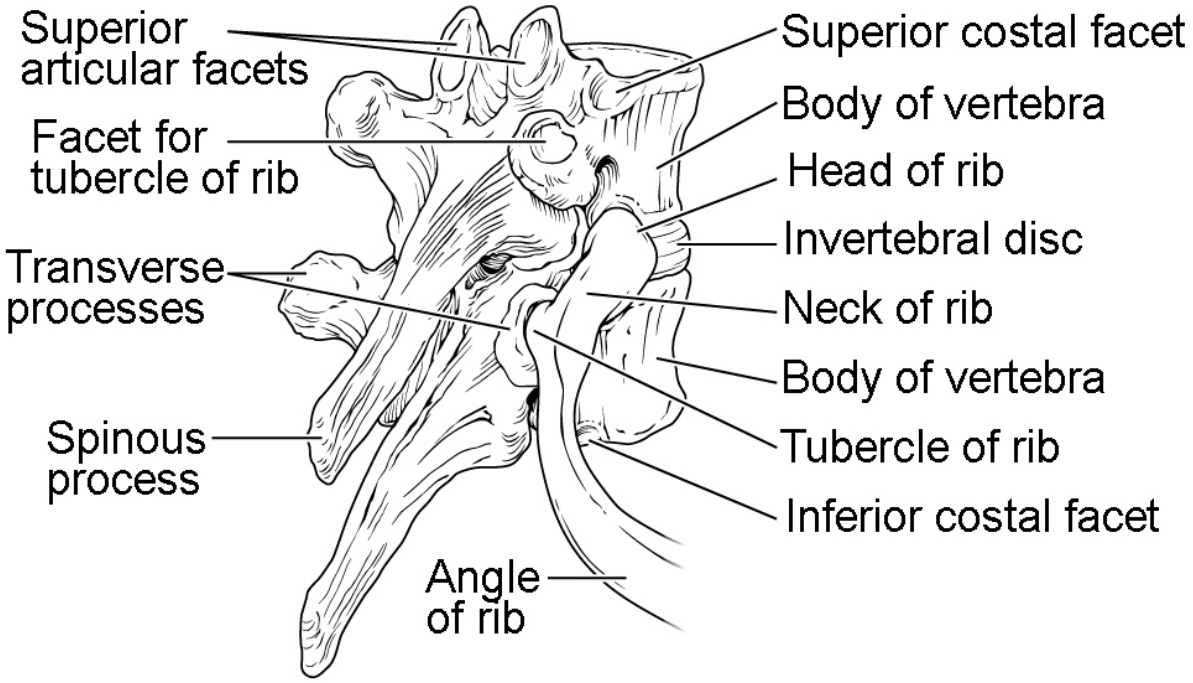


Figure 8. Rib Articulation in Thoracic Vertebrae. *Thoracic vertebrae have superior and inferior articular facets on the vertebral body for articulation with the head of a rib, and a transverse process facet for articulation with the rib tubercle.*

Lumbar Vertebrae

Lumbar vertebrae carry the greatest amount of body weight and are thus characterized by the large size and thickness of the vertebral body (Figure 9). They have short transverse processes and a short, blunt spinous process that projects posteriorly. The articular processes are large, with the superior process facing backward and the inferior facing forward.

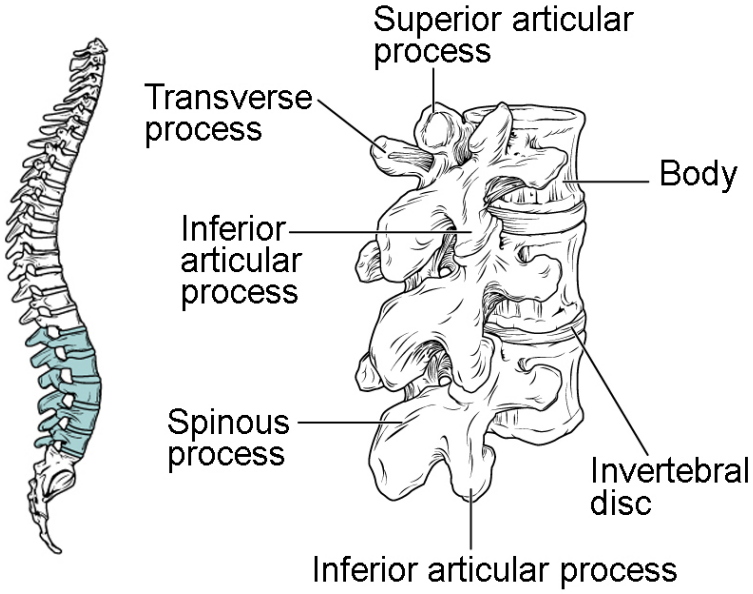


Figure 9. Lumbar Vertebrae. *Lumbar vertebrae are characterized by having a large, thick body and a short, rounded spinous process.*

Sacrum and Coccyx

The sacrum is a triangular-shaped bone that is thick and wide across its superior base where it is weight bearing and then tapers down to an inferior, non-weight bearing apex (Figure 10). It is formed by the fusion of five sacral vertebrae, a process that does not begin until after the age of 20. On the anterior surface of the older adult sacrum, the lines of vertebral fusion can be seen as four transverse ridges. On the posterior surface, running down the midline, is the **median sacral crest**, a bumpy ridge that is the remnant of the fused spinous processes (median = "midline"; while medial = "toward, but not necessarily at, the midline"). Similarly, the fused transverse processes of the sacral vertebrae form the **lateral sacral crest**.

The **sacral promontory** is the anterior lip of the superior base of the sacrum. Lateral to this is the roughened auricular surface, which joins with the ilium portion of the hipbone to form the immobile sacroiliac joints of the

pelvis. Passing inferiorly through the sacrum is a bony tunnel called the **sacral canal**, which terminates at the **sacral hiatus** near the inferior tip of the sacrum. The anterior and posterior surfaces of the sacrum have a series of paired openings called ***sacral foramina*** (singular = foramen) that connect to the sacral canal. Each of these openings is called a **posterior (dorsal) sacral foramen** or **anterior (ventral) sacral foramen**. These openings allow for the anterior and posterior branches of the sacral spinal nerves to exit the sacrum. The **superior articular process of the sacrum**, one of which is found on either side of the superior opening of the sacral canal, articulates with the inferior articular processes from the L5 vertebra.

The coccyx, or tailbone, is derived from the fusion of four very small coccygeal vertebrae (see Figure 10). It articulates with the inferior tip of the sacrum. It is not weight bearing in the standing position, but may receive some body weight when sitting.

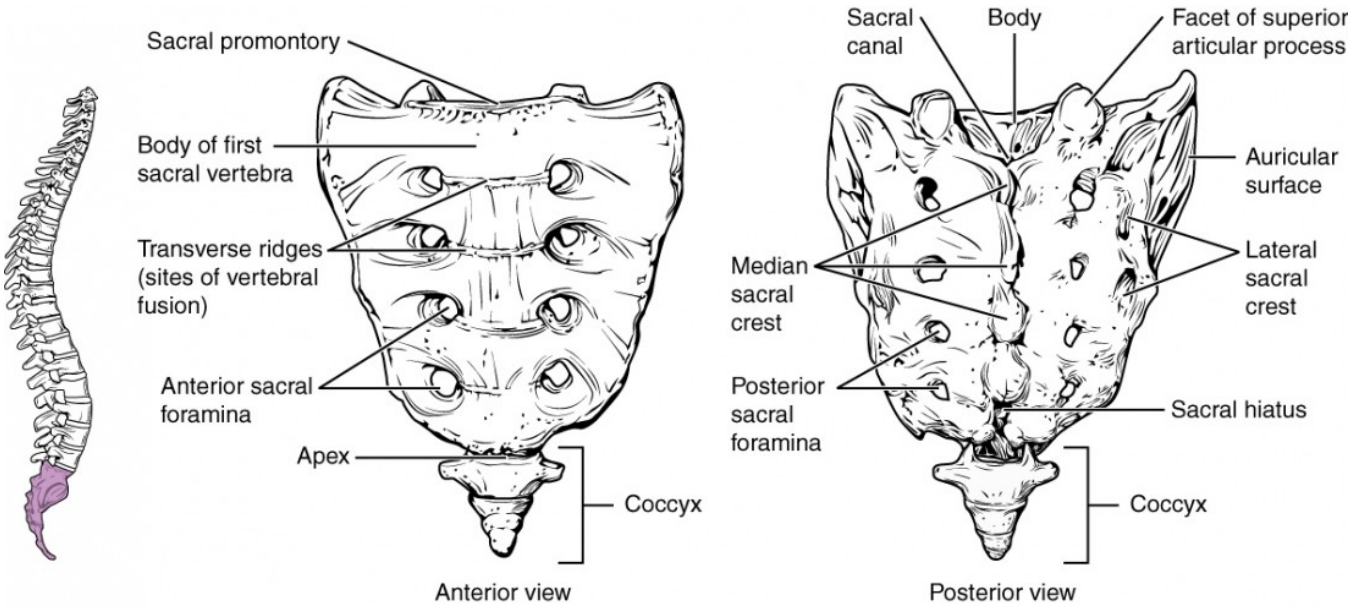


Figure 10. Sacrum and Coccyx. *The sacrum is formed from the fusion of five sacral vertebrae, whose lines of fusion are indicated by the transverse ridges. The fused spinous processes form the median sacral crest, while the lateral sacral crest arises from the fused transverse processes. The coccyx is formed by the fusion of four small coccygeal vertebrae.*

Intervertebral Discs and Ligaments of the Vertebral Column

The bodies of adjacent vertebrae are strongly anchored to each other by an intervertebral disc. This structure provides padding between the bones during weight bearing, and because it can change shape, also allows for movement between the vertebrae. Although the total amount of movement available between any two adjacent vertebrae is small, when these movements are summed together along the entire length of the vertebral column, large body movements can be produced. Ligaments that extend along the length of the vertebral column also contribute to its overall support and stability.

Intervertebral Disc

An **intervertebral disc** is a fibrocartilaginous pad that fills the gap between adjacent vertebral bodies (see Figure 5). Each disc is anchored to the bodies of its adjacent vertebrae, thus strongly uniting these. The discs also provide padding between vertebrae during weight bearing. Because of this, intervertebral discs are thin in the cervical region and thickest in the lumbar region, which carries the most body weight. In total, the intervertebral discs account for approximately 25 percent of your body height between the top of the pelvis and the base of the skull. Intervertebral discs are also flexible and can change shape to allow for movements of the vertebral column.

Each intervertebral disc consists of two parts. The **anulus fibrosus** is the tough, fibrous outer layer of the disc. It forms a circle (anulus = “ring” or “circle”) and is firmly anchored to the outer margins of the adjacent vertebral bodies. Inside is the **nucleus pulposus**, consisting of a softer, more gel-like material. It has a high water content

that serves to resist compression and thus is important for weight bearing. With increasing age, the water content of the nucleus pulposus gradually declines. This causes the disc to become thinner, decreasing total body height somewhat, and reduces the flexibility and range of motion of the disc, making bending more difficult.

The gel-like nature of the nucleus pulposus also allows the intervertebral disc to change shape as one vertebra rocks side to side or forward and back in relation to its neighbors during movements of the vertebral column. Thus, bending forward causes compression of the anterior portion of the disc but expansion of the posterior disc. If the posterior anulus fibrosus is weakened due to injury or increasing age, the pressure exerted on the disc when bending forward and lifting a heavy object can cause the nucleus pulposus to protrude posteriorly through the anulus fibrosus, resulting in a herniated disc ("ruptured" or "slipped" disc) (Figure 11). The posterior bulging of the nucleus pulposus can cause compression of a spinal nerve at the point where it exits through the intervertebral foramen, with resulting pain and/or muscle weakness in those body regions supplied by that nerve. The most common sites for disc herniation are the L4/L5 or L5/S1 intervertebral discs, which can cause sciatica, a widespread pain that radiates from the lower back down the thigh and into the leg. Similar injuries of the C5/C6 or C6/C7 intervertebral discs, following forcible hyperflexion of the neck from a collision accident or football injury, can produce pain in the neck, shoulder, and upper limb.

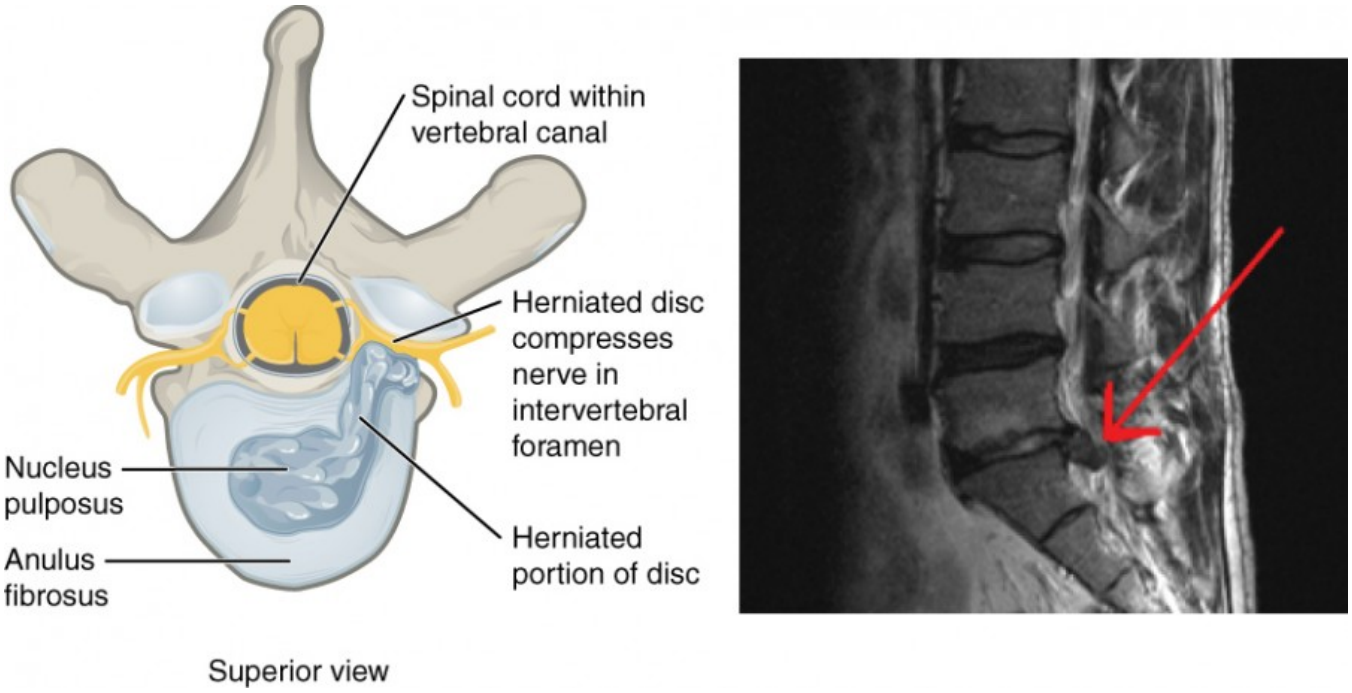


Figure 11. Herniated Intervertebral Disc. *Weakening of the anulus fibrosus can result in herniation (protrusion) of the nucleus pulposus and compression of a spinal nerve, resulting in pain and/or muscle weakness in the body regions supplied by that nerve.*

Watch this animation to see what it means to "slip" a disk.
Watch this video online: https://youtu.be/ggcDWKYRah8

Ligaments of the Vertebral Column

Adjacent vertebrae are united by ligaments that run the length of the vertebral column along both its posterior and anterior aspects (Figure 12). These serve to resist excess forward or backward bending movements of the vertebral column, respectively.

The **anterior longitudinal ligament** runs down the anterior side of the entire vertebral column, uniting the vertebral bodies. It serves to resist excess backward bending of the vertebral column. Protection against this movement is particularly important in the neck, where extreme posterior bending of the head and neck can stretch or tear this ligament, resulting in a painful whiplash injury. Prior to the mandatory installation of seat headrests, whiplash injuries were common for passengers involved in a rear-end automobile collision.

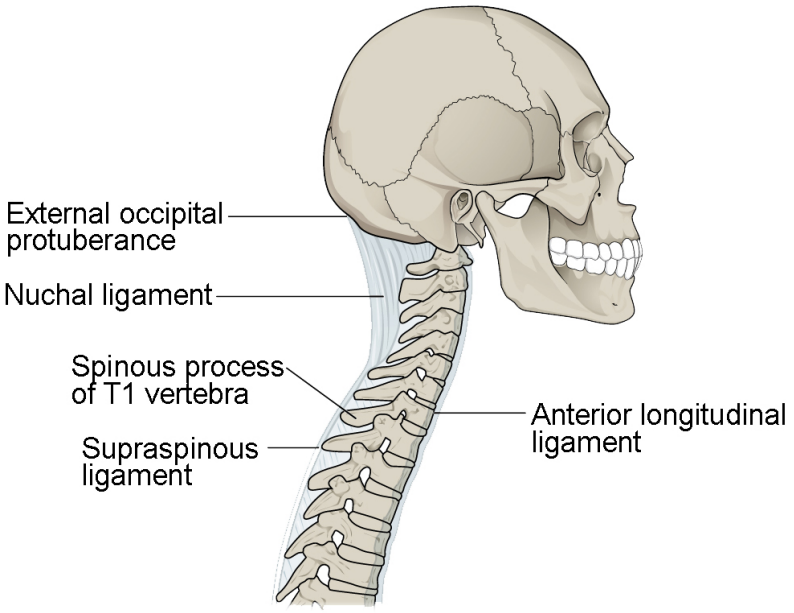


Figure 12. Ligaments of Vertebral Column. *The anterior longitudinal ligament runs the length of the vertebral column, uniting the anterior sides of the vertebral bodies. The supraspinous ligament connects the spinous processes of the thoracic and lumbar vertebrae. In the posterior neck, the supraspinous ligament enlarges to form the nuchal ligament, which attaches to the cervical spinous processes and to the base of the skull.*

The **supraspinous ligament** is located on the posterior side of the vertebral column, where it interconnects the spinous processes of the thoracic and lumbar vertebrae. This strong ligament supports the vertebral column during forward bending motions. In the posterior neck, where the cervical spinous processes are short, the supraspinous ligament expands to become the **nuchal ligament** (nuchae = “nape” or “back of the neck”). The nuchal ligament is attached to the cervical spinous processes and extends upward and posteriorly to attach to the midline base of the skull, out to the external occipital protuberance. It supports the skull and prevents it from falling forward. This ligament is much larger and stronger in four-legged animals such as cows, where the large skull hangs off the front end of the vertebral column. You can easily feel this ligament by first extending your head backward and pressing down on the posterior midline of your neck. Then tilt your head forward and you will fill the nuchal ligament popping out as it tightens to limit anterior bending of the head and neck.

Additional ligaments are located inside the vertebral canal, next to the spinal cord, along the length of the vertebral column. The **posterior longitudinal ligament** is found anterior to the spinal cord, where it is attached to the posterior sides of the vertebral bodies. Posterior to the spinal cord is the **ligamentum flavum** (“yellow ligament”). This consists of a series of short, paired ligaments, each of which interconnects the lamina regions of adjacent vertebrae. The ligamentum flavum has large numbers of elastic fibers, which have a yellowish color, allowing it to stretch and then pull back. Both of these ligaments provide important support for the vertebral column when bending forward.

Use this tool to identify the bones, intervertebral discs, and ligaments of the vertebral column. The thickest portions of the anterior longitudinal ligament and the supraspinous ligament are found in which regions of the vertebral column?

Career Connections: Chiropractor

Chiropractors are health professionals who use nonsurgical techniques to help patients with musculoskeletal system problems that involve the bones, muscles, ligaments, tendons, or nervous system. They treat problems such as neck pain, back pain, joint pain, or headaches. Chiropractors focus on the patient’s overall

health and can also provide counseling related to lifestyle issues, such as diet, exercise, or sleep problems. If needed, they will refer the patient to other medical specialists.

Chiropractors use a drug-free, hands-on approach for patient diagnosis and treatment. They will perform a physical exam, assess the patient's posture and spine, and may perform additional diagnostic tests, including taking X-ray images. They primarily use manual techniques, such as spinal manipulation, to adjust the patient's spine or other joints. They can recommend therapeutic or rehabilitative exercises, and some also include acupuncture, massage therapy, or ultrasound as part of the treatment program. In addition to those in general practice, some chiropractors specialize in sport injuries, neurology, orthopaedics, pediatrics, nutrition, internal disorders, or diagnostic imaging.

To become a chiropractor, students must have 3–4 years of undergraduate education, attend an accredited, four-year Doctor of Chiropractic (D.C.) degree program, and pass a licensure examination to be licensed for practice in their state. With the aging of the baby-boom generation, employment for chiropractors is expected to increase.

THE THORACIC CAGE

Learning Objectives

- Discuss the components that make up the thoracic cage
- Identify the parts of the sternum and define the sternal angle
- Discuss the parts of a rib and rib classifications

The thoracic cage (rib cage) forms the thorax (chest) portion of the body. It consists of the 12 pairs of ribs with their costal cartilages and the sternum (Figure 1). The ribs are anchored posteriorly to the 12 thoracic vertebrae (T1–T12). The thoracic cage protects the heart and lungs.

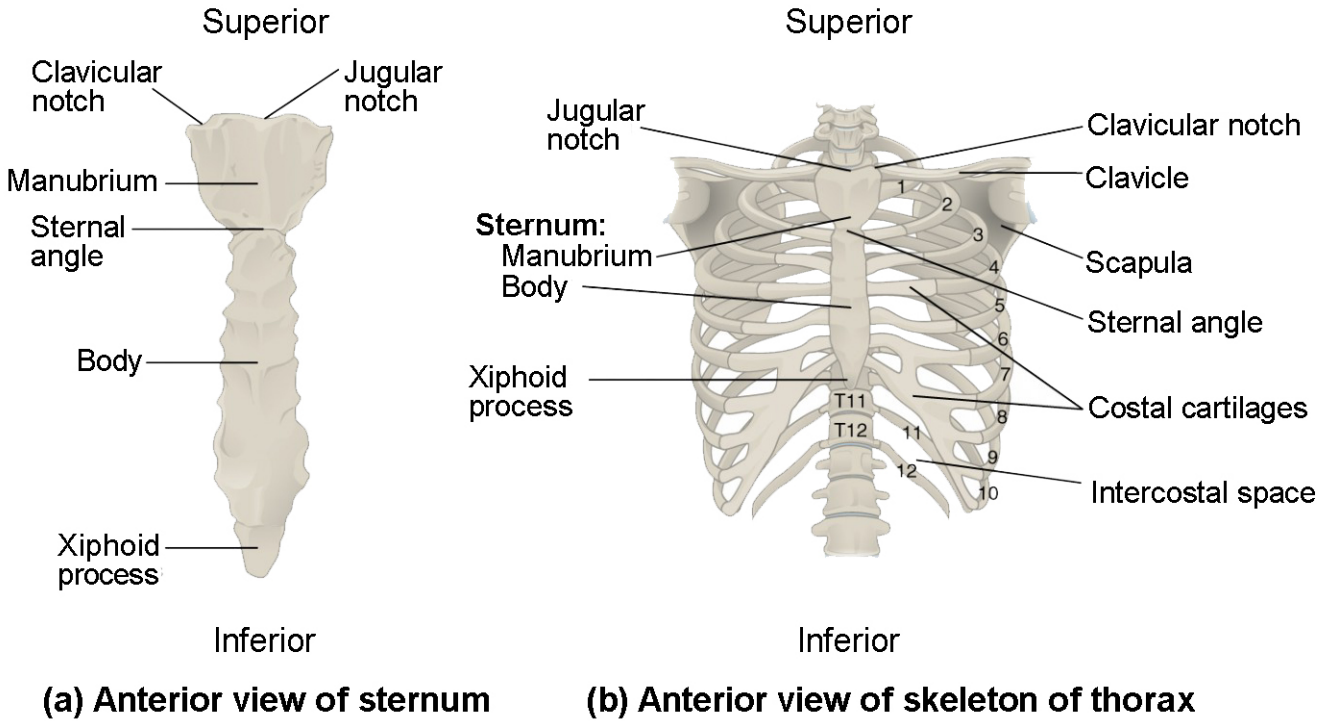


Figure 1. Thoracic Cage. *The thoracic cage is formed by the (a) sternum and (b) 12 pairs of ribs with their costal cartilages. The ribs are anchored posteriorly to the 12 thoracic vertebrae. The sternum consists of the manubrium, body, and xiphoid process. The ribs are classified as true ribs (1–7) and false ribs (8–12). The last two pairs of false ribs are also known as floating ribs (11–12).*

Sternum

The sternum is the elongated bony structure that anchors the anterior thoracic cage. It consists of three parts: the manubrium, body, and xiphoid process. The **manubrium** is the wider, superior portion of the sternum. The top of the manubrium has a shallow, U-shaped border called the **jugular (suprasternal) notch**. This can be easily felt at the anterior base of the neck, between the medial ends of the clavicles. The **clavicular notch** is the shallow depression located on either side at the superior-lateral margins of the manubrium. This is the site of the sternoclavicular joint, between the sternum and clavicle. The first ribs also attach to the manubrium.

The elongated, central portion of the sternum is the body. The manubrium and body join together at the **sternal angle**, so called because the junction between these two components is not flat, but forms a slight bend. The second rib attaches to the sternum at the sternal angle. Since the first rib is hidden behind the clavicle, the second rib is the highest rib that can be identified by palpation. Thus, the sternal angle and second rib are important landmarks for the identification and counting of the lower ribs. Ribs 3–7 attach to the sternal body.

The inferior tip of the sternum is the **xiphoid process**. This small structure is cartilaginous early in life, but gradually becomes ossified starting during middle age.

Ribs

Each rib is a curved, flattened bone that contributes to the wall of the thorax. The ribs articulate posteriorly with the T1–T12 thoracic vertebrae, and most attach anteriorly via their costal cartilages to the sternum. There are 12 pairs of ribs. The ribs are numbered 1–12 in accordance with the thoracic vertebrae.

Parts of a Typical Rib

The posterior end of a typical rib is called the **head of the rib**. This region articulates primarily with the costal facet located on the body of the same numbered thoracic vertebra and to a lesser degree, with the costal facet located on the body of the next higher vertebra. Lateral to the head is the narrowed **neck of the rib**. A small bump on the posterior rib surface is the **tubercle of the rib**, which articulates with the facet located on the transverse process of the same numbered vertebra. The remainder of the rib is the **body of the rib** (shaft). Just lateral to the tubercle is the **angle of the rib**, the point at which the rib has its greatest degree of curvature. The angles of the ribs form the most posterior extent of the thoracic cage. In the anatomical position, the angles align with the medial border of the scapula. A shallow **costal groove** for the passage of blood vessels and a nerve is found along the inferior margin of each rib.

Rib Classifications

The bony ribs do not extend anteriorly completely around to the sternum. Instead, each rib ends in a **costal cartilage**. These cartilages are made of hyaline cartilage and can extend for several inches. Most ribs are then attached, either directly or indirectly, to the sternum via their costal cartilage (see Figure 1). The ribs are classified into three groups based on their relationship to the sternum.

Ribs 1–7 are classified as **true ribs** (vertebrosternal ribs). The costal cartilage from each of these ribs attaches directly to the sternum. Ribs 8–12 are called **false ribs** (vertebrochondral ribs). The costal cartilages from these ribs do not attach directly to the sternum. For ribs 8–10, the costal cartilages are attached to the cartilage of the next higher rib. Thus, the cartilage of rib 10 attaches to the cartilage of rib 9, rib 9 then attaches to rib 8, and rib 8 is attached to rib 7. The last two false ribs (11–12) are also called **floating ribs** (vertebral ribs). These are short ribs that do not attach to the sternum at all. Instead, their small costal cartilages terminate within the musculature of the lateral abdominal wall.

EMBRYONIC DEVELOPMENT OF THE AXIAL SKELETON

Learning Objectives

- Discuss the two types of embryonic bone development within the skull
- Describe the development of the vertebral column and thoracic cage

The axial skeleton begins to form during early embryonic development. However, growth, remodeling, and ossification (bone formation) continue for several decades after birth before the adult skeleton is fully formed. Knowledge of the developmental processes that give rise to the skeleton is important for understanding the abnormalities that may arise in skeletal structures.

Development of the Skull

During the third week of embryonic development, a rod-like structure called the **notochord** develops dorsally along the length of the embryo. The tissue overlying the notochord enlarges and forms the neural tube, which will give

rise to the brain and spinal cord. By the fourth week, mesoderm tissue located on either side of the notochord thickens and separates into a repeating series of block-like tissue structures, each of which is called a **somite**. As the somites enlarge, each one will split into several parts. The most medial of these parts is called a **sclerotome**. The sclerotomes consist of an embryonic tissue called mesenchyme, which will give rise to the fibrous connective tissues, cartilages, and bones of the body.

The bones of the skull arise from mesenchyme during embryonic development in two different ways. The first mechanism produces the bones that form the top and sides of the brain case. This involves the local accumulation of mesenchymal cells at the site of the future bone. These cells then differentiate directly into bone producing cells, which form the skull bones through the process of intramembranous ossification. As the brain case bones grow in the fetal skull, they remain separated from each other by large areas of dense connective tissue, each of which is called a **fontanelle** (Figure 7.33). The fontanelles are the soft spots on an infant's head. They are important during birth because these areas allow the skull to change shape as it squeezes through the birth canal. After birth, the fontanelles allow for continued growth and expansion of the skull as the brain enlarges. The largest fontanelle is located on the anterior head, at the junction of the frontal and parietal bones. The fontanelles decrease in size and disappear by age 2. However, the skull bones remained separated from each other at the sutures, which contain dense fibrous connective tissue that unites the adjacent bones. The connective tissue of the sutures allows for continued growth of the skull bones as the brain enlarges during childhood growth.

The second mechanism for bone development in the skull produces the facial bones and floor of the brain case. This also begins with the localized accumulation of mesenchymal cells. However, these cells differentiate into cartilage cells, which produce a hyaline cartilage model of the future bone. As this cartilage model grows, it is gradually converted into bone through the process of endochondral ossification. This is a slow process and the cartilage is not completely converted to bone until the skull achieves its full adult size.

At birth, the brain case and orbits of the skull are disproportionally large compared to the bones of the jaws and lower face. This reflects the relative underdevelopment of the maxilla and mandible, which lack teeth, and the small sizes of the paranasal sinuses and nasal cavity. During early childhood, the mastoid process enlarges, the two halves of the mandible and frontal bone fuse together to form single bones, and the paranasal sinuses enlarge. The jaws also expand as the teeth begin to appear. These changes all contribute to the rapid growth and enlargement of the face during childhood.

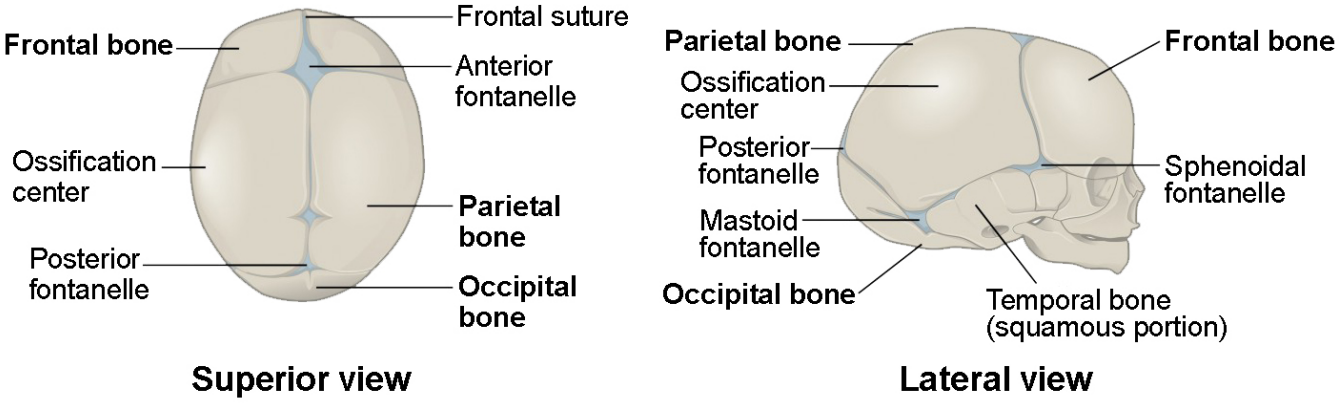


Figure 1. Newborn Skull. *The bones of the newborn skull are not fully ossified and are separated by large areas called fontanelles, which are filled with fibrous connective tissue. The fontanelles allow for continued growth of the skull after birth. At the time of birth, the facial bones are small and underdeveloped, and the mastoid process has not yet formed.*

Development of the Vertebral Column and Thoracic cage

Development of the vertebrae begins with the accumulation of mesenchyme cells from each sclerotome around the notochord. These cells differentiate into a hyaline cartilage model for each vertebra, which then grow and eventually ossify into bone through the process of endochondral ossification. As the developing vertebrae grow, the notochord largely disappears. However, small areas of notochord tissue persist between the adjacent vertebrae and this contributes to the formation of each intervertebral disc.

The ribs and sternum also develop from mesenchyme. The ribs initially develop as part of the cartilage model for each vertebra, but in the thorax region, the rib portion separates from the vertebra by the eighth week. The cartilage model of the rib then ossifies, except for the anterior portion, which remains as the costal cartilage. The sternum initially forms as paired hyaline cartilage models on either side of the anterior midline, beginning during the fifth week of development. The cartilage models of the ribs become attached to the lateral sides of the developing sternum. Eventually, the two halves of the cartilaginous sternum fuse together along the midline and then ossify into bone. The manubrium and body of the sternum are converted into bone first, with the xiphoid process remaining as cartilage until late in life.

View this video to review the two processes that give rise to the bones of the skull and body.

Watch this video online: https://youtu.be/p-3PuLXp9Wg

What are the two mechanisms by which the bones of the body are formed and which bones are formed by each mechanism?

Homeostatic Imbalances: Craniosynostosis

The premature closure (fusion) of a suture line is a condition called craniosynostosis. This error in the normal developmental process results in abnormal growth of the skull and deformity of the head. It is produced either by defects in the ossification process of the skull bones or failure of the brain to properly enlarge. Genetic factors are involved, but the underlying cause is unknown. It is a relatively common condition, occurring in approximately 1:2000 births, with males being more commonly affected. Primary craniosynostosis involves the early fusion of one cranial suture, whereas complex craniosynostosis results from the premature fusion of several sutures.

The early fusion of a suture in primary craniosynostosis prevents any additional enlargement of the cranial bones and skull along this line. Continued growth of the brain and skull is therefore diverted to other areas of the head, causing an abnormal enlargement of these regions. For example, the early disappearance of the anterior fontanelle and premature closure of the sagittal suture prevents growth across the top of the head. This is compensated by upward growth by the bones of the lateral skull, resulting in a long, narrow, wedge-shaped head. This condition, known as scaphocephaly, accounts for approximately 50 percent of craniosynostosis abnormalities. Although the skull is misshapen, the brain still has adequate room to grow and thus there is no accompanying abnormal neurological development.

In cases of complex craniosynostosis, several sutures close prematurely. The amount and degree of skull deformity is determined by the location and extent of the sutures involved. This results in more severe constraints on skull growth, which can alter or impede proper brain growth and development.

Cases of craniosynostosis are usually treated with surgery. A team of physicians will open the skull along the fused suture, which will then allow the skull bones to resume their growth in this area. In some cases, parts of the skull will be removed and replaced with an artificial plate. The earlier after birth that surgery is performed, the better the outcome. After treatment, most children continue to grow and develop normally and do not exhibit any neurological problems.

GLOSSARY: THE AXIAL SKELETON

alveolar process of the mandible: upper border of mandibular body that contains the lower teeth

alveolar process of the maxilla: curved, inferior margin of the maxilla that supports and anchors the upper teeth

angle of the mandible: rounded corner located at outside margin of the body and ramus junction

angle of the rib: portion of rib with greatest curvature; together, the rib angles form the most posterior extent of the thoracic cage

anterior (ventral) sacral foramen: one of the series of paired openings located on the anterior (ventral) side of the sacrum

anterior arch: anterior portion of the ring-like C1 (atlas) vertebra

anterior cranial fossa: shallowest and most anterior cranial fossa of the cranial base that extends from the frontal bone to the lesser wing of the sphenoid bone

anterior longitudinal ligament: ligament that runs the length of the vertebral column, uniting the anterior aspects of the vertebral bodies

anulus fibrosus: tough, fibrous outer portion of an intervertebral disc, which is strongly anchored to the bodies of the adjacent vertebrae

appendicular skeleton: all bones of the upper and lower limbs, plus the girdle bones that attach each limb to the axial skeleton

articular tubercle: smooth ridge located on the inferior skull, immediately anterior to the mandibular fossa

atlas: first cervical (C1) vertebra

axial skeleton: central, vertical axis of the body, including the skull, vertebral column, and thoracic cage

axis: second cervical (C2) vertebra

body of the rib: shaft portion of a rib

brain case: portion of the skull that contains and protects the brain, consisting of the eight bones that form the cranial base and rounded upper skull

calvaria: (also, skullcap) rounded top of the skull

carotid canal: zig-zag tunnel providing passage through the base of the skull for the internal carotid artery to the brain; begins anteromedial to the styloid process and terminates in the middle cranial cavity, near the posterior-lateral base of the sella turcica

cervical curve: posteriorly concave curvature of the cervical vertebral column region; a secondary curve of the vertebral column

cervical vertebrae: seven vertebrae numbered as C1–C7 that are located in the neck region of the vertebral column

clavicular notch: paired notches located on the superior-lateral sides of the sternal manubrium, for articulation with the clavicle

coccyx: small bone located at inferior end of the adult vertebral column that is formed by the fusion of four coccygeal vertebrae; also referred to as the “tailbone”

condylar process of the mandible: thickened upward projection from posterior margin of mandibular ramus

condyle: oval-shaped process located at the top of the condylar process of the mandible

coronal suture: joint that unites the frontal bone to the right and left parietal bones across the top of the skull

coronoid process of the mandible: flattened upward projection from the anterior margin of the mandibular ramus

costal cartilage: hyaline cartilage structure attached to the anterior end of each rib that provides for either direct or indirect attachment of most ribs to the sternum

costal facet: site on the lateral sides of a thoracic vertebra for articulation with the head of a rib

costal groove: shallow groove along the inferior margin of a rib that provides passage for blood vessels and a nerve

cranial cavity: interior space of the skull that houses the brain

cranium: skull

cribriform plate: small, flattened areas with numerous small openings, located to either side of the midline in the floor of the anterior cranial fossa; formed by the ethmoid bone

crista galli: small upward projection located at the midline in the floor of the anterior cranial fossa; formed by the ethmoid bone

dens: bony projection (odontoid process) that extends upward from the body of the C2 (axis) vertebra

ear ossicles: three small bones located in the middle ear cavity that serve to transmit sound vibrations to the inner ear

ethmoid air cell: one of several small, air-filled spaces located within the lateral sides of the ethmoid bone, between the orbit and upper nasal cavity

ethmoid bone: unpaired bone that forms the roof and upper, lateral walls of the nasal cavity, portions of the floor of the anterior cranial fossa and medial wall of orbit, and the upper portion of the nasal septum

external acoustic meatus: ear canal opening located on the lateral side of the skull

external occipital protuberance: small bump located at the midline on the posterior skull

facet: small, flattened area on a bone for an articulation (joint) with another bone, or for muscle attachment

facial bones: fourteen bones that support the facial structures and form the upper and lower jaws and the hard palate

false ribs: vertebrochondral ribs 8–12 whose costal cartilage either attaches indirectly to the sternum via the costal cartilage of the next higher rib or does not attach to the sternum at all

floating ribs: vertebral ribs 11–12 that do not attach to the sternum or to the costal cartilage of another rib

fontanelle: expanded area of fibrous connective tissue that separates the brain case bones of the skull prior to birth and during the first year after birth

foramen lacerum: irregular opening in the base of the skull, located inferior to the exit of carotid canal

foramen magnum: large opening in the occipital bone of the skull through which the spinal cord emerges and the vertebral arteries enter the cranium

foramen ovale of the middle cranial fossa: oval-shaped opening in the floor of the middle cranial fossa

foramen rotundum: round opening in the floor of the middle cranial fossa, located between the superior orbital fissure and foramen ovale

foramen spinosum: small opening in the floor of the middle cranial fossa, located lateral to the foramen ovale

frontal bone: unpaired bone that forms forehead, roof of orbit, and floor of anterior cranial fossa

frontal sinus: air-filled space within the frontal bone; most anterior of the paranasal sinuses

glabella: slight depression of frontal bone, located at the midline between the eyebrows

greater wings of sphenoid bone: lateral projections of the sphenoid bone that form the anterior wall of the middle cranial fossa and an area of the lateral skull

hard palate: bony structure that forms the roof of the mouth and floor of the nasal cavity, formed by the palatine process of the maxillary bones and the horizontal plate of the palatine bones

head of the rib: posterior end of a rib that articulates with the bodies of thoracic vertebrae

horizontal plate: medial extension from the palatine bone that forms the posterior quarter of the hard palate

hyoid bone: small, U-shaped bone located in upper neck that does not contact any other bone

hypoglossal canal: paired openings that pass anteriorly from the anterior-lateral margins of the foramen magnum deep to the occipital condyles

hypophyseal (pituitary) fossa: shallow depression on top of the sella turcica that houses the pituitary (hypophyseal) gland

inferior articular process: bony process that extends downward from the vertebral arch of a vertebra that articulates with the superior articular process of the next lower vertebra

inferior nasal concha: one of the paired bones that project from the lateral walls of the nasal cavity to form the largest and most inferior of the nasal conchae

infraorbital foramen: opening located on anterior skull, below the orbit

infratemporal fossa: space on lateral side of skull, below the level of the zygomatic arch and deep (medial) to the ramus of the mandible

internal acoustic meatus: opening into petrous ridge, located on the lateral wall of the posterior cranial fossa

intervertebral disc: structure located between the bodies of adjacent vertebrae that strongly joins the vertebrae; provides padding, weight bearing ability, and enables vertebral column movements

intervertebral foramen: opening located between adjacent vertebrae for exit of a spinal nerve

jugular (suprasternal) notch: shallow notch located on superior surface of sternal manubrium

jugular foramen: irregularly shaped opening located in the lateral floor of the posterior cranial cavity

kyphosis: (also, humpback or hunchback) excessive posterior curvature of the thoracic vertebral column region

lacrimal bone: paired bones that contribute to the anterior-medial wall of each orbit

lacrimal fossa: shallow depression in the anterior-medial wall of the orbit, formed by the lacrimal bone that gives rise to the nasolacrimal canal

lambdoid suture: inverted V-shaped joint that unites the occipital bone to the right and left parietal bones on the posterior skull

lamina: portion of the vertebral arch on each vertebra that extends between the transverse and spinous process

lateral pterygoid plate: paired, flattened bony projections of the sphenoid bone located on the inferior skull, lateral to the medial pterygoid plate

lateral sacral crest: paired irregular ridges running down the lateral sides of the posterior sacrum that was formed by the fusion of the transverse processes from the five sacral vertebrae

lesser wings of the sphenoid bone: lateral extensions of the sphenoid bone that form the bony lip separating the anterior and middle cranial fossae

ligamentum flavum: series of short ligaments that unite the lamina of adjacent vertebrae

lingula: small flap of bone located on the inner (medial) surface of mandibular ramus, next to the mandibular foramen

lordosis: (also, swayback) excessive anterior curvature of the lumbar vertebral column region

lumbar curve: posteriorly concave curvature of the lumbar vertebral column region; a secondary curve of the vertebral column

lumbar vertebrae: five vertebrae numbered as L1–L5 that are located in lumbar region (lower back) of the vertebral column

mandible: unpaired bone that forms the lower jaw bone; the only moveable bone of the skull

mandibular foramen: opening located on the inner (medial) surface of the mandibular ramus

mandibular fossa: oval depression located on the inferior surface of the skull

mandibular notch: large U-shaped notch located between the condylar process and coronoid process of the mandible

manubrium: expanded, superior portion of the sternum

mastoid process: large bony prominence on the inferior, lateral skull, just behind the earlobe

maxillary bone: (also, maxilla) paired bones that form the upper jaw and anterior portion of the hard palate

maxillary sinus: air-filled space located with each maxillary bone; largest of the paranasal sinuses

medial pterygoid plate: paired, flattened bony projections of the sphenoid bone located on the inferior skull medial to the lateral pterygoid plate; form the posterior portion of the nasal cavity lateral wall

median sacral crest: irregular ridge running down the midline of the posterior sacrum that was formed from the fusion of the spinous processes of the five sacral vertebrae

mental foramen: opening located on the anterior-lateral side of the mandibular body

mental protuberance: inferior margin of anterior mandible that forms the chin

middle cranial fossa: centrally located cranial fossa that extends from the lesser wings of the sphenoid bone to the petrous ridge

middle nasal concha: nasal concha formed by the ethmoid bone that is located between the superior and inferior conchae

mylohyoid line: bony ridge located along the inner (medial) surface of the mandibular body

nasal bone: paired bones that form the base of the nose

nasal cavity: opening through skull for passage of air

nasal conchae: curved bony plates that project from the lateral walls of the nasal cavity; include the superior and middle nasal conchae, which are parts of the ethmoid bone, and the independent inferior nasal conchae bone

nasal septum: flat, midline structure that divides the nasal cavity into halves, formed by the perpendicular plate of the ethmoid bone, vomer bone, and septal cartilage

nasolacrimal canal: passage for drainage of tears that extends downward from the medial-anterior orbit to the nasal cavity, terminating behind the inferior nasal conchae

neck of the rib: narrowed region of a rib, next to the rib head

notochord: rod-like structure along dorsal side of the early embryo; largely disappears during later development but does contribute to formation of the intervertebral discs

nuchal ligament: expanded portion of the supraspinous ligament within the posterior neck; interconnects the spinous processes of the cervical vertebrae and attaches to the base of the skull

nucleus pulposus: gel-like central region of an intervertebral disc; provides for padding, weight-bearing, and movement between adjacent vertebrae

occipital bone: unpaired bone that forms the posterior portions of the brain case and base of the skull

occipital condyle: paired, oval-shaped bony knobs located on the inferior skull, to either side of the foramen magnum

optic canal: opening spanning between middle cranial fossa and posterior orbit

orbit: bony socket that contains the eyeball and associated muscles

palatine bone: paired bones that form the posterior quarter of the hard palate and a small area in floor of the orbit

palatine process: medial projection from the maxilla bone that forms the anterior three quarters of the hard palate

paranasal sinuses: cavities within the skull that are connected to the conchae that serve to warm and humidify incoming air, produce mucus, and lighten the weight of the skull; consist of frontal, maxillary, sphenoidal, and ethmoidal sinuses

parietal bone: paired bones that form the upper, lateral sides of the skull

pedicle: portion of the vertebral arch that extends from the vertebral body to the transverse process

perpendicular plate of the ethmoid bone: downward, midline extension of the ethmoid bone that forms the superior portion of the nasal septum

petrous ridge: petrous portion of the temporal bone that forms a large, triangular ridge in the floor of the cranial cavity, separating the middle and posterior cranial fossae; houses the middle and inner ear structures

posterior (dorsal) sacral foramen: one of the series of paired openings located on the posterior (dorsal) side of the sacrum

posterior arch: posterior portion of the ring-like C1 (atlas) vertebra

posterior cranial fossa: deepest and most posterior cranial fossa; extends from the petrous ridge to the occipital bone

posterior longitudinal ligament: ligament that runs the length of the vertebral column, uniting the posterior sides of the vertebral bodies

primary curve: anteriorly concave curvatures of the thoracic and sacrococcygeal regions that are retained from the original fetal curvature of the vertebral column

pterion: H-shaped suture junction region that unites the frontal, parietal, temporal, and sphenoid bones on the lateral side of the skull

ramus of the mandible: vertical portion of the mandible

ribs: thin, curved bones of the chest wall

sacral canal: bony tunnel that runs through the sacrum

sacral foramina: series of paired openings for nerve exit located on both the anterior (ventral) and posterior (dorsal) aspects of the sacrum

sacral hiatus: inferior opening and termination of the sacral canal

sacral promontory: anterior lip of the base (superior end) of the sacrum

sacrococcygeal curve: anteriorly concave curvature formed by the sacrum and coccyx; a primary curve of the vertebral column

sacrum: single bone located near the inferior end of the adult vertebral column that is formed by the fusion of five sacral vertebrae; forms the posterior portion of the pelvis

sagittal suture: joint that unites the right and left parietal bones at the midline along the top of the skull

sclerotome: medial portion of a somite consisting of mesenchyme tissue that will give rise to bone, cartilage, and fibrous connective tissues

scoliosis: abnormal lateral curvature of the vertebral column

secondary curve: posteriorly concave curvatures of the cervical and lumbar regions of the vertebral column that develop after the time of birth

sella turcica: elevated area of sphenoid bone located at midline of the middle cranial fossa

septal cartilage: flat cartilage structure that forms the anterior portion of the nasal septum

skeleton: bones of the body

skull: bony structure that forms the head, face, and jaws, and protects the brain; consists of 22 bones

somite: one of the paired, repeating blocks of tissue located on either side of the notochord in the early embryo

sphenoid bone: unpaired bone that forms the central base of skull

sphenoid sinus: air-filled space located within the sphenoid bone; most posterior of the paranasal sinuses

spinous process: unpaired bony process that extends posteriorly from the vertebral arch of a vertebra

squamous suture: joint that unites the parietal bone to the squamous portion of the temporal bone on the lateral side of the skull

sternal angle: junction line between manubrium and body of the sternum and the site for attachment of the second rib to the sternum

sternum: flattened bone located at the center of the anterior chest

styloid process: downward projecting, elongated bony process located on the inferior aspect of the skull

stylomastoid foramen: opening located on inferior skull, between the styloid process and mastoid process

superior articular process of the sacrum: paired processes that extend upward from the sacrum to articulate (join) with the inferior articular processes from the L5 vertebra

superior articular process: bony process that extends upward from the vertebral arch of a vertebra that articulates with the inferior articular process of the next higher vertebra

superior nasal concha: smallest and most superiorly located of the nasal conchae; formed by the ethmoid bone

superior nuchal line: paired bony lines on the posterior skull that extend laterally from the external occipital protuberance

superior orbital fissure: irregularly shaped opening between the middle cranial fossa and the posterior orbit

supraorbital foramen: opening located on anterior skull, at the superior margin of the orbit

supraorbital margin: superior margin of the orbit

supraspinous ligament: ligament that interconnects the spinous processes of the thoracic and lumbar vertebrae

suture: junction line at which adjacent bones of the skull are united by fibrous connective tissue

temporal bone: paired bones that form the lateral, inferior portions of the skull, with squamous, mastoid, and petrous portions

temporal fossa: shallow space on the lateral side of the skull, above the level of the zygomatic arch

temporal process of the zygomatic bone: short extension from the zygomatic bone that forms the anterior portion of the zygomatic arch

thoracic cage: consists of 12 pairs of ribs and sternum

thoracic curve: anteriorly concave curvature of the thoracic vertebral column region; a primary curve of the vertebral column

thoracic vertebrae: twelve vertebrae numbered as T1–T12 that are located in the thoracic region (upper back) of the vertebral column

transverse foramen: opening found only in the transverse processes of cervical vertebrae

transverse process: paired bony processes that extends laterally from the vertebral arch of a vertebra

true ribs: vertebrosternal ribs 1–7 that attach via their costal cartilage directly to the sternum

tubercle of the rib: small bump on the posterior side of a rib for articulation with the transverse process of a thoracic vertebra

vertebral (spinal) canal: bony passageway within the vertebral column for the spinal cord that is formed by the series of individual vertebral foramina

vertebral arch: bony arch formed by the posterior portion of each vertebra that surrounds and protects the spinal cord

vertebral column: entire sequence of bones that extend from the skull to the tailbone

vertebral foramen: opening associated with each vertebra defined by the vertebral arch that provides passage for the spinal cord

vertebra: individual bone in the neck and back regions of the vertebral column

vomer bone: unpaired bone that forms the inferior and posterior portions of the nasal septum

xiphoid process: small process that forms the inferior tip of the sternum

zygomatic arch: elongated, free-standing arch on the lateral skull, formed anteriorly by the temporal process of the zygomatic bone and posteriorly by the zygomatic process of the temporal bone

zygomatic bone: cheekbone; paired bones that contribute to the lateral orbit and anterior zygomatic arch

zygomatic process of the temporal bone: extension from the temporal bone that forms the posterior portion of the zygomatic arch

PRACTICE TEST: THE AXIAL SKELETON

Review the material from this module by completing the practice in course online.

MODULE 9: THE APPENDICULAR SKELETON

INTRODUCTION TO THE APPENDICULAR SKELETON

Learning Objectives

- Discuss the bones of the pectoral and pelvic girdles, and describe how these unite the limbs with the axial skeleton
- Describe the bones of the upper limb, including the bones of the arm, forearm, wrist, and hand
- Identify the features of the pelvis and explain how these differ between the adult male and female pelvis
- Describe the bones of the lower limb, including the bones of the thigh, leg, ankle, and foot
- Describe the embryonic formation and growth of the limb bones

Your skeleton provides the internal supporting structure of the body. The adult axial skeleton consists of 80 bones that form the head and body trunk. Attached to this are the limbs, whose 126 bones constitute the appendicular skeleton. These bones are divided into two groups: the bones that are located within the limbs themselves, and the girdle bones that attach the limbs to the axial skeleton. The bones of the shoulder region form the pectoral girdle, which anchors the upper limb to the thoracic cage of the axial skeleton. The lower limb is attached to the vertebral column by the pelvic girdle.

Figure 1. Dancer. *The appendicular skeleton consists of the upper and lower limb bones, the bones of the hands and feet, and the bones that anchor the limbs to the axial skeleton. (credit: Melissa Dooley/flickr)*

Because of our upright stance, different functional demands are placed upon the upper and lower limbs. Thus, the bones of the lower limbs are adapted for weight-bearing support and stability, as well as for body locomotion via walking or running. In contrast, our upper limbs are not required for these functions. Instead, our upper limbs are highly mobile and can be utilized for a wide variety of activities. The large range of upper limb movements, coupled with the ability to easily manipulate objects with our hands and opposable thumbs, has allowed humans to construct the modern world in which we live.

THE PECTORAL GIRDLE

Learning Objectives

- Describe the bones that form the pectoral girdle
- List the functions of the pectoral girdle

The appendicular skeleton includes all of the limb bones, plus the bones that unite each limb with the axial skeleton (Figure 1).

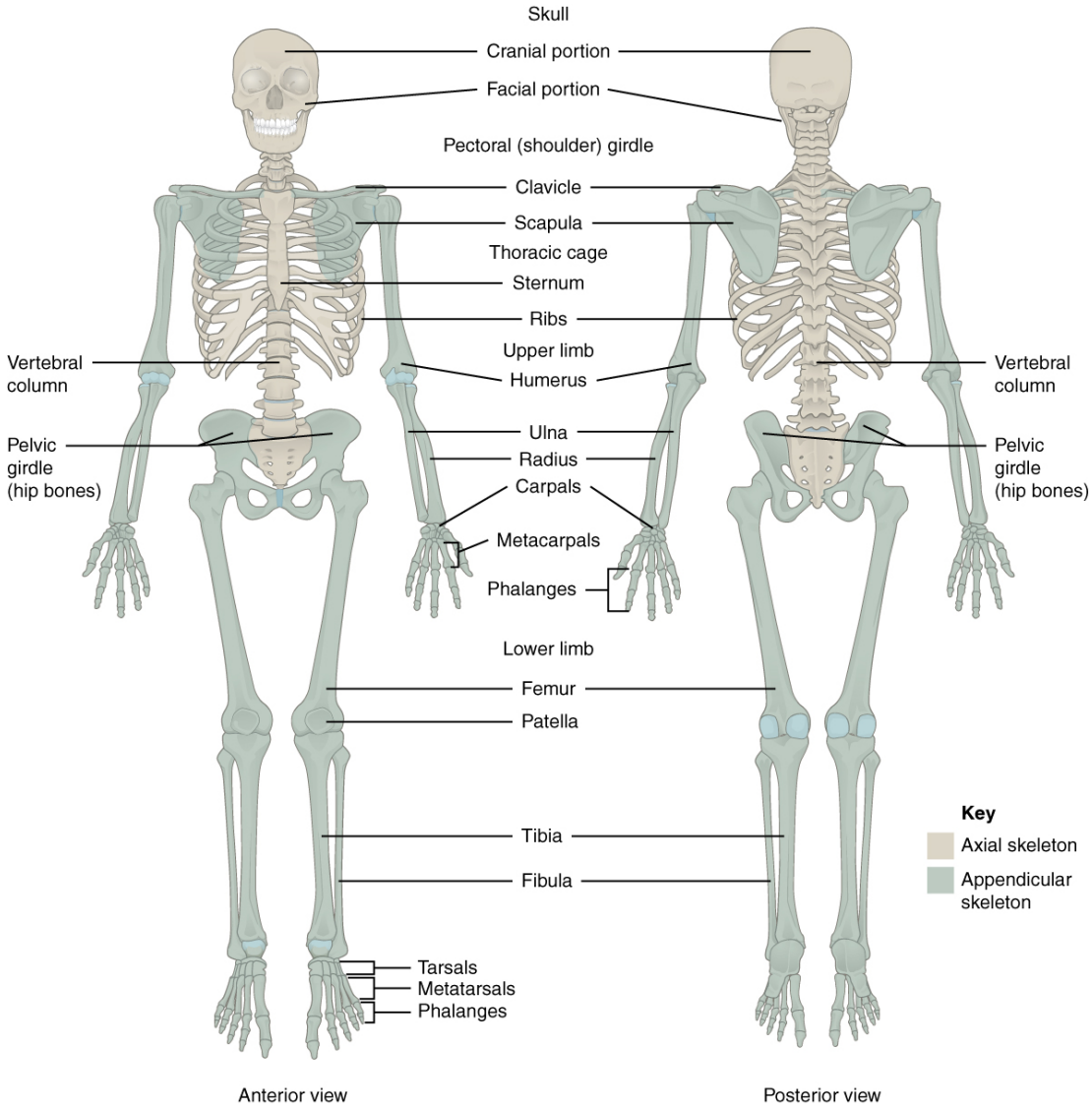


Figure 1. Axial and Appendicular Skeletons. *Click for larger image. The axial skeleton forms the central axis of the body and consists of the skull, vertebral column, and thoracic cage. The appendicular skeleton consists of the pectoral and pelvic girdles, the limb bones, and the bones of the hands and feet.*

The bones that attach each upper limb to the axial skeleton form the pectoral girdle (shoulder girdle). This consists of two bones, the scapula and clavicle (Figure 2). The clavicle (collarbone) is an S-shaped bone located on the anterior side of the shoulder. It is attached on its medial end to the sternum of the thoracic cage, which is part of the axial skeleton. The lateral end of the clavicle articulates (joins) with the scapula just above the shoulder joint. You can easily palpate, or feel with your fingers, the entire length of your clavicle.

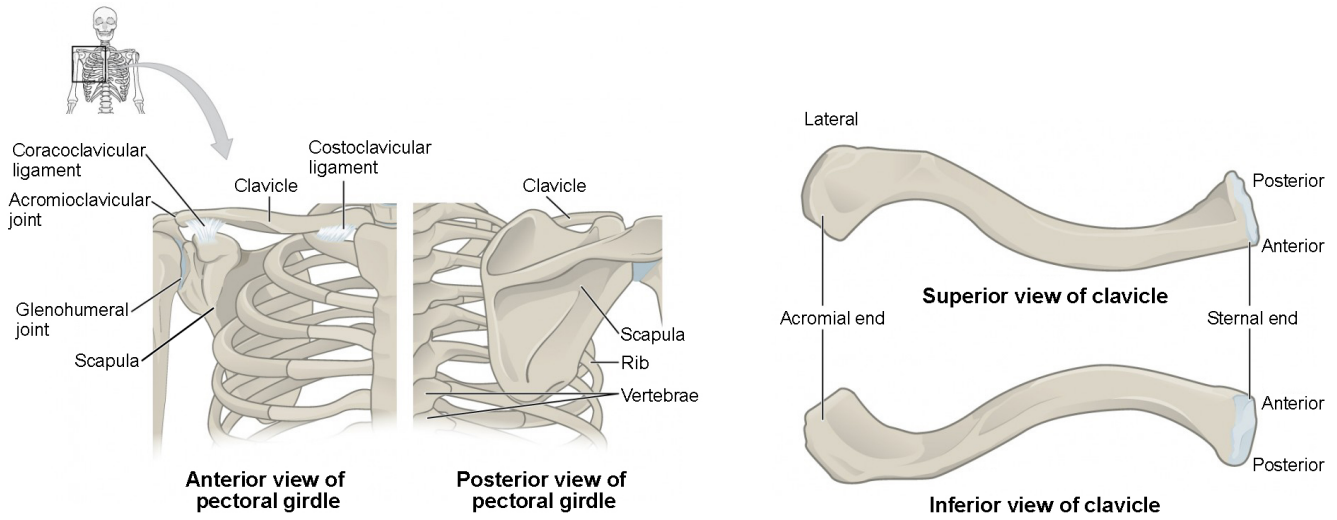


Figure 2. Pectoral Girdle. *The pectoral girdle consists of the clavicle and the scapula, which serve to attach the upper limb to the sternum of the axial skeleton.*

The **scapula** (shoulder blade) lies on the posterior aspect of the shoulder. It is supported by the **clavicle**, which also articulates with the humerus (arm bone) to form the shoulder joint. The scapula is a flat, triangular-shaped bone with a prominent ridge running across its posterior surface. This ridge extends out laterally, where it forms the bony tip of the shoulder and joins with the lateral end of the clavicle. By following along the clavicle, you can palpate out to the bony tip of the shoulder, and from there, you can move back across your posterior shoulder to follow the ridge of the scapula. Move your shoulder around and feel how the clavicle and scapula move together as a unit. Both of these bones serve as important attachment sites for muscles that aid with movements of the shoulder and arm.

The right and left pectoral girdles are not joined to each other, allowing each to operate independently. In addition, the clavicle of each **pectoral girdle** is anchored to the axial skeleton by a single, highly mobile joint. This allows for the extensive mobility of the entire pectoral girdle, which in turn enhances movements of the shoulder and upper limb.

Clavicle

The clavicle is the only long bone that lies in a horizontal position in the body (see Figure 2). The clavicle has several important functions. First, anchored by muscles from above, it serves as a strut that extends laterally to support the scapula. This in turn holds the shoulder joint superiorly and laterally from the body trunk, allowing for maximal freedom of motion for the upper limb. The clavicle also transmits forces acting on the upper limb to the sternum and axial skeleton. Finally, it serves to protect the underlying nerves and blood vessels as they pass between the trunk of the body and the upper limb.

The clavicle has three regions: the medial end, the lateral end, and the shaft. The medial end, known as the **sternal end of the clavicle**, has a triangular shape and articulates with the manubrium portion of the sternum. This forms the **sternoclavicular joint**, which is the only bony articulation between the pectoral girdle of the upper limb and the axial skeleton. This joint allows considerable mobility, enabling the clavicle and scapula to move in upward/downward and anterior/posterior directions during shoulder movements. The sternoclavicular joint is indirectly supported by the **costoclavicular ligament** (*costo–* = “rib”), which spans the sternal end of the clavicle and the underlying first rib. The lateral or **acromial end of the clavicle** articulates with the acromion of the scapula, the portion of the scapula that forms the bony tip of the shoulder. There are some sex differences in the morphology of the clavicle. In women, the clavicle tends to be shorter, thinner, and less curved. In men, the

clavicle is heavier and longer, and has a greater curvature and rougher surfaces where muscles attach, features that are more pronounced in manual workers.

The clavicle is the most commonly fractured bone in the body. Such breaks often occur because of the force exerted on the clavicle when a person falls onto his or her outstretched arms, or when the lateral shoulder receives a strong blow. Because the sternoclavicular joint is strong and rarely dislocated, excessive force results in the breaking of the clavicle, usually between the middle and lateral portions of the bone. If the fracture is complete, the shoulder and lateral clavicle fragment will drop due to the weight of the upper limb, causing the person to support the sagging limb with their other hand. Muscles acting across the shoulder will also pull the shoulder and lateral clavicle anteriorly and medially, causing the clavicle fragments to override. The clavicle overlies many important blood vessels and nerves for the upper limb, but fortunately, due to the anterior displacement of a broken clavicle, these structures are rarely affected when the clavicle is fractured.

Scapula

The scapula is also part of the pectoral girdle and thus plays an important role in anchoring the upper limb to the body. The scapula is located on the posterior side of the shoulder. It is surrounded by muscles on both its anterior (deep) and posterior (superficial) sides, and thus does not articulate with the ribs of the thoracic cage.

The scapula has several important landmarks (Figure 3). The three margins or borders of the scapula, named for their positions within the body, are the **superior border of the scapula**, the **medial border of the scapula**, and the **lateral border of the scapula**. The **suprascapular notch** is located lateral to the midpoint of the superior border. The corners of the triangular scapula, at either end of the medial border, are the **superior angle of the scapula,** located between the medial and superior borders, and the **inferior angle of the scapula**, located between the medial and lateral borders. The inferior angle is the most inferior portion of the scapula, and is particularly important because it serves as the attachment point for several powerful muscles involved in shoulder and upper limb movements. The remaining corner of the scapula, between the superior and lateral borders, is the location of the **glenoid cavity** (glenoid fossa). This shallow depression articulates with the humerus bone of the arm to form the **glenohumeral joint** (shoulder joint). The small bony bumps located immediately above and below the glenoid cavity are the **supraglenoid tubercle** and the **infraglenoid tubercle**, respectively. These provide attachments for muscles of the arm.

The scapula also has two prominent projections. Toward the lateral end of the superior border, between the suprascapular notch and glenoid cavity, is the hook-like **coracoid process** (*coracoid* = “shaped like a crow’s beak”). This process projects anteriorly and curves laterally. At the shoulder, the coracoid process is located inferior to the lateral end of the clavicle. It is anchored to the clavicle by a strong ligament, and serves as the attachment site for muscles of the anterior chest and arm. On the posterior aspect, the **spine of the scapula** is a long and prominent ridge that runs across its upper portion. Extending laterally from the spine is a flattened and expanded region called the **acromion** or **acromial process**. The acromion forms the bony tip of the superior shoulder region and articulates with the lateral end of the clavicle, forming the **acromioclavicular joint** (see Figure 2). Together, the clavicle, acromion, and spine of the scapula form a V-shaped bony line that provides for the attachment of neck and back muscles that act on the shoulder, as well as muscles that pass across the shoulder joint to act on the arm.

The scapula has three depressions, each of which is called a **fossa** (plural = *fossae*). Two of these are found on the posterior scapula, above and below the scapular spine. Superior to the spine is the narrow **supraspinous fossa**, and inferior to the spine is the broad **infraspinous fossa**. The anterior (deep) surface of the scapula forms the broad **subscapular fossa**. All of these fossae provide large surface areas for the attachment of muscles that cross the shoulder joint to act on the humerus.

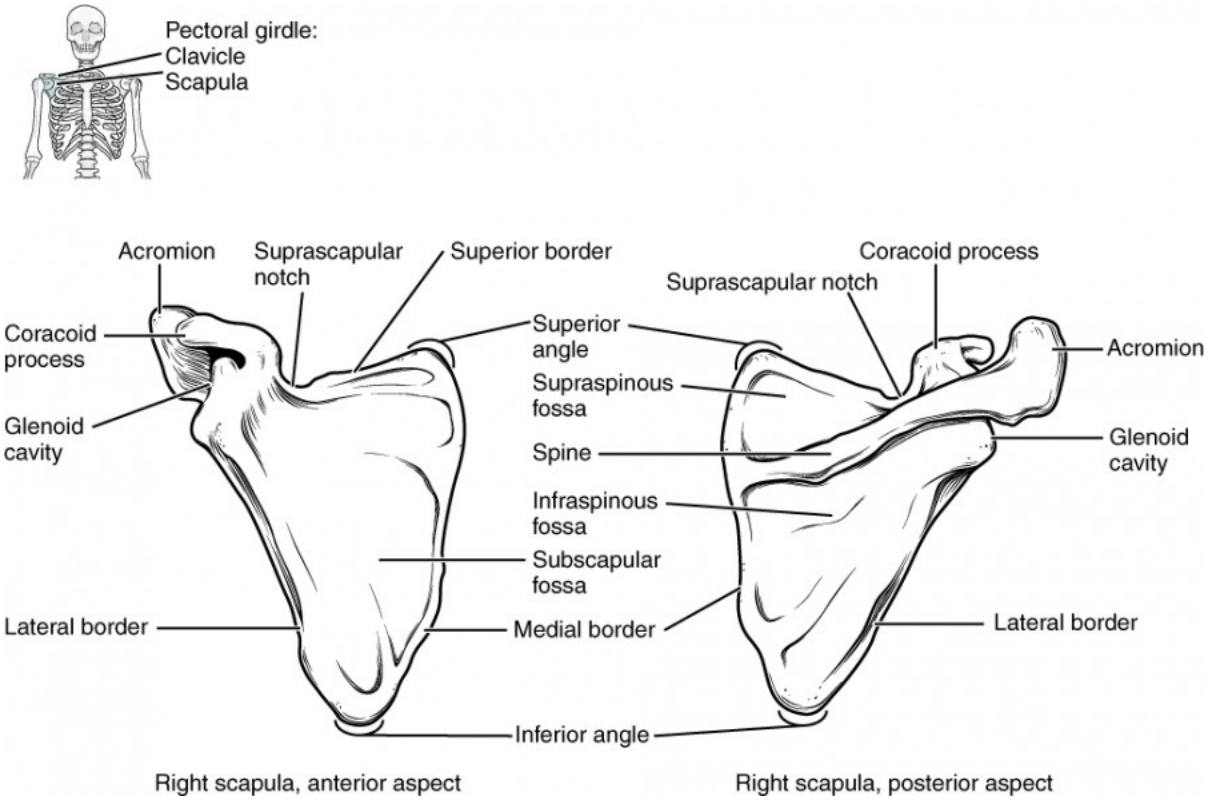


Figure 3. Scapula. *The isolated scapula is shown here from its anterior (deep) side and its posterior (superficial) side.*

The acromioclavicular joint transmits forces from the upper limb to the clavicle. The ligaments around this joint are relatively weak. A hard fall onto the elbow or outstretched hand can stretch or tear the acromioclavicular ligaments, resulting in a moderate injury to the joint. However, the primary support for the acromioclavicular joint comes from a very strong ligament called the coracoclavicular ligament (see Figure 2). This connective tissue band anchors the coracoid process of the scapula to the inferior surface of the acromial end of the clavicle and thus provides important indirect support for the acromioclavicular joint. Following a strong blow to the lateral shoulder, such as when a hockey player is driven into the boards, a complete dislocation of the acromioclavicular joint can result. In this case, the acromion is thrust under the acromial end of the clavicle, resulting in ruptures of both the acromioclavicular and coracoclavicular ligaments. The scapula then separates from the clavicle, with the weight of the upper limb pulling the shoulder downward. This dislocation injury of the acromioclavicular joint is known as a “shoulder separation” and is common in contact sports such as hockey, football, or martial arts.

BONES OF THE UPPER LIMB

Learning Objectives

- Identify the divisions of the upper limb and describe the bones in each region
- List the bones and bony landmarks that articulate at each joint of the upper limb

The upper limb is divided into three regions. These consist of the **arm**, located between the shoulder and elbow joints; the **forearm**, which is between the elbow and wrist joints; and the **hand**, which is located distal to the wrist. There are 30 bones in each upper limb. The **humerus** is the single bone of the upper arm, and the **ulna** (medially) and the **radius** (laterally) are the paired bones of the forearm. The base of the hand contains eight bones, each called a **carpal bone**, and the palm of the hand is formed by five bones, each called a **metacarpal bone**. The fingers and thumb contain a total of 14 bones, each of which is a **phalanx bone of the hand**.

Humerus

The humerus is the single bone of the upper arm region (Figure 1). At its proximal end is the **head of the humerus**. This is the large, round, smooth region that faces medially. The head articulates with the glenoid cavity of the scapula to form the glenohumeral (shoulder) joint. The margin of the smooth area of the head is the **anatomical neck** of the humerus. Located on the lateral side of the proximal humerus is an expanded bony area called the **greater tubercle**. The smaller **lesser tubercle** of the humerus is found on the anterior aspect of the humerus. Both the greater and lesser tubercles serve as attachment sites for muscles that act across the shoulder joint. Passing between the greater and lesser tubercles is the narrow **intertubercular groove (sulcus)**, which is also known as the **bicipital groove** because it provides passage for a tendon of the biceps brachii muscle. The **surgical neck** is located at the base of the expanded, proximal end of the humerus, where it joins the narrow **shaft of the humerus**. The surgical neck is a common site of arm fractures. The **deltoid tuberosity** is a roughened, V-shaped region located on the lateral side in the middle of the humerus shaft. As its name indicates, it is the site of attachment for the deltoid muscle.

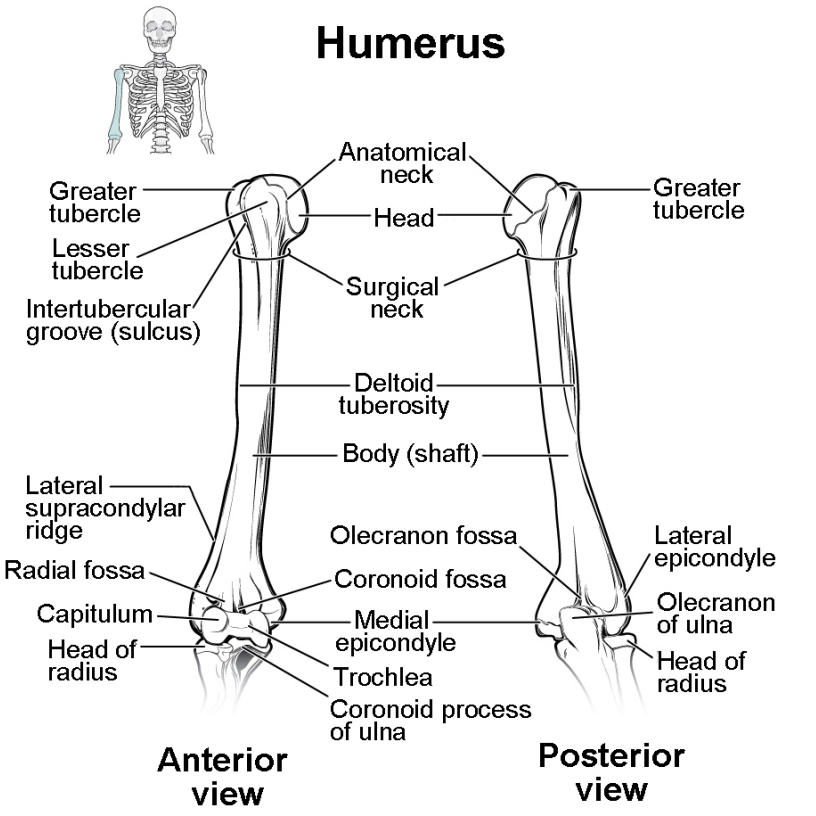


Figure 1. Humerus and Elbow Joint. *The humerus is the single bone of the upper arm region. It articulates with the radius and ulna bones of the forearm to form the elbow joint.*

Distally, the humerus becomes flattened. The prominent bony projection on the medial side is the **medial epicondyle of the humerus**. The much smaller **lateral epicondyle of the humerus** is found on the lateral side of the distal humerus. The roughened ridge of bone above the lateral epicondyle is the **lateral supracondylar ridge**. All of these areas are attachment points for muscles that act on the forearm, wrist, and hand. The powerful grasping muscles of the anterior forearm arise from the medial epicondyle, which is thus larger and more robust than the lateral epicondyle that gives rise to the weaker posterior forearm muscles.

The distal end of the humerus has two articulation areas, which join the ulna and radius bones of the forearm to form the **elbow joint**. The more medial of these areas is the **trochlea**, a spindle- or pulley-shaped region (trochlea = “pulley”), which articulates with the ulna bone. Immediately lateral to the trochlea is the **capitulum** (“small head”), a knob-like structure located on the anterior surface of the distal humerus. The capitulum articulates with the radius bone of the forearm. Just above these bony areas are two small depressions. These spaces accommodate the forearm bones when the elbow is fully bent (flexed). Superior to the trochlea is the **coronoid fossa**, which receives the coronoid process of the ulna, and above the capitulum is the **radial fossa**, which receives the head of the radius when the elbow is flexed. Similarly, the posterior humerus has the **olecranon fossa**, a larger depression that receives the olecranon process of the ulna when the forearm is fully extended.

Ulna

The ulna is the medial bone of the forearm. It runs parallel to the radius, which is the lateral bone of the forearm (Figure 2). The proximal end of the ulna resembles a crescent wrench with its large, C-shaped **trochlear notch**. This region articulates with the trochlea of the humerus as part of the elbow joint. The inferior margin of the trochlear notch is formed by a prominent lip of bone called the **coronoid process of the ulna**. Just below this on the anterior ulna is a roughened area called the **ulnar tuberosity**. To the lateral side and slightly inferior to the trochlear notch is a small, smooth area called the **radial notch of the ulna**. This area is the site of articulation between the proximal radius and the ulna, forming the **proximal radioulnar joint**. The posterior and superior portions of the proximal ulna make up the **olecranon process**, which forms the bony tip of the elbow.

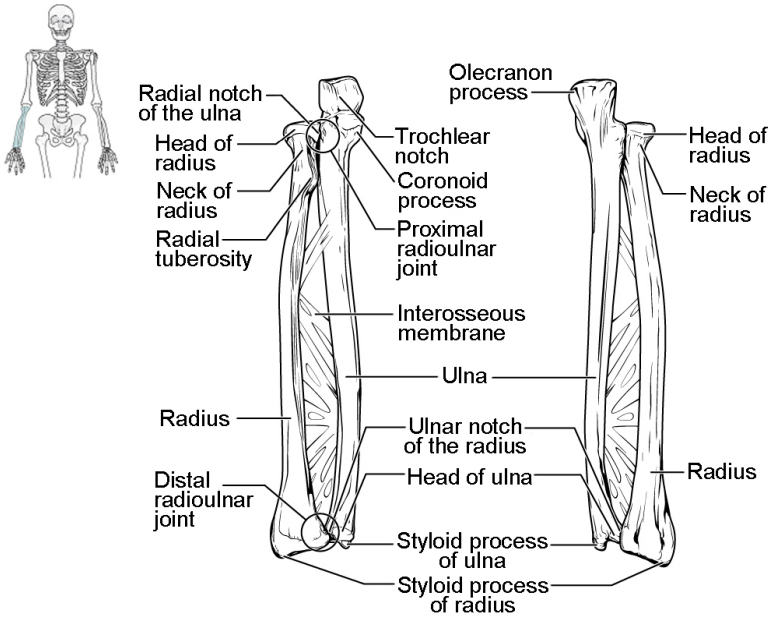


Figure 2. Ulna and Radius. *The ulna is located on the medial side of the forearm, and the radius is on the lateral side. These bones are attached to each other by an interosseous membrane.*

More distal is the **shaft of the ulna**. The lateral side of the shaft forms a ridge called the **interosseous border of the ulna**. This is the line of attachment for the **interosseous membrane of the forearm**, a sheet of dense connective tissue that unites the ulna and radius bones. The small, rounded area that forms the distal end is the **head of the ulna**. Projecting from the posterior side of the ulnar head is the **styloid process of the ulna**, a short bony projection. This serves as an attachment point for a connective tissue structure that unites the distal ends of the ulna and radius.

In the anatomical position, with the elbow fully extended and the palms facing forward, the arm and forearm do not form a straight line. Instead, the forearm deviates laterally by 5–15 degrees from the line of the arm. This deviation is called the carrying angle. It allows the forearm and hand to swing freely or to carry an object without hitting the hip. The carrying angle is larger in females to accommodate their wider pelvis.

Radius

The radius runs parallel to the ulna, on the lateral (thumb) side of the forearm (see Figure 2). The **head of the radius** is a disc-shaped structure that forms the proximal end. The small depression on the surface of the head articulates with the capitulum of the humerus as part of the elbow joint, whereas the smooth, outer margin of the head articulates with the radial notch of the ulna at the proximal radioulnar joint.

The **neck of the radius** is the narrowed region immediately below the expanded head. Inferior to this point on the medial side is the **radial tuberosity**, an oval-shaped, bony protuberance that serves as a muscle attachment point.

The **shaft of the radius** is slightly curved and has a small ridge along its medial side. This ridge forms the **interosseous border of the radius**, which, like the similar border of the ulna, is the line of attachment for the interosseous membrane that unites the two forearm bones.

The distal end of the radius has a smooth surface for articulation with two carpal bones to form the **radiocarpal joint** or wrist joint (Figure 3 and Figure 4). On the medial side of the distal radius is the **ulnar notch of the radius**. This shallow depression articulates with the head of the ulna, which together form the **distal radioulnar joint**. The lateral end of the radius has a pointed projection called the **styloid process of the radius**. This provides attachment for ligaments that support the lateral side of the wrist joint. Compared to the styloid process of the ulna, the styloid

process of the radius projects more distally, thereby limiting the range of movement for lateral deviations of the hand at the wrist joint.

Watch this video to see how fractures of the distal radius bone can affect the wrist joint. Explain the problems that may occur if a fracture of the distal radius involves the joint surface of the radiocarpal joint of the wrist.

Carpal Bones

The wrist and base of the hand are formed by a series of eight small carpal bones (see Figure 3).

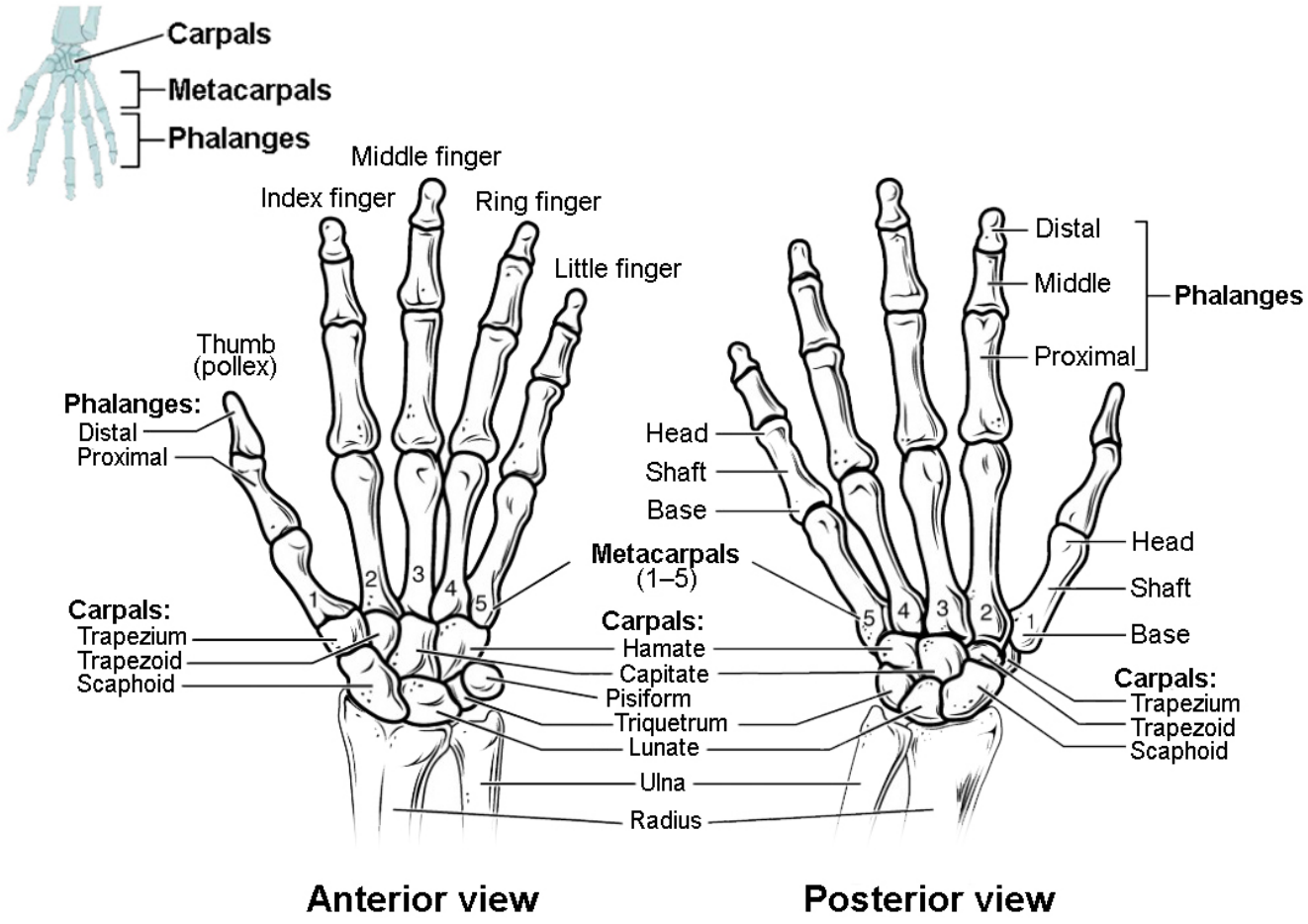


Figure 3. Bones of the Wrist and Hand. *The eight carpal bones form the base of the hand. These are arranged into proximal and distal rows of four bones each. The metacarpal bones form the palm of the hand. The thumb and fingers consist of the phalanx bones.*

The carpal bones are arranged in two rows, forming a proximal row of four carpal bones and a distal row of four carpal bones. The bones in the proximal row, running from the lateral (thumb) side to the medial side, are the **scaphoid** (“boat-shaped”), **lunate** (“moon-shaped”), **triquetrum** (“three-cornered”), and **pisiform** (“pea-shaped”) bones. The small, rounded pisiform bone articulates with the anterior surface of the triquetrum bone. The pisiform thus projects anteriorly, where it forms the bony bump that can be felt at the medial base of your hand. The distal bones (lateral to medial) are the **trapezium** (“table”), **trapezoid** (“resembles a table”), **capitate** (“head-shaped”), and **hamate** (“hooked bone”) bones. The hamate bone is characterized by a prominent bony extension on its anterior side called the **hook of the hamate bone**.

A helpful mnemonic for remembering the arrangement of the carpal bones is “So Long To Pinky, Here Comes The Thumb.” This mnemonic starts on the lateral side and names the proximal bones from lateral to medial

(scaphoid, lunate, triquetrum, pisiform), then makes a U-turn to name the distal bones from medial to lateral (hamate, capitate, trapezoid, trapezium). Thus, it starts and finishes on the lateral side.

The carpal bones form the base of the hand. This can be seen in the radiograph (X-ray image) of the hand that shows the relationships of the hand bones to the skin creases of the hand (see Figure 4). Within the carpal bones, the four proximal bones are united to each other by ligaments to form a unit. Only three of these bones, the scaphoid, lunate, and triquetrum, contribute to the radiocarpal joint. The scaphoid and lunate bones articulate directly with the distal end of the radius, whereas the triquetrum bone articulates with a fibrocartilaginous pad that spans the radius and styloid process of the ulna. The distal end of the ulna thus does not directly articulate with any of the carpal bones.

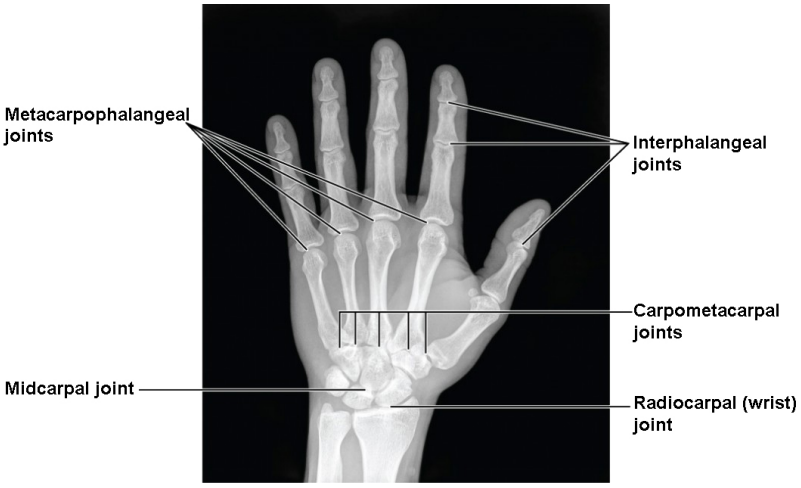


Figure 4. Bones of the Hand. *This radiograph shows the position of the bones within the hand. Note the carpal bones that form the base of the hand. (credit: modification of work by Trace Meek)*

The four distal carpal bones are also held together as a group by ligaments. The proximal and distal rows of carpal bones articulate with each other to form the **midcarpal joint** (see Figure 4). Together, the radiocarpal and midcarpal joints are responsible for all movements of the hand at the wrist. The distal carpal bones also articulate with the metacarpal bones of the hand.

In the articulated hand, the carpal bones form a U-shaped grouping. A strong ligament called the **flexor retinaculum** spans the top of this U-shaped area to maintain this grouping of the carpal bones. The flexor retinaculum is attached laterally to the trapezium and scaphoid bones, and medially to the hamate and pisiform bones. Together, the carpal bones and the flexor retinaculum form a passageway called the **carpal tunnel**, with the carpal bones forming the walls and floor, and the flexor retinaculum forming the roof of this space (Figure 5).

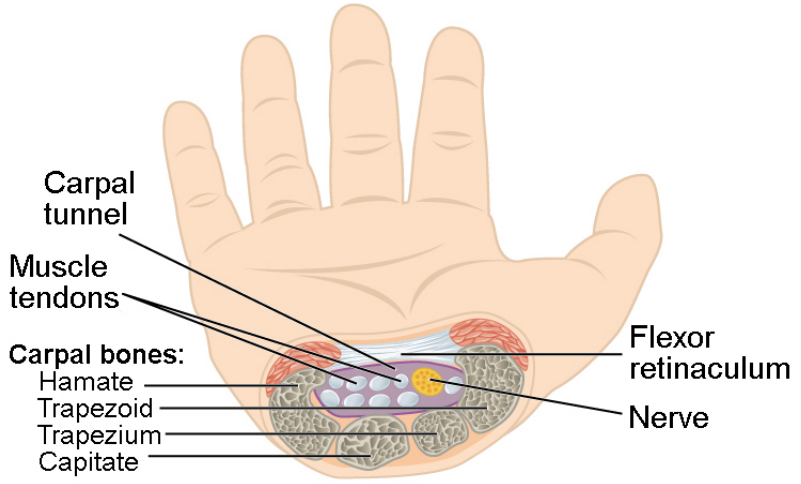


Figure 5. Carpal Tunnel. *The carpal tunnel is the passageway by which nine muscle tendons and a major nerve enter the hand from the anterior forearm. The walls and floor of the carpal tunnel are formed by the U-shaped grouping of the carpal bones, and the roof is formed by the flexor retinaculum, a strong ligament that anteriorly unites the bones.*

The tendons of nine muscles of the anterior forearm and an important nerve pass through this narrow tunnel to enter the hand. Overuse of the muscle tendons or wrist injury can produce inflammation and swelling within this space. This produces compression of the nerve, resulting in carpal tunnel syndrome, which is characterized by pain or numbness, and muscle weakness in those areas of the hand supplied by this nerve.

Metacarpal Bones

The palm of the hand contains five elongated metacarpal bones. These bones lie between the carpal bones of the wrist and the bones of the fingers and thumb (see Figure 3). The proximal end of each metacarpal bone articulates with one of the distal carpal bones. Each of these articulations is a **carpometacarpal joint** (see Figure 4). The expanded distal end of each metacarpal bone articulates at the **metacarpophalangeal**

joint with the proximal phalanx bone of the thumb or one of the fingers. The distal end also forms the knuckles of the hand, at the base of the fingers. The metacarpal bones are numbered 1–5, beginning at the thumb.

The first metacarpal bone, at the base of the thumb, is separated from the other metacarpal bones. This allows it a freedom of motion that is independent of the other metacarpal bones, which is very important for thumb mobility. The remaining metacarpal bones are united together to form the palm of the hand. The second and third metacarpal bones are firmly anchored in place and are immobile. However, the fourth and fifth metacarpal bones have limited anterior-posterior mobility, a motion that is greater for the fifth bone. This mobility is important during power gripping with the hand (Figure 6). The anterior movement of these bones, particularly the fifth metacarpal bone, increases the strength of contact for the medial hand during gripping actions.

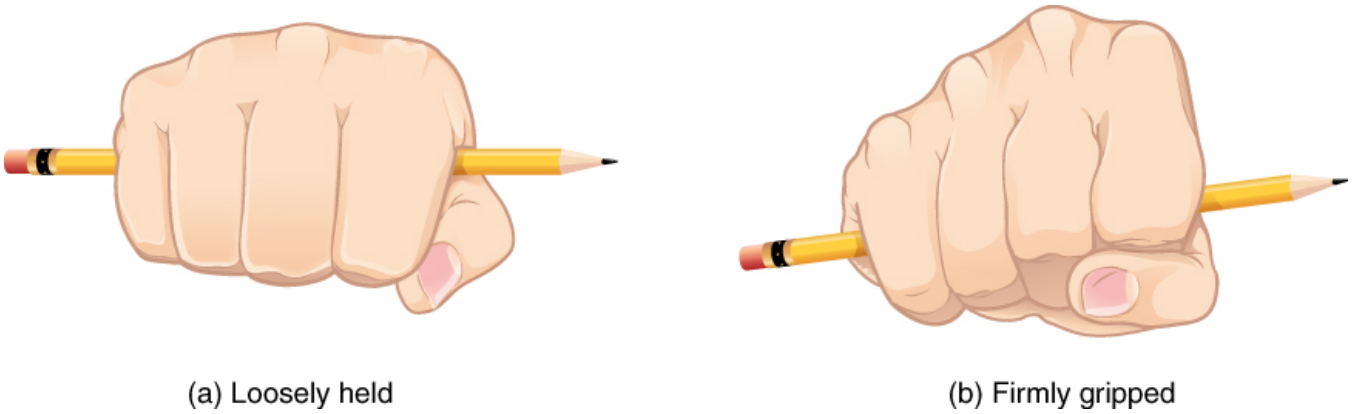


Figure 6. Hand During Gripping. *During tight gripping—compare (b) to (a)—the fourth and, particularly, the fifth metatarsal bones are pulled anteriorly. This increases the contact between the object and the medial side of the hand, thus improving the firmness of the grip.*

Phalanx Bones

The fingers and thumb contain 14 bones, each of which is called a phalanx bone (plural = *phalanges*), named after the ancient Greek phalanx (a rectangular block of soldiers). The thumb (*pollex*) is digit number 1 and has two phalanges, a proximal phalanx, and a distal phalanx bone (see Figure 3). Digits 2 (index finger) through 5 (little finger) have three phalanges each, called the proximal, middle, and distal phalanx bones. An **interphalangeal joint** is one of the articulations between adjacent phalanges of the digits (see Figure 4).

Visit this site to explore the bones and joints of the hand. What are the three arches of the hand, and what is the importance of these during the gripping of an object?

Disorders of the Appendicular System: Fractures of the Upper Limb Bones

Due to our constant use of the hands and the rest of our upper limbs, an injury to any of these areas will cause a significant loss of functional ability. Many fractures result from a hard fall onto an outstretched hand. The resulting transmission of force up the limb may result in a fracture of the humerus, radius, or scaphoid bones. These injuries are especially common in elderly people whose bones are weakened due to osteoporosis.

Falls onto the hand or elbow, or direct blows to the arm, can result in fractures of the humerus (Figure 7). Following a fall, fractures at the surgical neck, the region at which the expanded proximal end of the humerus joins with the shaft, can result in an impacted fracture, in which the distal portion of the humerus is driven into the proximal portion. Falls or blows to the arm can also produce transverse or spiral fractures of the humeral shaft.

In children, a fall onto the tip of the elbow frequently results in a distal humerus fracture. In these, the olecranon of the ulna is driven upward, resulting in a fracture across the distal humerus, above both epicondyles (supracondylar fracture), or a fracture between the epicondyles, thus separating one or both of the epicondyles from the body of the humerus (intercondylar fracture). With these injuries, the immediate concern is possible compression of the artery to the forearm due to swelling of the surrounding tissues. If compression occurs, the resulting ischemia (lack of oxygen) due to reduced blood flow can quickly produce irreparable damage to the forearm muscles. In addition, four major nerves for shoulder and upper limb muscles are closely associated with different regions of the humerus, and thus, humeral fractures may also damage these nerves.

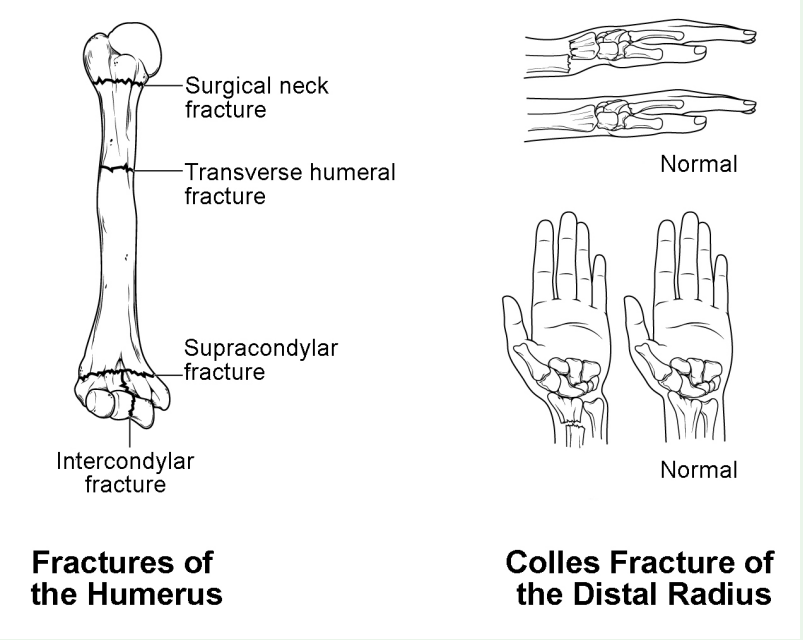


Figure 7. Fractures of the Humerus and Radius. *Falls or direct blows can result in fractures of the surgical neck or shaft of the humerus. Falls onto the elbow can fracture the distal humerus. A Colles fracture of the distal radius is the most common forearm fracture.*

Another frequent injury following a fall onto an outstretched hand is a Colles fracture ("col-lees") of the distal radius (see Figure 7). This involves a complete transverse fracture across the distal radius that drives the separated distal fragment of the radius posteriorly and superiorly. This injury results in a characteristic "dinner fork" bend of the forearm just above the wrist due to the posterior displacement of the hand. This is the most frequent forearm fracture and is a common injury in persons over the age of 50, particularly in older women with osteoporosis. It also commonly occurs following a high-speed fall onto the hand during activities such as snowboarding or skating.

The most commonly fractured carpal bone is the scaphoid, often resulting from a fall onto the hand. Deep pain at the lateral wrist may yield an initial diagnosis of a wrist sprain, but a radiograph taken several weeks after the injury, after tissue swelling has subsided, will reveal the fracture. Due to the poor blood supply to the scaphoid bone, healing will be slow and there is the danger of bone necrosis and subsequent degenerative joint disease of the wrist.

Watch this video to learn about a Colles fracture, a break of the distal radius, usually caused by falling onto an outstretched hand. When would surgery be required and how would the fracture be repaired in this case?

Watch this video online: https://youtu.be/HKcQ3XaU8Fk

Self-Check Questions

Visit your course online to take a quiz to check your understanding of Bones of the Upper Limb:

THE PELVIC GIRDLE AND PELVIS

Learning Objectives

- Define the pelvic girdle and describe the bones and ligaments of the pelvis
- Explain the three regions of the hip bone and identify their bony landmarks
- Describe the openings of the pelvis and the boundaries of the greater and lesser pelvis

The **pelvic girdle** (hip girdle) is formed by a single bone, the **hip bone** or **coxal bone** (coxal = "hip"), which serves as the attachment point for each lower limb. Each hip bone, in turn, is firmly joined to the axial skeleton via its attachment to the sacrum of the vertebral column. The right and left hip bones also converge anteriorly to attach to each other. The bony **pelvis** is the entire structure formed by the two hip bones, the sacrum, and, attached inferiorly to the sacrum, the coccyx (Figure 1).

Unlike the bones of the pectoral girdle, which are highly mobile to enhance the range of upper limb movements, the bones of the pelvis are strongly united to each other to form a largely immobile, weight-bearing structure. This is important for stability because it enables the weight of the body to be easily transferred laterally from the vertebral column, through the pelvic girdle and hip joints, and into either lower limb whenever the other limb is not bearing weight. Thus, the immobility of the pelvis provides a strong foundation for the upper body as it rests on top of the mobile lower limbs.

Figure 1. Pelvis. *The pelvic girdle is formed by a single hip bone. The hip bone attaches the lower limb to the axial skeleton through its articulation with the sacrum. The right and left hip bones, plus the sacrum and the coccyx, together form the pelvis.*

Hip Bone

The hip bone, or coxal bone, forms the pelvic girdle portion of the pelvis. The paired hip bones are the large, curved bones that form the lateral and anterior aspects of the pelvis. Each adult hip bone is formed by three separate bones that fuse together during the late teenage years. These bony components are the ilium, ischium, and pubis (Figure 2). These names are retained and used to define the three regions of the adult hip bone.

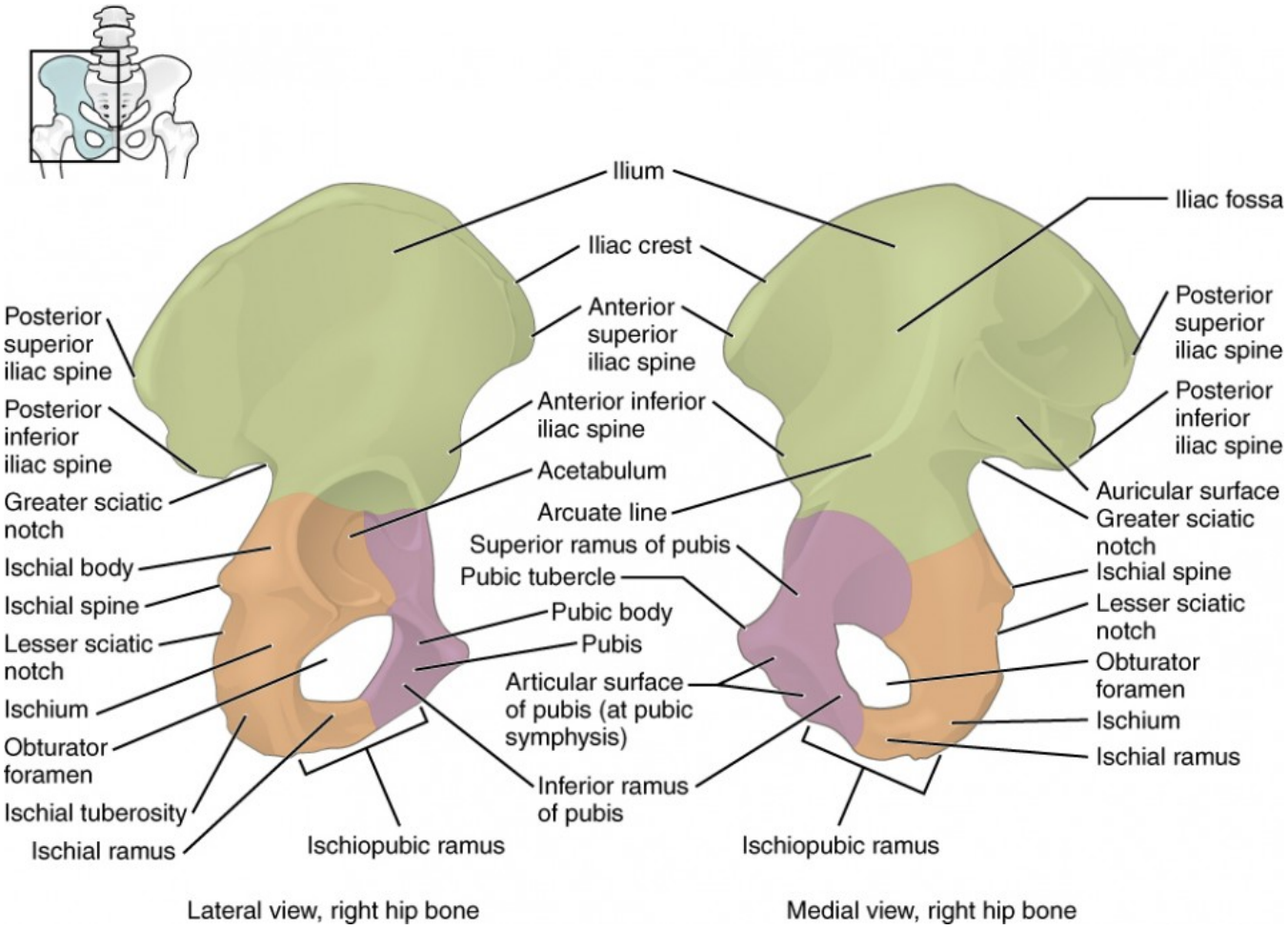


Figure 2. The Hip Bone. *The adult hip bone consists of three regions. The ilium forms the large, fan-shaped superior portion, the ischium forms the posteroinferior portion, and the pubis forms the anteromedial portion.*

The **ilium** is the fan-like, superior region that forms the largest part of the hip bone. It is firmly united to the sacrum at the largely immobile **sacroiliac joint** (see Figure 1). The **ischium** forms the posteroinferior region of each hip bone. It supports the body when sitting. The **pubis** forms the anterior portion of the hip bone. The pubis curves medially, where it joins to the pubis of the opposite hip bone at a specialized joint called the **pubic symphysis**.

Ilium

When you place your hands on your waist, you can feel the arching, superior margin of the ilium along your waistline (see Figure 2). This curved, superior margin of the ilium is the **iliac crest**. The rounded, anterior termination of the iliac crest is the **anterior superior iliac spine**. This important bony landmark can be felt at your anterolateral hip. Inferior to the anterior superior iliac spine is a rounded protuberance called the **anterior inferior iliac spine**. Both of these iliac spines serve as attachment points for muscles of the thigh. Posteriorly, the iliac crest curves downward to terminate as the **posterior superior iliac spine**. Muscles and ligaments surround but do not cover this bony landmark, thus sometimes producing a depression seen as a “dimple” located on the lower back. More inferiorly is the **posterior inferior iliac spine**. This is located at the inferior end of a large, roughened area called the **auricular surface of the ilium**. The auricular surface articulates with the auricular surface of the sacrum to form the sacroiliac joint. Both the posterior superior and posterior inferior iliac spines serve as attachment points for the muscles and very strong ligaments that support the sacroiliac joint.

The shallow depression located on the anteromedial (internal) surface of the upper ilium is called the **iliac fossa**. The inferior margin of this space is formed by the **arcuate line of the ilium**, the ridge formed by the pronounced change in curvature between the upper and lower portions of the ilium. The large, inverted U-shaped indentation located on the posterior margin of the lower ilium is called the **greater sciatic notch**.

Ischium

The ischium forms the posterolateral portion of the hip bone (see Figure 2). The large, roughened area of the inferior ischium is the **ischial tuberosity**. This serves as the attachment for the posterior thigh muscles and also carries the weight of the body when sitting. You can feel the ischial tuberosity if you wiggle your pelvis against the seat of a chair. Projecting superiorly and anteriorly from the ischial tuberosity is a narrow segment of bone called the **ischial ramus**. The slightly curved posterior margin of the ischium above the ischial tuberosity is the **lesser sciatic notch**. The bony projection separating the lesser sciatic notch and greater sciatic notch is the **ischial spine**.

Pubis

The pubis forms the anterior portion of the hip bone (see Figure 2). The enlarged medial portion of the pubis is the **pubic body**. Located superiorly on the pubic body is a small bump called the **pubic tubercle**. The **superior pubic ramus** is the segment of bone that passes laterally from the pubic body to join the ilium. The narrow ridge running along the superior margin of the superior pubic ramus is the **pectineal line** of the pubis.

The pubic body is joined to the pubic body of the opposite hip bone by the pubic symphysis. Extending downward and laterally from the body is the **inferior pubic ramus**. The **pubic arch** is the bony structure formed by the pubic symphysis, and the bodies and inferior pubic rami of the adjacent pubic bones. The inferior pubic ramus extends downward to join the ischial ramus. Together, these form the single **ischiopubic ramus**, which extends from the pubic body to the ischial tuberosity. The inverted V-shape formed as the ischiopubic rami from both sides come together at the pubic symphysis is called the **subpubic angle**.

Pelvis

The pelvis consists of four bones: the right and left hip bones, the sacrum, and the coccyx (see Figure 1). The pelvis has several important functions. Its primary role is to support the weight of the upper body when sitting and to transfer this weight to the lower limbs when standing. It serves as an attachment point for trunk and lower limb muscles, and also protects the internal pelvic organs. When standing in the anatomical position, the pelvis is tilted anteriorly. In this position, the anterior superior iliac spines and the pubic tubercles lie in the same vertical plane, and the anterior (internal) surface of the sacrum faces forward and downward.

The three areas of each hip bone, the ilium, pubis, and ischium, converge centrally to form a deep, cup-shaped cavity called the **acetabulum**. This is located on the lateral side of the hip bone and is part of the hip joint. The large opening in the anteroinferior hip bone between the ischium and pubis is the **obturator foramen**. This space is largely filled in by a layer of connective tissue and serves for the attachment of muscles on both its internal and external surfaces.

Several ligaments unite the bones of the pelvis (Figure 3). The largely immobile sacroiliac joint is supported by a pair of strong ligaments that are attached between the sacrum and ilium portions of the hip bone. These are the **anterior sacroiliac ligament** on the anterior side of the joint and the **posterior sacroiliac ligament** on the posterior side. Also spanning the sacrum and hip bone are two additional ligaments. The **sacrospinous ligament** runs from the sacrum to the ischial spine, and the **sacrotuberous ligament** runs from the sacrum to the ischial tuberosity. These ligaments help to support and immobilize the sacrum as it carries the weight of the body.

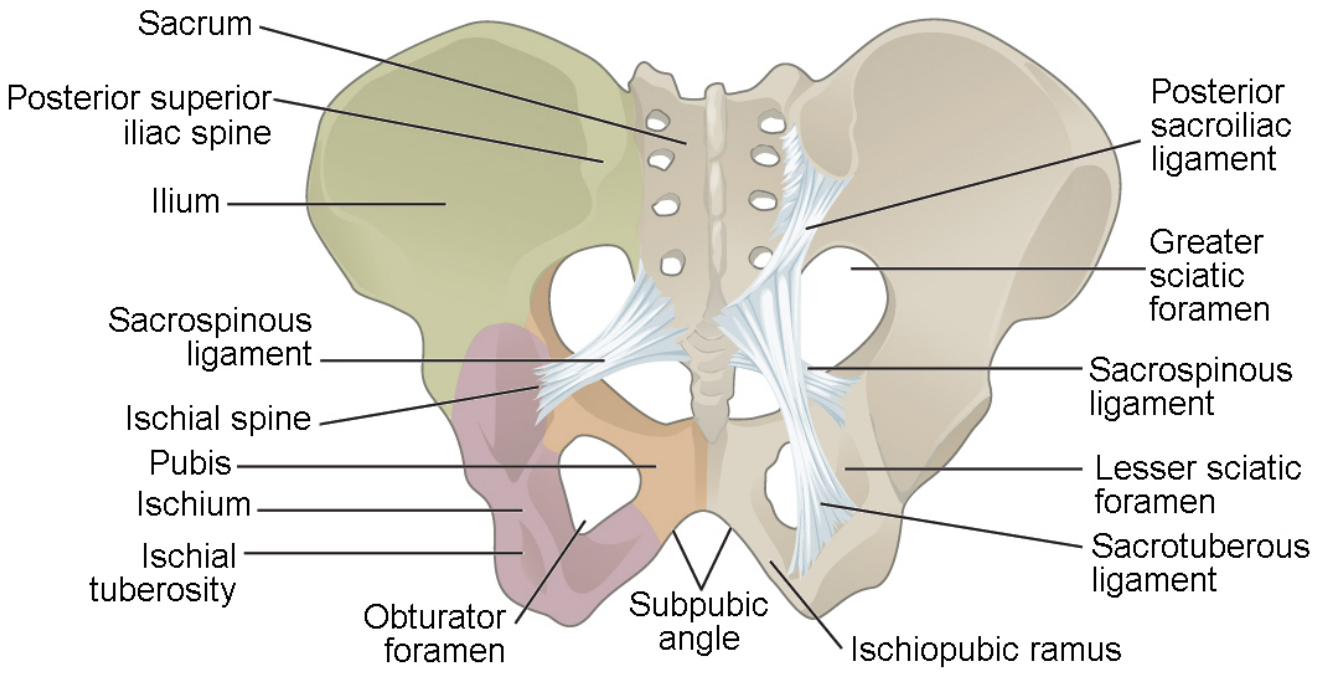


Figure 3. Ligaments of the Pelvis. *The posterior sacroiliac ligament supports the sacroiliac joint. The sacrospinous ligament spans the sacrum to the ischial spine, and the sacrotuberous ligament spans the sacrum to the ischial tuberosity. The sacrospinous and sacrotuberous ligaments contribute to the formation of the greater and lesser sciatic foramens.*

Watch this video for a 3-D view of the pelvis and its associated ligaments. What is the large opening in the bony pelvis, located between the ischium and pubic regions, and what two parts of the pubis contribute to the formation of this opening?

Watch this video online: https://youtu.be/jpScugJrA8g

The sacrospinous and sacrotuberous ligaments also help to define two openings on the posterolateral sides of the pelvis through which muscles, nerves, and blood vessels for the lower limb exit. The superior opening is the **greater sciatic foramen**. This large opening is formed by the greater sciatic notch of the hip bone, the sacrum, and the sacrospinous ligament. The smaller, more inferior **lesser sciatic foramen** is formed by the lesser sciatic notch of the hip bone, together with the sacrospinous and sacrotuberous ligaments.

The space enclosed by the bony pelvis is divided into two regions (Figure 4). The broad, superior region, defined laterally by the large, fan-like portion of the upper hip bone, is called the **greater pelvis** (greater pelvic cavity; false pelvis). This broad area is occupied by portions of the small and large intestines, and because it is more closely associated with the abdominal cavity, it is sometimes referred to as the false pelvis. More inferiorly, the narrow, rounded space of the **lesser pelvis** (lesser pelvic cavity; true pelvis) contains the bladder and other pelvic organs, and thus is also known as the true pelvis. The **pelvic brim** (also known as the **pelvic inlet**) forms the superior margin of the lesser pelvis, separating it from the greater pelvis. The pelvic brim is defined by a line formed by the upper margin of the pubic symphysis anteriorly, and the pectineal line of the pubis, the arcuate line of the ilium, and the sacral promontory (the anterior margin of the superior sacrum) posteriorly. The inferior limit of the lesser pelvic cavity is called the **pelvic outlet**. This large opening is defined by the inferior margin of the pubic symphysis anteriorly, and the ischiopubic ramus, the ischial tuberosity, the sacrotuberous ligament, and the inferior tip of the coccyx posteriorly. Because of the anterior tilt of the pelvis, the lesser pelvis is also angled, giving it an anterosuperior (pelvic inlet) to posteroinferior (pelvic outlet) orientation.

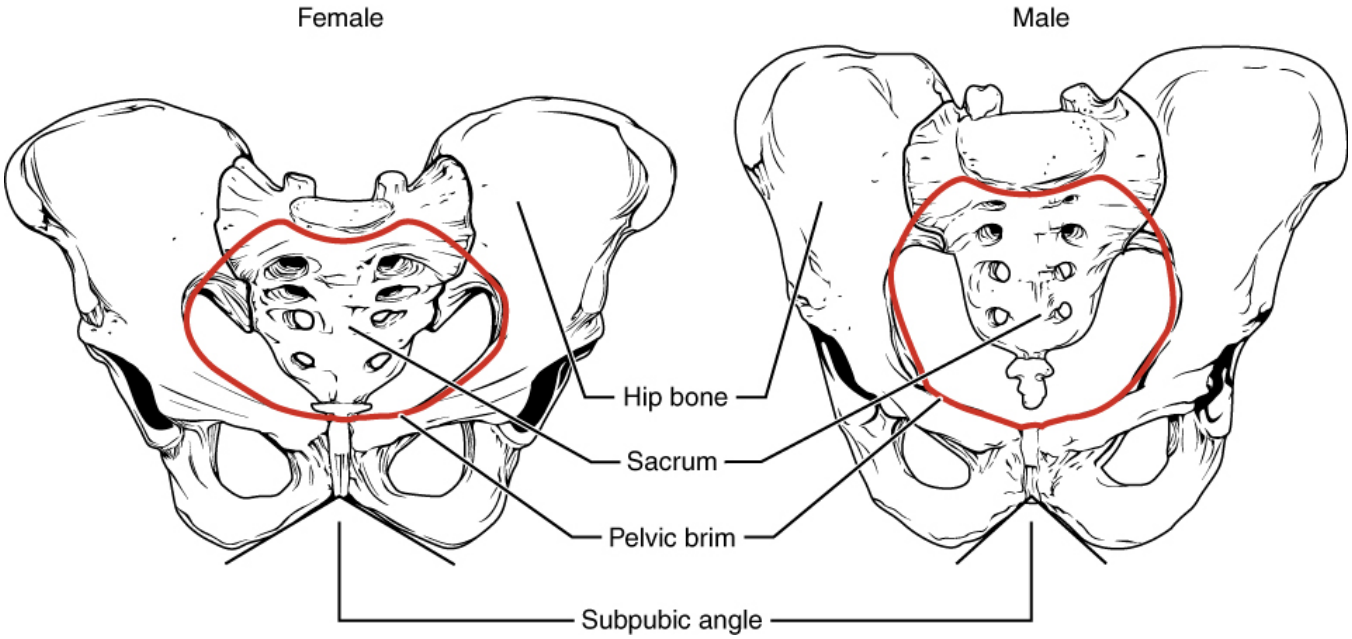


Figure 4. Male and Female Pelvis. *The female pelvis is adapted for childbirth and is broader, with a larger subpubic angle, a rounder pelvic brim, and a wider and more shallow lesser pelvic cavity than the male pelvis.*

Comparison of the Female and Male Pelvis

The differences between the adult female and male pelvis relate to function and body size. In general, the bones of the male pelvis are thicker and heavier, adapted for support of the male's heavier physical build and stronger muscles. The greater sciatic notch of the male hip bone is narrower and deeper than the broader notch of females. Because the female pelvis is adapted for childbirth, it is wider than the male pelvis, as evidenced by the distance between the anterior superior iliac spines (see Figure 4). The ischial tuberosities of females are also farther apart, which increases the size of the pelvic outlet. Because of this increased pelvic width, the subpubic angle is larger in females (greater than 80 degrees) than it is in males (less than 70 degrees). The female sacrum is wider, shorter, and less curved, and the sacral promontory projects less into the pelvic cavity, thus giving the female pelvic inlet (pelvic brim) a more rounded or oval shape compared to males. The lesser pelvic cavity of females is also wider and more shallow than the narrower, deeper, and tapering lesser pelvis of males. Because of the obvious differences between female and male hip bones, this is the one bone of the body that allows for the most accurate sex determination. Table 1 provides an overview of the general differences between the female and male pelvis.

Table 1. Overview of Differences between the Female and Male Pelvis

	Female pelvis	Male pelvis
Pelvic weight	Bones of the pelvis are lighter and thinner	Bones of the pelvis are thicker and heavier
Pelvic inlet shape	Pelvic inlet has a round or oval shape	Pelvic inlet is heart-shaped
Lesser pelvic cavity shape	Lesser pelvic cavity is shorter and wider	Lesser pelvic cavity is longer and narrower
Subpubic angle	Subpubic angle is greater than 80 degrees	Subpubic angle is less than 70 degrees
Pelvic outlet shape	Pelvic outlet is rounded and larger	Pelvic outlet is smaller

Career Connection: Forensic Pathology and Forensic Anthropology

A forensic pathologist (also known as a medical examiner) is a medically trained physician who has been specifically trained in pathology to examine the bodies of the deceased to determine the cause of death. A forensic pathologist applies his or her understanding of disease as well as toxins, blood and DNA analysis, firearms and ballistics, and other factors to assess the cause and manner of death. At times, a forensic pathologist will be called to testify under oath in situations that involve a possible crime. Forensic pathology is a field that has received much media attention on television shows or following a high-profile death.

While forensic pathologists are responsible for determining whether the cause of someone's death was natural, a suicide, accidental, or a homicide, there are times when uncovering the cause of death is more complex, and other skills are needed. Forensic anthropology brings the tools and knowledge of physical anthropology and human osteology (the study of the skeleton) to the task of investigating a death. A forensic anthropologist assists medical and legal professionals in identifying human remains. The science behind forensic anthropology involves the study of archaeological excavation; the examination of hair; an understanding of plants, insects, and footprints; the ability to determine how much time has elapsed since the person died; the analysis of past medical history and toxicology; the ability to determine whether there are any postmortem injuries or alterations of the skeleton; and the identification of the decedent (deceased person) using skeletal and dental evidence.

Due to the extensive knowledge and understanding of excavation techniques, a forensic anthropologist is an integral and invaluable team member to have on-site when investigating a crime scene, especially when the recovery of human skeletal remains is involved. When remains are bought to a forensic anthropologist for examination, he or she must first determine whether the remains are in fact human. Once the remains have been identified as belonging to a person and not to an animal, the next step is to approximate the individual's age, sex, race, and height. The forensic anthropologist does not determine the cause of death, but rather provides information to the forensic pathologist, who will use all of the data collected to make a final determination regarding the cause of death.

BONES OF THE LOWER LIMB

Learning Objectives

- Identify the divisions of the lower limb and describe the bones of each region
- Describe the bones and bony landmarks that articulate at each joint of the lower limb

Like the upper limb, the lower limb is divided into three regions. The **thigh** is that portion of the lower limb located between the hip joint and knee joint. The **leg** is specifically the region between the knee joint and the ankle joint. Distal to the ankle is the **foot**. The lower limb contains 30 bones. These are the femur, patella, tibia, fibula, tarsal bones, metatarsal bones, and phalanges. The **femur** is the single bone of the thigh. The **patella** is the kneecap and articulates with the distal femur. The **tibia** is the larger, weight-bearing bone located on the medial side of the leg, and the **fibula** is the thin bone of the lateral leg. The bones of the foot are divided into three groups. The posterior portion of the foot is formed by a group of seven bones, each of which is known as a **tarsal bone**, whereas the mid-foot contains five elongated bones, each of which is a **metatarsal bone**. The toes contain 14 small bones, each of which is a **phalanx bone of the foot**.

Femur

The femur, or thigh bone, is the single bone of the thigh region (Figure 1). It is the longest and strongest bone of the body, and accounts for approximately one-quarter of a person's total height. The rounded, proximal end is the **head of the femur**, which articulates with the acetabulum of the hip bone to form the **hip joint**. The **fovea capitis** is a minor indentation on the medial side of the femoral head that serves as the site of attachment for the **ligament of the head of the femur**. This ligament spans the femur and acetabulum, but is weak and provides little support for the hip joint. It does, however, carry an important artery that supplies the head of the femur.

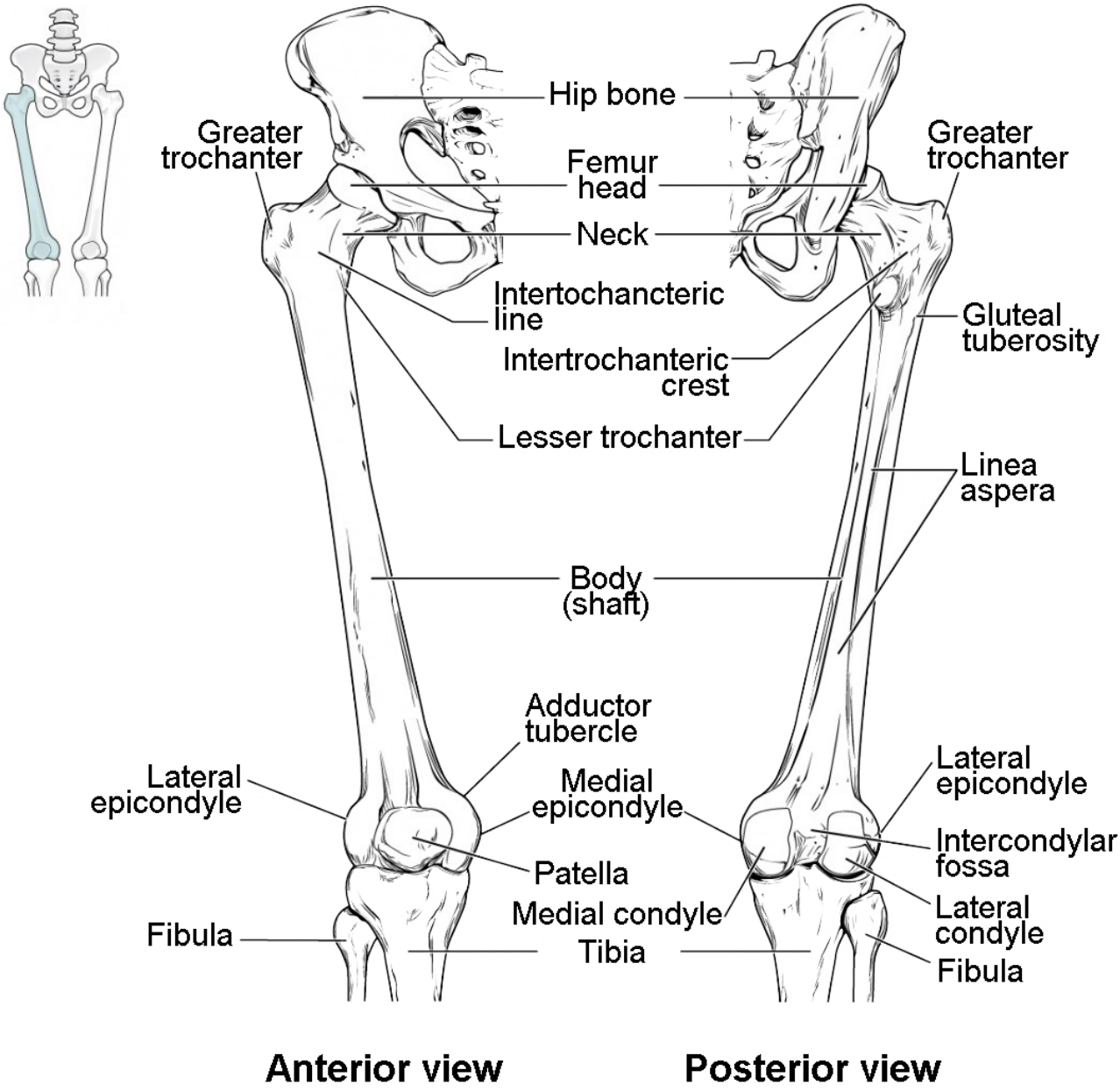


Figure 1. Femur and Patella. *The femur is the single bone of the thigh region. It articulates superiorly with the hip bone at the hip joint, and inferiorly with the tibia at the knee joint. The patella only articulates with the distal end of the femur.*

The narrowed region below the head is the **neck of the femur**. This is a common area for fractures of the femur. The **greater trochanter** is the large, upward, bony projection located above the base of the neck. Multiple muscles that act across the hip joint attach to the greater trochanter, which, because of its projection from the femur, gives additional leverage to these muscles. The greater trochanter can be felt just under the skin on the lateral side of your upper thigh. The **lesser trochanter** is a small, bony prominence that lies on the medial aspect of the femur,

just below the neck. A single, powerful muscle attaches to the lesser trochanter. Running between the greater and lesser trochanters on the anterior side of the femur is the roughened **intertrochanteric line**. The trochanters are also connected on the posterior side of the femur by the larger **intertrochanteric crest**.

The elongated **shaft of the femur** has a slight anterior bowing or curvature. At its proximal end, the posterior shaft has the **gluteal tuberosity**, a roughened area extending inferiorly from the greater trochanter. More inferiorly, the gluteal tuberosity becomes continuous with the **linea aspera** ("rough line"). This is the roughened ridge that passes distally along the posterior side of the mid-femur. Multiple muscles of the hip and thigh regions make long, thin attachments to the femur along the linea aspera.

The distal end of the femur has medial and lateral bony expansions. On the lateral side, the smooth portion that covers the distal and posterior aspects of the lateral expansion is the **lateral condyle of the femur**. The roughened area on the outer, lateral side of the condyle is the **lateral epicondyle of the femur**. Similarly, the smooth region of the distal and posterior medial femur is the **medial condyle of the femur**, and the irregular outer, medial side of this is the **medial epicondyle of the femur**. The lateral and medial condyles articulate with the tibia to form the knee joint. The epicondyles provide attachment for muscles and supporting ligaments of the knee. The **adductor tubercle** is a small bump located at the superior margin of the medial epicondyle. Posteriorly, the medial and lateral condyles are separated by a deep depression called the **intercondylar fossa**. Anteriorly, the smooth surfaces of the condyles join together to form a wide groove called the **patellar surface**, which provides for articulation with the patella bone. The combination of the medial and lateral condyles with the patellar surface gives the distal end of the femur a horseshoe (U) shape.

Watch this video to view how a fracture of the mid-femur is surgically repaired. How are the two portions of the broken femur stabilized during surgical repair of a fractured femur?

Watch this video online: https://youtu.be/1S1nrCwm1qc

Patella

The patella (kneecap) is largest sesamoid bone of the body (see Figure 1). A sesamoid bone is a bone that is incorporated into the tendon of a muscle where that tendon crosses a joint. The sesamoid bone articulates with the underlying bones to prevent damage to the muscle tendon due to rubbing against the bones during movements of the joint. The patella is found in the tendon of the quadriceps femoris muscle, the large muscle of the anterior thigh that passes across the anterior knee to attach to the tibia. The patella articulates with the patellar surface of the femur and thus prevents rubbing of the muscle tendon against the distal femur. The patella also lifts the tendon away from the knee joint, which increases the leverage power of the quadriceps femoris muscle as it acts across the knee. The patella does not articulate with the tibia.

Visit this site to perform a virtual knee replacement surgery. The prosthetic knee components must be properly aligned to function properly. How is this alignment ensured?

Homeostatic Imbalances: Runner's Knee

Runner's knee, also known as patellofemoral syndrome, is the most common overuse injury among runners. It is most frequent in adolescents and young adults, and is more common in females. It often results from excessive running, particularly downhill, but may also occur in athletes who do a lot of knee bending, such as jumpers, skiers, cyclists, weight lifters, and soccer players. It is felt as a dull, aching pain around the front of the knee and deep to the patella. The pain may be felt when walking or running, going up or down stairs, kneeling or squatting, or after sitting with the knee bent for an extended period.

Patellofemoral syndrome may be initiated by a variety of causes, including individual variations in the shape and movement of the patella, a direct blow to the patella, or flat feet or improper shoes that cause excessive turning in or out of the feet or leg. These factors may cause in an imbalance in the muscle pull that acts on the patella, resulting in an abnormal tracking of the patella that allows it to deviate too far toward the lateral side of the patellar surface on the distal femur.

Because the hips are wider than the knee region, the femur has a diagonal orientation within the thigh, in contrast to the vertically oriented tibia of the leg (Figure 2). The Q-angle is a measure of how far the femur is angled laterally away from vertical. The Q-angle is normally 10–15 degrees, with females typically having a larger Q-angle due to their wider pelvis. During extension of the knee, the quadriceps femoris muscle pulls the patella both superiorly and laterally, with the lateral pull greater in women due to their large Q-angle. This makes women more vulnerable to developing patellofemoral syndrome than men. Normally, the large lip on the lateral side of the patellar surface of the femur compensates for the lateral pull on the patella, and thus helps to maintain its proper tracking.

However, if the pull produced by the medial and lateral sides of the quadriceps femoris muscle is not properly balanced, abnormal tracking of the patella toward the lateral side may occur. With continued use, this produces pain and could result in damage to the articulating surfaces of the patella and femur, and the possible future development of arthritis. Treatment generally involves stopping the activity that produces knee pain for a period of time, followed by a gradual resumption of activity. Proper strengthening of the quadriceps femoris muscle to correct for imbalances is also important to help prevent reoccurrence.

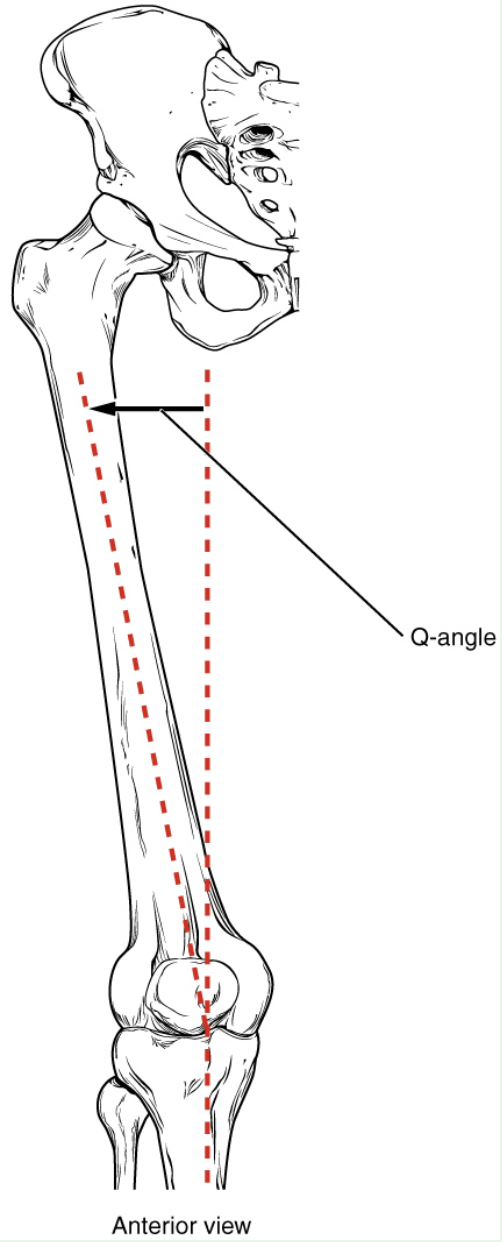


Figure 2. The Q-Angle. *The Q-angle is a measure of the amount of lateral deviation of the femur from the vertical line of the tibia. Adult females have a larger Q-angle due to their wider pelvis than adult males.*

Tibia

The tibia (shin bone) is the medial bone of the leg and is larger than the fibula, with which it is paired (Figure 3). The tibia is the main weight-bearing bone of the lower leg and the second longest bone of the body, after the femur. The medial side of the tibia is located immediately under the skin, allowing it to be easily palpated down the entire length of the medial leg.

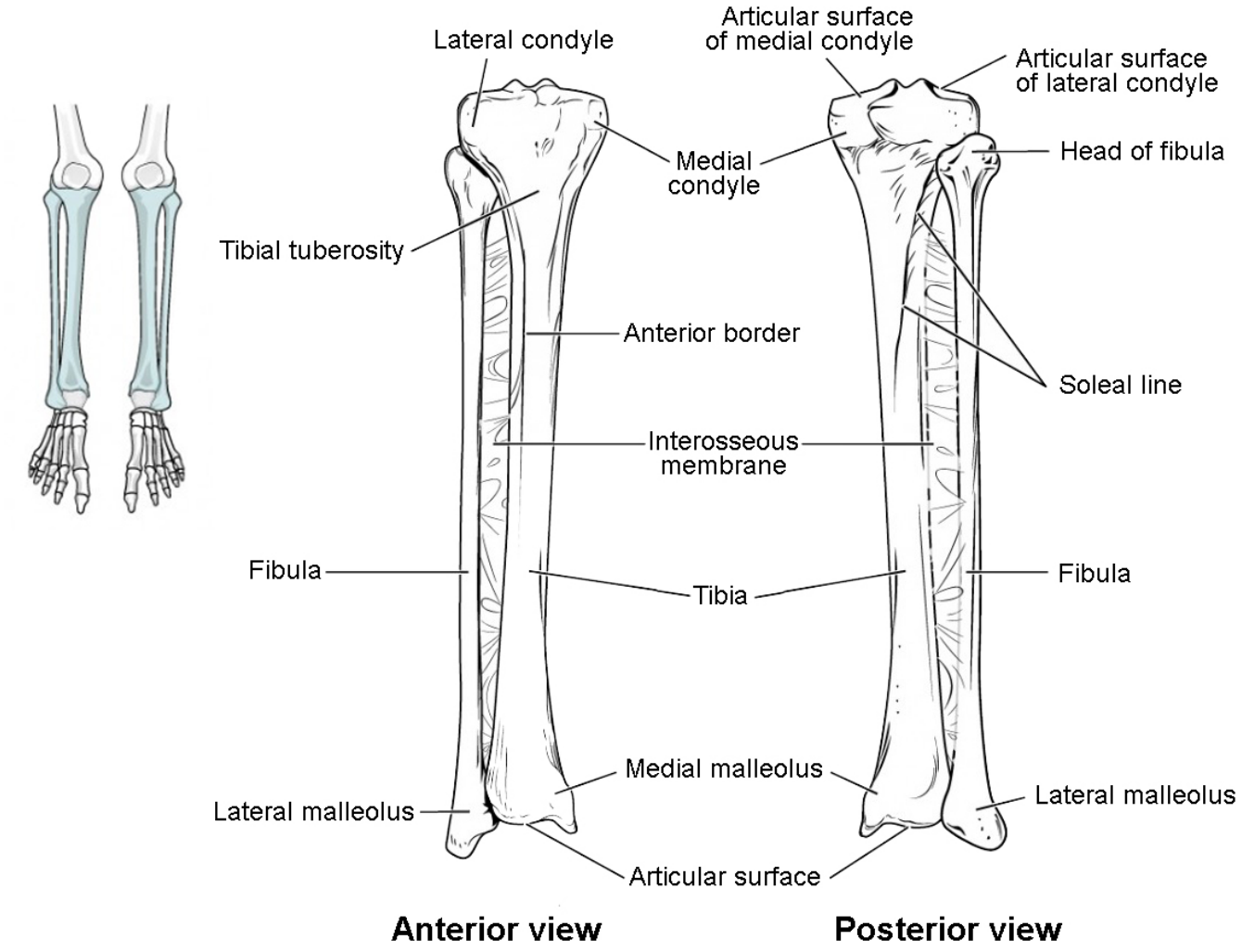


Figure 3. Tibia and Fibula. *The tibia is the larger, weight-bearing bone located on the medial side of the leg. The fibula is the slender bone of the lateral side of the leg and does not bear weight.*

The proximal end of the tibia is greatly expanded. The two sides of this expansion form the **medial condyle of the tibia** and the **lateral condyle of the tibia**. The tibia does not have epicondyles. The top surface of each condyle is smooth and flattened. These areas articulate with the medial and lateral condyles of the femur to form the **knee joint**. Between the articulating surfaces of the tibial condyles is the **intercondylar eminence**, an irregular, elevated area that serves as the inferior attachment point for two supporting ligaments of the knee.

The **tibial tuberosity** is an elevated area on the anterior side of the tibia, near its proximal end. It is the final site of attachment for the muscle tendon associated with the patella. More inferiorly, the **shaft of the tibia** becomes triangular in shape. The anterior apex of this triangle forms the **anterior border of the tibia**, which begins at the tibial tuberosity and runs inferiorly along the length of the tibia. Both the anterior border and the medial side of the triangular shaft are located immediately under the skin and can be easily palpated along the entire length of the tibia. A small ridge running down the lateral side of the tibial shaft is the **interosseous border of the tibia**. This is for the attachment of the **interosseous membrane of the leg**, the sheet of dense connective tissue that unites the tibia and fibula bones. Located on the posterior side of the tibia is the **soleal line**, a diagonally running, roughened ridge that begins below the base of the lateral condyle, and runs down and medially across the proximal third of the posterior tibia. Muscles of the posterior leg attach to this line.

The large expansion found on the medial side of the distal tibia is the **medial malleolus** (“little hammer”). This forms the large bony bump found on the medial side of the ankle region. Both the smooth surface on the inside of the medial malleolus and the smooth area at the distal end of the tibia articulate with the talus bone of the foot as part of the ankle joint. On the lateral side of the distal tibia is a wide groove called the **fibular notch**. This area articulates with the distal end of the fibula, forming the **distal tibiofibular joint**.

Fibula

The fibula is the slender bone located on the lateral side of the leg (see Figure 3). The fibula does not bear weight. It serves primarily for muscle attachments and thus is largely surrounded by muscles. Only the proximal and distal ends of the fibula can be palpated.

The **head of the fibula** is the small, knob-like, proximal end of the fibula. It articulates with the inferior aspect of the lateral tibial condyle, forming the **proximal tibiofibular joint**. The thin **shaft of the fibula** has the **interosseous border of the fibula**, a narrow ridge running down its medial side for the attachment of the interosseous membrane that spans the fibula and tibia. The distal end of the fibula forms the **lateral malleolus**, which forms the easily palpated bony bump on the lateral side of the ankle. The deep (medial) side of the lateral malleolus articulates with the talus bone of the foot as part of the ankle joint. The distal fibula also articulates with the fibular notch of the tibia.

Tarsal Bones

The posterior half of the foot is formed by seven tarsal bones (Figure 4).

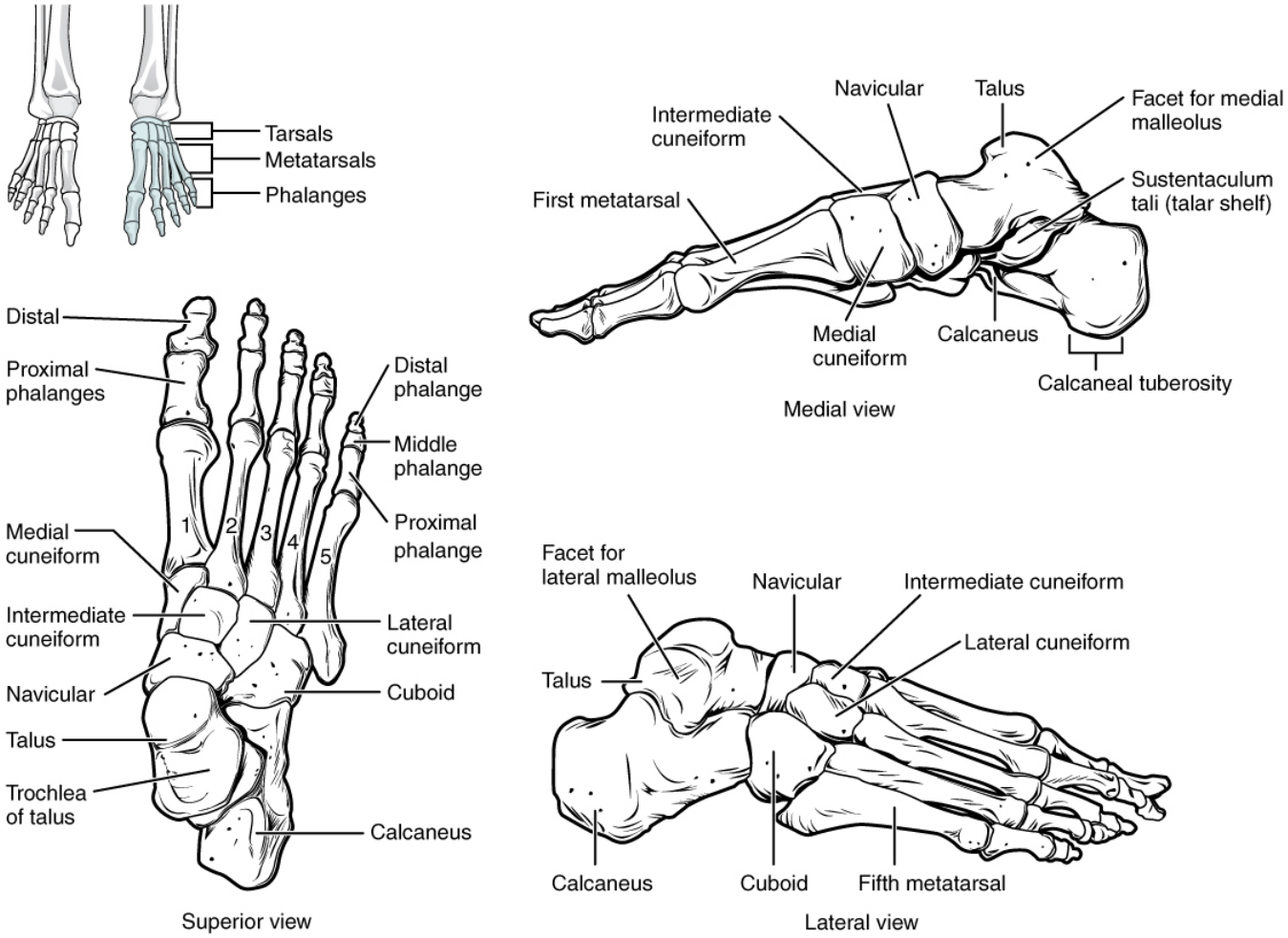


Figure 4. Bones of the Foot. *The bones of the foot are divided into three groups. The posterior foot is formed by the seven tarsal bones. The mid-foot has the five metatarsal bones. The toes contain the phalanges.*

The most superior bone is the **talus**. This has a relatively square-shaped, upper surface that articulates with the tibia and fibula to form the **ankle joint**. Three areas of articulation form the ankle joint: The superomedial surface of the talus bone articulates with the medial malleolus of the tibia, the top of the talus articulates with the distal end of the tibia, and the lateral side of the talus articulates with the lateral malleolus of the fibula. Inferiorly, the talus articulates with the **calcaneus** (heel bone), the largest bone of the foot, which forms the heel. Body weight is

transferred from the tibia to the talus to the calcaneus, which rests on the ground. The medial calcaneus has a prominent bony extension called the **sustentaculum tali** ("support for the talus") that supports the medial side of the talus bone.

The **cuboid** bone articulates with the anterior end of the calcaneus bone. The cuboid has a deep groove running across its inferior surface, which provides passage for a muscle tendon. The talus bone articulates anteriorly with the **navicular** bone, which in turn articulates anteriorly with the three cuneiform ("wedge-shaped") bones. These bones are the **medial cuneiform**, the **intermediate cuneiform**, and the **lateral cuneiform**. Each of these bones has a broad superior surface and a narrow inferior surface, which together produce the transverse (medial-lateral) curvature of the foot. The navicular and lateral cuneiform bones also articulate with the medial side of the cuboid bone.

Use this tutorial to review the bones of the foot. Which tarsal bones are in the proximal, intermediate, and distal groups?

Metatarsal Bones

The anterior half of the foot is formed by the five metatarsal bones, which are located between the tarsal bones of the posterior foot and the phalanges of the toes (see Figure 4). These elongated bones are numbered 1–5, starting with the medial side of the foot. The first metatarsal bone is shorter and thicker than the others. The second metatarsal is the longest. The **base of the metatarsal bone** is the proximal end of each metatarsal bone. These articulate with the cuboid or cuneiform bones. The base of the fifth metatarsal has a large, lateral expansion that provides for muscle attachments. This expanded base of the fifth metatarsal can be felt as a bony bump at the midpoint along the lateral border of the foot. The expanded distal end of each metatarsal is the **head of the metatarsal bone**. Each metatarsal bone articulates with the proximal phalanx of a toe to form a **metatarsophalangeal joint**. The heads of the metatarsal bones also rest on the ground and form the ball (anterior end) of the foot.

Phalanges

The toes contain a total of 14 phalanx bones (phalanges), arranged in a similar manner as the phalanges of the fingers (see Figure 4). The toes are numbered 1–5, starting with the big toe (**hallux**). The big toe has two phalanx bones, the proximal and distal phalanges. The remaining toes all have proximal, middle, and distal phalanges. A joint between adjacent phalanx bones is called an interphalangeal joint.

View this link to learn about a bunion, a localized swelling on the medial side of the foot, next to the first metatarsophalangeal joint, at the base of the big toe. What is a bunion and what type of shoe is most likely to cause this to develop?

Arches of the Foot

When the foot comes into contact with the ground during walking, running, or jumping activities, the impact of the body weight puts a tremendous amount of pressure and force on the foot. During running, the force applied to each foot as it contacts the ground can be up to 2.5 times your body weight. The bones, joints, ligaments, and muscles of the foot absorb this force, thus greatly reducing the amount of shock that is passed superiorly into the lower limb and body. The arches of the foot play an important role in this shock-absorbing ability. When weight is applied to the foot, these arches will flatten somewhat, thus absorbing energy. When the weight is removed, the arch rebounds, giving "spring" to the step. The arches also serve to distribute body weight side to side and to either end of the foot.

The foot has a transverse arch, a medial longitudinal arch, and a lateral longitudinal arch (see Figure 4). The transverse arch forms the medial-lateral curvature of the mid-foot. It is formed by the wedge shapes of the cuneiform bones and bases (proximal ends) of the first to fourth metatarsal bones. This arch helps to distribute body weight from side to side within the foot, thus allowing the foot to accommodate uneven terrain.

The longitudinal arches run down the length of the foot. The lateral longitudinal arch is relatively flat, whereas the medial longitudinal arch is larger (taller). The longitudinal arches are formed by the tarsal bones posteriorly and the metatarsal bones anteriorly. These arches are supported at either end, where they contact the ground. Posteriorly, this support is provided by the calcaneus bone and anteriorly by the heads (distal ends) of the metatarsal bones. The talus bone, which receives the weight of the body, is located at the top of the longitudinal arches. Body weight is then conveyed from the talus to the ground by the anterior and posterior ends of these arches.

Strong ligaments unite the adjacent foot bones to prevent disruption of the arches during weight bearing. On the bottom of the foot, additional ligaments tie together the anterior and posterior ends of the arches. These ligaments have elasticity, which allows them to stretch somewhat during weight bearing, thus allowing the longitudinal arches to spread. The stretching of these ligaments stores energy within the foot, rather than passing these forces into the leg. Contraction of the foot muscles also plays an important role in this energy absorption. When the weight is removed, the elastic ligaments recoil and pull the ends of the arches closer together. This recovery of the arches releases the stored energy and improves the energy efficiency of walking.

Stretching of the ligaments that support the longitudinal arches can lead to pain. This can occur in overweight individuals, with people who have jobs that involve standing for long periods of time (such as a waitress), or walking or running long distances. If stretching of the ligaments is prolonged, excessive, or repeated, it can result in a gradual lengthening of the supporting ligaments, with subsequent depression or collapse of the longitudinal arches, particularly on the medial side of the foot. This condition is called pes planus (“flat foot” or “fallen arches”).

Self-Check Questions

Visit your course online to take a quiz to check your understanding of Bones of the Lower Limb:

DEVELOPMENT OF THE APPENDICULAR SKELETON

Learning Objectives

- Describe the growth and development of the embryonic limb buds
- Discuss the appearance of primary and secondary ossification centers

Embryologically, the appendicular skeleton arises from mesenchyme, a type of embryonic tissue that can differentiate into many types of tissues, including bone or muscle tissue. Mesenchyme gives rise to the bones of the upper and lower limbs, as well as to the pectoral and pelvic girdles. Development of the limbs begins near the end of the fourth embryonic week, with the upper limbs appearing first. Thereafter, the development of the upper and lower limbs follows similar patterns, with the lower limbs lagging behind the upper limbs by a few days.

Limb Growth

Each upper and lower limb initially develops as a small bulge called a **limb bud**, which appears on the lateral side of the early embryo. The upper limb bud appears near the end of the fourth week of development, with the lower limb bud appearing shortly after (Figure 1).

Initially, the limb buds consist of a core of mesenchyme covered by a layer of ectoderm. The ectoderm at the end of the limb bud thickens to form a narrow crest called the **apical ectodermal ridge**. This ridge stimulates the underlying mesenchyme to rapidly proliferate, producing the outgrowth of the developing limb. As the limb bud elongates, cells located farther from the apical ectodermal ridge slow their rates of cell division and begin to differentiate. In this way, the limb develops along a proximal-to-distal axis.

During the sixth week of development, the distal ends of the upper and lower limb buds expand and flatten into a paddle shape. This region will become the hand or foot. The wrist or ankle areas then appear as a constriction that develops at the base of the paddle. Shortly after this, a second constriction on the limb bud appears at the future site of the elbow or knee. Within the paddle, areas of tissue undergo cell death, producing separations between the growing fingers and toes. Also during the sixth week of development, mesenchyme within the limb buds begins to differentiate into hyaline cartilage that will form models of the future limb bones.

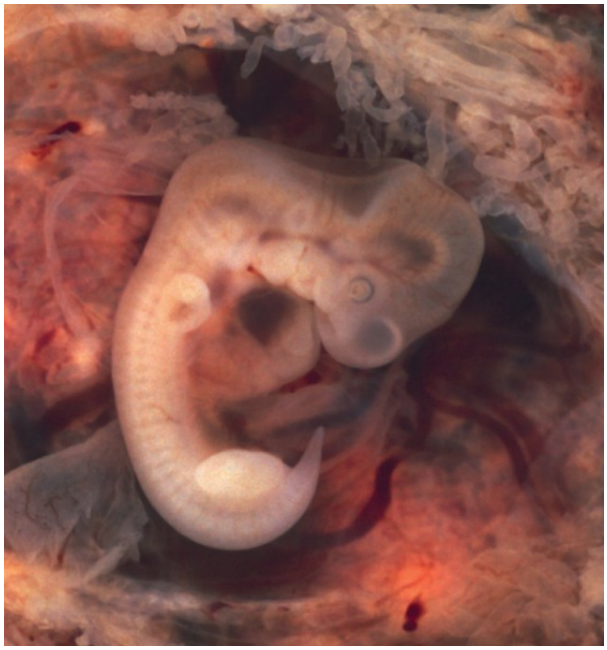


Figure 1. Embryo at Seven Weeks. *Limb buds are visible in an embryo at the end of the seventh week of development (embryo derived from an ectopic pregnancy). (credit: Ed Uthman/flickr)*

The early outgrowth of the upper and lower limb buds initially has the limbs positioned so that the regions that will become the palm of the hand or the bottom of the foot are facing medially toward the body, with the future thumb or big toe both oriented toward the head. During the seventh week of development, the upper limb rotates laterally by 90 degrees, so that the palm of the hand faces anteriorly and the thumb points laterally. In contrast, the lower limb undergoes a 90-degree medial rotation, thus bringing the big toe to the medial side of the foot.

Watch this animation to follow the development and growth of the upper and lower limb buds. On what days of embryonic development do these events occur: (a) first appearance of the upper limb bud (limb ridge); (b) the flattening of the distal limb to form the handplate or footplate; and (c) the beginning of limb rotation?

Watch this video online: https://youtu.be/VpbdqGJ9LWk

Ossification of Appendicular Bones

All of the girdle and limb bones, except for the clavicle, develop by the process of endochondral ossification. This process begins as the mesenchyme within the limb bud differentiates into hyaline cartilage to form cartilage models for future bones. By the twelfth week, a primary ossification center will have appeared in the diaphysis (shaft) region of the long bones, initiating the process that converts the cartilage model into bone. A secondary ossification center will appear in each epiphysis (expanded end) of these bones at a later time, usually after birth. The primary and secondary ossification centers are separated by the epiphyseal plate, a layer of growing hyaline cartilage. This plate is located between the diaphysis and each epiphysis. It continues to grow and is responsible for the lengthening of the bone. The epiphyseal plate is retained for many years, until the bone reaches its final, adult size, at which time the epiphyseal plate disappears and the epiphysis fuses to the diaphysis. (Seek additional content on ossification in the chapter on bone tissue.)

Small bones, such as the phalanges, will develop only one secondary ossification center and will thus have only a single epiphyseal plate. Large bones, such as the femur, will develop several secondary ossification centers, with an epiphyseal plate associated with each secondary center. Thus, ossification of the femur begins at the end of the seventh week with the appearance of the primary ossification center in the diaphysis, which rapidly expands to ossify the shaft of the bone prior to birth. Secondary ossification centers develop at later times.

Ossification of the distal end of the femur, to form the condyles and epicondyles, begins shortly before birth. Secondary ossification centers also appear in the femoral head late in the first year after birth, in the greater trochanter during the fourth year, and in the lesser trochanter between the ages of 9 and 10 years. Once these areas have ossified, their fusion to the diaphysis and the disappearance of each epiphyseal plate follow a reversed sequence. Thus, the lesser trochanter is the first to fuse, doing so at the onset of puberty (around 11 years of age), followed by the greater trochanter approximately 1 year later.

The femoral head fuses between the ages of 14–17 years, whereas the distal condyles of the femur are the last to fuse, between the ages of 16–19 years. Knowledge of the age at which different epiphyseal plates disappear is important when interpreting radiographs taken of children. Since the cartilage of an epiphyseal plate is less dense than bone, the plate will appear dark in a radiograph image. Thus, a normal epiphyseal plate may be mistaken for a bone fracture.

The clavicle is the one appendicular skeleton bone that does not develop via endochondral ossification. Instead, the clavicle develops through the process of intramembranous ossification. During this process, mesenchymal cells differentiate directly into bone-producing cells, which produce the clavicle directly, without first making a cartilage model. Because of this early production of bone, the clavicle is the first bone of the body to begin ossification, with ossification centers appearing during the fifth week of development. However, ossification of the clavicle is not complete until age 25.

Disorders of the Appendicular System: Congenital Clubfoot

Clubfoot, also known as talipes, is a congenital (present at birth) disorder of unknown cause and is the most common deformity of the lower limb. It affects the foot and ankle, causing the foot to be twisted inward at a sharp angle, like the head of a golf club (Figure 2). Clubfoot has a frequency of about 1 out of every 1,000 births, and is twice as likely to occur in a male child as in a female child. In 50 percent of cases, both feet are affected.

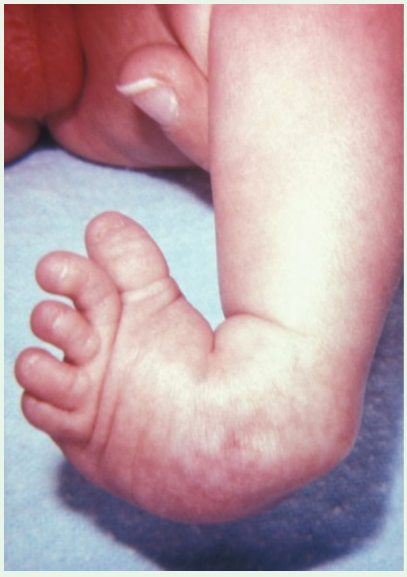


Figure 2. Clubfoot. Clubfoot is a common deformity of the ankle and foot that is present at birth. Most cases are corrected without surgery, and affected individuals will grow up to lead normal, active lives. (credit: James W. Hanson)

At birth, children with a clubfoot have the heel turned inward and the anterior foot twisted so that the lateral side of the foot is facing inferiorly, commonly due to ligaments or leg muscles attached to the foot that are shortened or abnormally tight. These pull the foot into an abnormal position, resulting in bone deformities. Other symptoms may include bending of the ankle that lifts the heel of the foot and an extremely high foot arch. Due to the limited range of motion in the affected foot, it is difficult to place the foot into the correct position. Additionally, the affected foot may be shorter than normal, and the calf muscles are usually underdeveloped on the affected side. Despite the appearance, this is not a painful condition for newborns. However, it must be treated early to avoid future pain and impaired walking ability.

Although the cause of clubfoot is idiopathic (unknown), evidence indicates that fetal position within the uterus is not a contributing factor. Genetic factors are involved, because clubfoot tends to run within families. Cigarette smoking during pregnancy has been linked to the development of clubfoot, particularly in families with a history of clubfoot.

Previously, clubfoot required extensive surgery. Today, 90 percent of cases are successfully treated without surgery using new corrective casting techniques. The best chance for a full recovery requires that clubfoot treatment begin during the first 2 weeks after birth. Corrective casting gently stretches the foot, which is followed by the application of a holding cast to keep the foot in the proper

position. This stretching and casting is repeated weekly for several weeks. In severe cases, surgery may also be required, after which the foot typically remains in a cast for 6 to 8 weeks. After the cast is removed following either surgical or nonsurgical treatment, the child will be required to wear a brace part-time (at night) for up to 4 years. In addition, special exercises will be prescribed, and the child must also wear special shoes. Close monitoring by the parents and adherence to postoperative instructions are imperative in minimizing the risk of relapse.

Despite these difficulties, treatment for clubfoot is usually successful, and the child will grow up to lead a normal, active life. Numerous examples of individuals born with a clubfoot who went on to successful careers include Dudley Moore (comedian and actor), Damon Wayans (comedian and actor), Troy Aikman (three-time Super Bowl-winning quarterback), Kristi Yamaguchi (Olympic gold medalist in figure skating), Mia Hamm (two-time Olympic gold medalist in soccer), and Charles Woodson (Heisman trophy and Super Bowl winner).

ADDITIONAL LINKS

Interactive Links

- Notes on the skeletal system
- Images and practice on the skeletal system
- Manatomy overview of the skeletal system
- Interactive Skeletal Anatomy
- InnerBody Anatomy Explorer
- Skeletal System Games

Suggested App: Virtual Human Body

GLOSSARY: THE APPENDICULAR SYSTEM

acetabulum: large, cup-shaped cavity located on the lateral side of the hip bone; formed by the junction of the ilium, pubis, and ischium portions of the hip bone

acromial end of the clavicle: lateral end of the clavicle that articulates with the acromion of the scapula

acromial process: acromion of the scapula

acromioclavicular joint: articulation between the acromion of the scapula and the acromial end of the clavicle

acromion: flattened bony process that extends laterally from the scapular spine to form the bony tip of the shoulder

adductor tubercle: small, bony bump located on the superior aspect of the medial epicondyle of the femur

anatomical neck: line on the humerus located around the outside margin of the humeral head

ankle joint: joint that separates the leg and foot portions of the lower limb; formed by the articulations between the talus bone of the foot inferiorly, and the distal end of the tibia, medial malleolus of the tibia, and lateral malleolus of the fibula superiorly

anterior border of the tibia: narrow, anterior margin of the tibia that extends inferiorly from the tibial tuberosity

anterior inferior iliac spine: small, bony projection located on the anterior margin of the ilium, below the anterior superior iliac spine

anterior sacroiliac ligament: strong ligament between the sacrum and the ilium portions of the hip bone that supports the anterior side of the sacroiliac joint

anterior superior iliac spine: rounded, anterior end of the iliac crest

apical ectodermal ridge: enlarged ridge of ectoderm at the distal end of a limb bud that stimulates growth and elongation of the limb

arcuate line of the ilium: smooth ridge located at the inferior margin of the iliac fossa; forms the lateral portion of the pelvic brim

arm: region of the upper limb located between the shoulder and elbow joints; contains the humerus bone

auricular surface of the ilium: roughened area located on the posterior, medial side of the ilium of the hip bone; articulates with the auricular surface of the sacrum to form the sacroiliac joint

base of the metatarsal bone: expanded, proximal end of each metatarsal bone

bicipital groove: intertubercular groove; narrow groove located between the greater and lesser tubercles of the humerus

calcaneus: heel bone; posterior, inferior tarsal bone that forms the heel of the foot

capitate: from the lateral side, the third of the four distal carpal bones; articulates with the scaphoid and lunate proximally, the trapezoid laterally, the hamate medially, and primarily with the third metacarpal distally

capitulum: knob-like bony structure located anteriorly on the lateral, distal end of the humerus

carpal bone: one of the eight small bones that form the wrist and base of the hand; these are grouped as a proximal row consisting of (from lateral to medial) the scaphoid, lunate, triquetrum, and pisiform bones, and a distal row containing (from lateral to medial) the trapezium, trapezoid, capitate, and hamate bones

carpal tunnel: passageway between the anterior forearm and hand formed by the carpal bones and flexor retinaculum

carpometacarpal joint: articulation between one of the carpal bones in the distal row and a metacarpal bone of the hand

clavicle: collarbone; elongated bone that articulates with the manubrium of the sternum medially and the acromion of the scapula laterally

coracoclavicular ligament: strong band of connective tissue that anchors the coracoid process of the scapula to the lateral clavicle; provides important indirect support for the acromioclavicular joint

coracoid process: short, hook-like process that projects anteriorly and laterally from the superior margin of the scapula

coronoid fossa: depression on the anterior surface of the humerus above the trochlea; this space receives the coronoid process of the ulna when the elbow is maximally flexed

coronoid process of the ulna: projecting bony lip located on the anterior, proximal ulna; forms the inferior margin of the trochlear notch

costoclavicular ligament: band of connective tissue that unites the medial clavicle with the first rib

coxal bone: hip bone

cuboid: tarsal bone that articulates posteriorly with the calcaneus bone, medially with the lateral cuneiform bone, and anteriorly with the fourth and fifth metatarsal bones

deltoid tuberosity: roughened, V-shaped region located laterally on the mid-shaft of the humerus

distal radioulnar joint: articulation between the head of the ulna and the ulnar notch of the radius

distal tibiofibular joint: articulation between the distal fibula and the fibular notch of the tibia

elbow joint: joint located between the upper arm and forearm regions of the upper limb; formed by the articulations between the trochlea of the humerus and the trochlear notch of the ulna, and the capitulum of the humerus and the head of the radius

femur: thigh bone; the single bone of the thigh

fibula: thin, non-weight-bearing bone found on the lateral side of the leg

fibular notch: wide groove on the lateral side of the distal tibia for articulation with the fibula at the distal tibiofibular joint

flexor retinaculum: strong band of connective tissue at the anterior wrist that spans the top of the U-shaped grouping of the carpal bones to form the roof of the carpal tunnel

foot: portion of the lower limb located distal to the ankle joint

forearm: region of the upper limb located between the elbow and wrist joints; contains the radius and ulna bones

fossa: (plural = fossae) shallow depression on the surface of a bone

fovea capitis: minor indentation on the head of the femur that serves as the site of attachment for the ligament to the head of the femur

glenohumeral joint: shoulder joint; formed by the articulation between the glenoid cavity of the scapula and the head of the humerus

glenoid cavity: (also, glenoid fossa) shallow depression located on the lateral scapula, between the superior and lateral borders

gluteal tuberosity: roughened area on the posterior side of the proximal femur, extending inferiorly from the base of the greater trochanter

greater pelvis: (also, greater pelvic cavity or false pelvis) broad space above the pelvic brim defined laterally by the fan-like portion of the upper ilium

greater sciatic foramen: pelvic opening formed by the greater sciatic notch of the hip bone, the sacrum, and the sacrospinous ligament

greater sciatic notch: large, U-shaped indentation located on the posterior margin of the ilium, superior to the ischial spine

greater trochanter: large, bony expansion of the femur that projects superiorly from the base of the femoral neck

greater tubercle: enlarged prominence located on the lateral side of the proximal humerus

hallux: big toe; digit 1 of the foot

hamate: from the lateral side, the fourth of the four distal carpal bones; articulates with the lunate and triquetrum proximally, the fourth and fifth metacarpals distally, and the capitate laterally

hand: region of the upper limb distal to the wrist joint

head of the femur: rounded, proximal end of the femur that articulates with the acetabulum of the hip bone to form the hip joint

head of the fibula: small, knob-like, proximal end of the fibula; articulates with the inferior aspect of the lateral condyle of the tibia

head of the humerus: smooth, rounded region on the medial side of the proximal humerus; articulates with the glenoid fossa of the scapula to form the glenohumeral (shoulder) joint

head of the metatarsal bone: expanded, distal end of each metatarsal bone

head of the radius: disc-shaped structure that forms the proximal end of the radius; articulates with the capitulum of the humerus as part of the elbow joint, and with the radial notch of the ulna as part of the proximal radioulnar joint

head of the ulna: small, rounded distal end of the ulna; articulates with the ulnar notch of the distal radius, forming the distal radioulnar joint

hip bone: coxal bone; single bone that forms the pelvic girdle; consists of three areas, the ilium, ischium, and pubis

hip joint: joint located at the proximal end of the lower limb; formed by the articulation between the acetabulum of the hip bone and the head of the femur

hook of the hamate bone: bony extension located on the anterior side of the hamate carpal bone

humerus: single bone of the upper arm

iliac crest: curved, superior margin of the ilium

iliac fossa: shallow depression found on the anterior and medial surfaces of the upper ilium

ilium: superior portion of the hip bone

inferior angle of the scapula: inferior corner of the scapula located where the medial and lateral borders meet

inferior pubic ramus: narrow segment of bone that passes inferiorly and laterally from the pubic body; joins with the ischial ramus to form the ischiopubic ramus

infraglenoid tubercle: small bump or roughened area located on the lateral border of the scapula, near the inferior margin of the glenoid cavity

infraspinous fossa: broad depression located on the posterior scapula, inferior to the spine

intercondylar eminence: irregular elevation on the superior end of the tibia, between the articulating surfaces of the medial and lateral condyles

intercondylar fossa: deep depression on the posterior side of the distal femur that separates the medial and lateral condyles

intermediate cuneiform: middle of the three cuneiform tarsal bones; articulates posteriorly with the navicular bone, medially with the medial cuneiform bone, laterally with the lateral cuneiform bone, and anteriorly with the second metatarsal bone

interosseous border of the fibula: small ridge running down the medial side of the fibular shaft; for attachment of the interosseous membrane between the fibula and tibia

interosseous border of the radius: narrow ridge located on the medial side of the radial shaft; for attachment of the interosseous membrane between the ulna and radius bones

interosseous border of the tibia: small ridge running down the lateral side of the tibial shaft; for attachment of the interosseous membrane between the tibia and fibula

interosseous border of the ulna: narrow ridge located on the lateral side of the ulnar shaft; for attachment of the interosseous membrane between the ulna and radius

interosseous membrane of the forearm: sheet of dense connective tissue that unites the radius and ulna bones

interosseous membrane of the leg: sheet of dense connective tissue that unites the shafts of the tibia and fibula bones

interphalangeal joint: articulation between adjacent phalanx bones of the hand or foot digits

intertrochanteric crest: short, prominent ridge running between the greater and lesser trochanters on the posterior side of the proximal femur

intertrochanteric line: small ridge running between the greater and lesser trochanters on the anterior side of the proximal femur

intertubercular groove (sulcus): bicipital groove; narrow groove located between the greater and lesser tubercles of the humerus

ischial ramus: bony extension projecting anteriorly and superiorly from the ischial tuberosity; joins with the inferior pubic ramus to form the ischiopubic ramus

ischial spine: pointed, bony projection from the posterior margin of the ischium that separates the greater sciatic notch and lesser sciatic notch

ischial tuberosity: large, roughened protuberance that forms the posteroinferior portion of the hip bone; weight-bearing region of the pelvis when sitting

ischiopubic ramus: narrow extension of bone that connects the ischial tuberosity to the pubic body; formed by the junction of the ischial ramus and inferior pubic ramus

ischium: posteroinferior portion of the hip bone

knee joint: joint that separates the thigh and leg portions of the lower limb; formed by the articulations between the medial and lateral condyles of the femur, and the medial and lateral condyles of the tibia

lateral border of the scapula: diagonally oriented lateral margin of the scapula

lateral condyle of the femur: smooth, articulating surface that forms the distal and posterior sides of the lateral expansion of the distal femur

lateral condyle of the tibia: lateral, expanded region of the proximal tibia that includes the smooth surface that articulates with the lateral condyle of the femur as part of the knee joint

lateral cuneiform: most lateral of the three cuneiform tarsal bones; articulates posteriorly with the navicular bone, medially with the intermediate cuneiform bone, laterally with the cuboid bone, and anteriorly with the third metatarsal bone

lateral epicondyle of the femur: roughened area of the femur located on the lateral side of the lateral condyle

lateral epicondyle of the humerus: small projection located on the lateral side of the distal humerus

lateral malleolus: expanded distal end of the fibula

lateral supracondylar ridge: narrow, bony ridge located along the lateral side of the distal humerus, superior to the lateral epicondyle

leg: portion of the lower limb located between the knee and ankle joints

lesser pelvis: (also, lesser pelvic cavity or true pelvis) narrow space located within the pelvis, defined superiorly by the pelvic brim (pelvic inlet) and inferiorly by the pelvic outlet

lesser sciatic foramen: pelvic opening formed by the lesser sciatic notch of the hip bone, the sacrospinous ligament, and the sacrotuberous ligament

lesser sciatic notch: shallow indentation along the posterior margin of the ischium, inferior to the ischial spine

lesser trochanter: small, bony projection on the medial side of the proximal femur, at the base of the femoral neck

lesser tubercle: small, bony prominence located on anterior side of the proximal humerus

ligament of the head of the femur: ligament that spans the acetabulum of the hip bone and the fovea capitis of the femoral head

limb bud: small elevation that appears on the lateral side of the embryo during the fourth or fifth week of development, which gives rise to an upper or lower limb

linea aspera: longitudinally running bony ridge located in the middle third of the posterior femur

lunate: from the lateral side, the second of the four proximal carpal bones; articulates with the radius proximally, the capitate and hamate distally, the scaphoid laterally, and the triquetrum medially

medial border of the scapula: elongated, medial margin of the scapula

medial condyle of the femur: smooth, articulating surface that forms the distal and posterior sides of the medial expansion of the distal femur

medial condyle of the tibia: medial, expanded region of the proximal tibia that includes the smooth surface that articulates with the medial condyle of the femur as part of the knee joint

medial cuneiform: most medial of the three cuneiform tarsal bones; articulates posteriorly with the navicular bone, laterally with the intermediate cuneiform bone, and anteriorly with the first and second metatarsal bones

medial epicondyle of the femur: roughened area of the distal femur located on the medial side of the medial condyle

medial epicondyle of the humerus: enlarged projection located on the medial side of the distal humerus

medial malleolus: bony expansion located on the medial side of the distal tibia

metacarpal bone: one of the five long bones that form the palm of the hand; numbered 1–5, starting on the lateral (thumb) side of the hand

metacarpophalangeal joint: articulation between the distal end of a metacarpal bone of the hand and a proximal phalanx bone of the thumb or a finger

metatarsal bone: one of the five elongated bones that forms the anterior half of the foot; numbered 1–5, starting on the medial side of the foot

metatarsophalangeal joint: articulation between a metatarsal bone of the foot and the proximal phalanx bone of a toe

midcarpal joint: articulation between the proximal and distal rows of the carpal bones; contributes to movements of the hand at the wrist

navicular: tarsal bone that articulates posteriorly with the talus bone, laterally with the cuboid bone, and anteriorly with the medial, intermediate, and lateral cuneiform bones

neck of the femur: narrowed region located inferior to the head of the femur

neck of the radius: narrowed region immediately distal to the head of the radius

obturator foramen: large opening located in the anterior hip bone, between the pubis and ischium regions

olecranon fossa: large depression located on the posterior side of the distal humerus; this space receives the olecranon process of the ulna when the elbow is fully extended

olecranon process: expanded posterior and superior portions of the proximal ulna; forms the bony tip of the elbow

patella: kneecap; the largest sesamoid bone of the body; articulates with the distal femur

patellar surface: smooth groove located on the anterior side of the distal femur, between the medial and lateral condyles; site of articulation for the patella

pectineal line: narrow ridge located on the superior surface of the superior pubic ramus

pectoral girdle: shoulder girdle; the set of bones, consisting of the scapula and clavicle, which attaches each upper limb to the axial skeleton

pelvic brim: pelvic inlet; the dividing line between the greater and lesser pelvic regions; formed by the superior margin of the pubic symphysis, the pectineal lines of each pubis, the arcuate lines of each ilium, and the sacral promontory

pelvic girdle: hip girdle; consists of a single hip bone, which attaches a lower limb to the sacrum of the axial skeleton

pelvic inlet: pelvic brim

pelvic outlet: inferior opening of the lesser pelvis; formed by the inferior margin of the pubic symphysis, right and left ischiopubic rami and sacrotuberous ligaments, and the tip of the coccyx

pelvis: ring of bone consisting of the right and left hip bones, the sacrum, and the coccyx

phalanx bone of the foot: (plural = phalanges) one of the 14 bones that form the toes; these include the proximal and distal phalanges of the big toe, and the proximal, middle, and distal phalanx bones of toes two through five

phalanx bone of the hand: (plural = phalanges) one of the 14 bones that form the thumb and fingers; these include the proximal and distal phalanges of the thumb, and the proximal, middle, and distal phalanx bones of the fingers two through five

pisiform: from the lateral side, the fourth of the four proximal carpal bones; articulates with the anterior surface of the triquetrum

pollex: (also, thumb) digit 1 of the hand

posterior inferior iliac spine: small, bony projection located at the inferior margin of the auricular surface on the posterior ilium

posterior sacroiliac ligament: strong ligament spanning the sacrum and ilium of the hip bone that supports the posterior side of the sacroiliac joint

posterior superior iliac spine: rounded, posterior end of the iliac crest

proximal radioulnar joint: articulation formed by the radial notch of the ulna and the head of the radius

proximal tibiofibular joint: articulation between the head of the fibula and the inferior aspect of the lateral condyle of the tibia

pubic arch: bony structure formed by the pubic symphysis, and the bodies and inferior pubic rami of the right and left pubic bones

pubic body: enlarged, medial portion of the pubis region of the hip bone

pubic symphysis: joint formed by the articulation between the pubic bodies of the right and left hip bones

pubic tubercle: small bump located on the superior aspect of the pubic body

pubis: anterior portion of the hip bone

radial fossa: small depression located on the anterior humerus above the capitulum; this space receives the head of the radius when the elbow is maximally flexed

radial notch of the ulna: small, smooth area on the lateral side of the proximal ulna; articulates with the head of the radius as part of the proximal radioulnar joint

radial tuberosity: oval-shaped, roughened protuberance located on the medial side of the proximal radius

radiocarpal joint: wrist joint, located between the forearm and hand regions of the upper limb; articulation formed proximally by the distal end of the radius and the fibrocartilaginous pad that unites the distal radius and ulna bone, and distally by the scaphoid, lunate, and triquetrum carpal bones

radius: bone located on the lateral side of the forearm

sacroiliac joint: joint formed by the articulation between the auricular surfaces of the sacrum and ilium

sacrospinous ligament: ligament that spans the sacrum to the ischial spine of the hip bone

sacrotuberous ligament: ligament that spans the sacrum to the ischial tuberosity of the hip bone

scaphoid: from the lateral side, the first of the four proximal carpal bones; articulates with the radius proximally, the trapezoid, trapezium, and captitate distally, and the lunate medially

scapula: shoulder blade bone located on the posterior side of the shoulder

shaft of the femur: cylindrically shaped region that forms the central portion of the femur

shaft of the fibula: elongated, slender portion located between the expanded ends of the fibula

shaft of the humerus: narrow, elongated, central region of the humerus

shaft of the radius: narrow, elongated, central region of the radius

shaft of the tibia: triangular-shaped, central portion of the tibia

shaft of the ulna: narrow, elongated, central region of the ulna

soleal line: small, diagonally running ridge located on the posterior side of the proximal tibia

spine of the scapula: prominent ridge passing mediolaterally across the upper portion of the posterior scapular surface

sternal end of the clavicle: medial end of the clavicle that articulates with the manubrium of the sternum

sternoclavicular joint: articulation between the manubrium of the sternum and the sternal end of the clavicle; forms the only bony attachment between the pectoral girdle of the upper limb and the axial skeleton

styloid process of the radius: pointed projection located on the lateral end of the distal radius

styloid process of the ulna: short, bony projection located on the medial end of the distal ulna

subpubic angle: inverted V-shape formed by the convergence of the right and left ischiopubic rami; this angle is greater than 80 degrees in females and less than 70 degrees in males

subscapular fossa: broad depression located on the anterior (deep) surface of the scapula

superior angle of the scapula: corner of the scapula between the superior and medial borders of the scapula

superior border of the scapula: superior margin of the scapula

superior pubic ramus: narrow segment of bone that passes laterally from the pubic body to join the ilium

supraglenoid tubercle: small bump located at the superior margin of the glenoid cavity

suprascapular notch: small notch located along the superior border of the scapula, medial to the coracoid process

supraspinous fossa: narrow depression located on the posterior scapula, superior to the spine

surgical neck: region of the humerus where the expanded, proximal end joins with the narrower shaft

sustentaculum tali: bony ledge extending from the medial side of the calcaneus bone

talus: tarsal bone that articulates superiorly with the tibia and fibula at the ankle joint; also articulates inferiorly with the calcaneus bone and anteriorly with the navicular bone

tarsal bone: one of the seven bones that make up the posterior foot; includes the calcaneus, talus, navicular, cuboid, medial cuneiform, intermediate cuneiform, and lateral cuneiform bones

thigh: portion of the lower limb located between the hip and knee joints

tibial tuberosity: elevated area on the anterior surface of the proximal tibia

tibia: shin bone; the large, weight-bearing bone located on the medial side of the leg

trapezium: from the lateral side, the first of the four distal carpal bones; articulates with the scaphoid proximally, the first and second metacarpals distally, and the trapezoid medially

trapezoid: from the lateral side, the second of the four distal carpal bones; articulates with the scaphoid proximally, the second metacarpal distally, the trapezium laterally, and the capitate medially

triquetrum: from the lateral side, the third of the four proximal carpal bones; articulates with the lunate laterally, the hamate distally, and has a facet for the pisiform

trochlear notch: large, C-shaped depression located on the anterior side of the proximal ulna; articulates at the elbow with the trochlea of the humerus

trochlea: pulley-shaped region located medially at the distal end of the humerus; articulates at the elbow with the trochlear notch of the ulna

ulnar notch of the radius: shallow, smooth area located on the medial side of the distal radius; articulates with the head of the ulna at the distal radioulnar joint

ulnar tuberosity: roughened area located on the anterior, proximal ulna inferior to the coronoid process

ulna: bone located on the medial side of the forearm

PRACTICE TEST: THE APPENDICULAR SYSTEM

Review the material from this module by completing the practice in course online.

MODULE 10: JOINTS

INTRODUCTION TO JOINTS

Learning Objectives

- Discuss both functional and structural classifications for body joints
- Describe the characteristic features for fibrous, cartilaginous, and synovial joints and give examples of each
- Define and identify the different body movements
- Discuss the structure of specific body joints and the movements allowed by each
- Explain the development of body joints

The adult human body has 206 bones, and with the exception of the hyoid bone in the neck, each bone is connected to at least one other bone. Joints are the location where bones come together. Many joints allow for movement between the bones. At these joints, the articulating surfaces of the adjacent bones can move smoothly against each other. However, the bones of other joints may be joined to each other by connective tissue or cartilage. These joints are designed for stability and provide for little or no movement.

Joint stability and movement are related to each other. This means that stable joints allow for little or no mobility between the adjacent bones. Conversely, joints that provide the most movement between bones are the least stable. Understanding the relationship between joint structure and function will help to explain why particular types of joints are found in certain areas of the body.

Figure 1. Girl Kayaking. *Without joints, body movements would be impossible. (credit: Graham Richardson/flickr.com)*

The articulating surfaces of bones at stable types of joints, with little or no mobility, are strongly united to each other. For example, most of the joints of the skull are held together by fibrous connective tissue and do not allow for movement between the adjacent bones. This lack of mobility is important, because the skull bones serve to protect the brain.

Similarly, other joints united by fibrous connective tissue allow for very little movement, which provides stability and weight-bearing support for the body. For example, the tibia and fibula of the leg are tightly united to give stability to the body when standing. At other joints, the bones are held together by cartilage, which permits limited movements between the bones. Thus, the joints of the vertebral column only allow for small movements between

adjacent vertebrae, but when added together, these movements provide the flexibility that allows your body to twist, or bend to the front, back, or side.

In contrast, at joints that allow for wide ranges of motion, the articulating surfaces of the bones are not directly united to each other. Instead, these surfaces are enclosed within a space filled with lubricating fluid, which allows the bones to move smoothly against each other. These joints provide greater mobility, but since the bones are free to move in relation to each other, the joint is less stable. Most of the joints between the bones of the appendicular skeleton are this freely moveable type of joint. These joints allow the muscles of the body to pull on a bone and thereby produce movement of that body region. Your ability to kick a soccer ball, pick up a fork, and dance the tango depend on mobility at these types of joints.

CLASSIFICATION OF JOINTS

Learning Objectives

- Distinguish between the functional and structural classifications for joints
- Describe the three functional types of joints and give an example of each
- List the three types of diarthrodial joints

A **joint**, also called an **articulation**, is any place where adjacent bones or bone and cartilage come together (articulate with each other) to form a connection. Joints are classified both structurally and functionally. Structural classifications of joints take into account whether the adjacent bones are strongly anchored to each other by fibrous connective tissue or cartilage, or whether the adjacent bones articulate with each other within a fluid-filled space called a **joint cavity**. Functional classifications describe the degree of movement available between the bones, ranging from immobile, to slightly mobile, to freely moveable joints. The amount of movement available at a particular joint of the body is related to the functional requirements for that joint. Thus immobile or slightly moveable joints serve to protect internal organs, give stability to the body, and allow for limited body movement. In contrast, freely moveable joints allow for much more extensive movements of the body and limbs.

Structural Classification of Joints

The structural classification of joints is based on whether the articulating surfaces of the adjacent bones are directly connected by fibrous connective tissue or cartilage, or whether the articulating surfaces contact each other within a fluid-filled joint cavity. These differences serve to divide the joints of the body into three structural classifications. A **fibrous joint** is where the adjacent bones are united by fibrous connective tissue. At a **cartilaginous joint**, the bones are joined by hyaline cartilage or fibrocartilage. At a **synovial joint**, the articulating surfaces of the bones are not directly connected, but instead come into contact with each other within a joint cavity that is filled with a lubricating fluid. Synovial joints allow for free movement between the bones and are the most common joints of the body.

Functional Classification of Joints

The functional classification of joints is determined by the amount of mobility found between the adjacent bones. Joints are thus functionally classified as a synarthrosis or immobile joint, an amphiarthrosis or slightly moveable joint, or as a diarthrosis, which is a freely moveable joint (arthroun = “to fasten by a joint”). Depending on their

location, fibrous joints may be functionally classified as a synarthrosis (immobile joint) or an amphiarthrosis (slightly mobile joint). Cartilaginous joints are also functionally classified as either a synarthrosis or an amphiarthrosis joint. All synovial joints are functionally classified as a diarthrosis joint.

Synarthrosis

An immobile or nearly immobile joint is called a **synarthrosis**. The immobile nature of these joints provide for a strong union between the articulating bones. This is important at locations where the bones provide protection for internal organs. Examples include sutures, the fibrous joints between the bones of the skull that surround and protect the brain (Figure 1), and the manubriosternal joint, the cartilaginous joint that unites the manubrium and body of the sternum for protection of the heart.

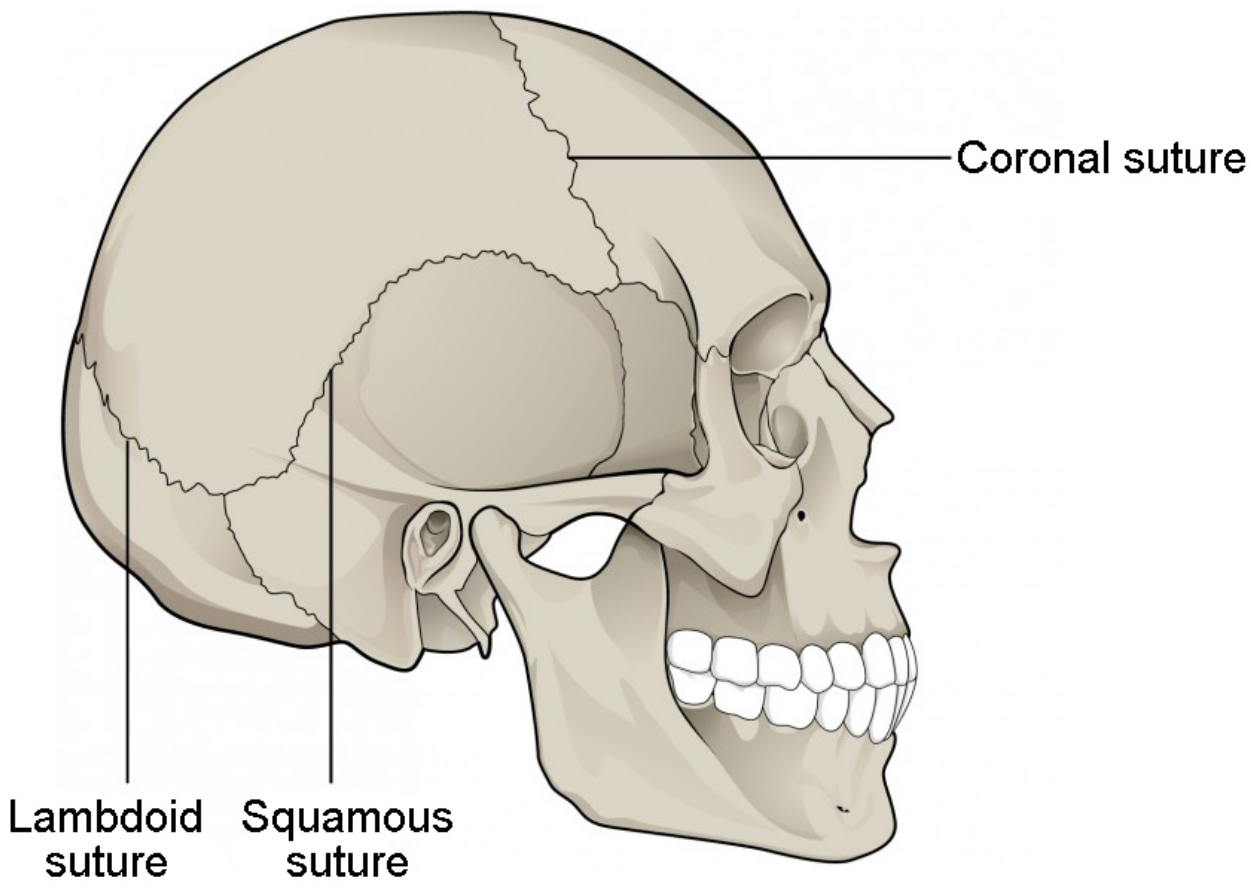


Figure 1. Suture Joints of Skull. *The suture joints of the skull are an example of a synarthrosis, an immobile or essentially immobile joint.*

Amphiarthrosis

An **amphiarthrosis** is a joint that has limited mobility. An example of this type of joint is the cartilaginous joint that unites the bodies of adjacent vertebrae. Filling the gap between the vertebrae is a thick pad of fibrocartilage called an intervertebral disc (Figure 2). Each intervertebral disc strongly unites the vertebrae but still allows for a limited amount of movement between them. However, the small movements available between adjacent vertebrae can sum together along the length of the vertebral column to provide for large ranges of body movements.

Another example of an amphiarthrosis is the pubic symphysis of the pelvis. This is a cartilaginous joint in which the pubic regions of the right and left hip bones are strongly anchored to each other by fibrocartilage. This joint normally has very little mobility. The strength of the pubic symphysis is important in conferring weight-bearing stability to the pelvis.

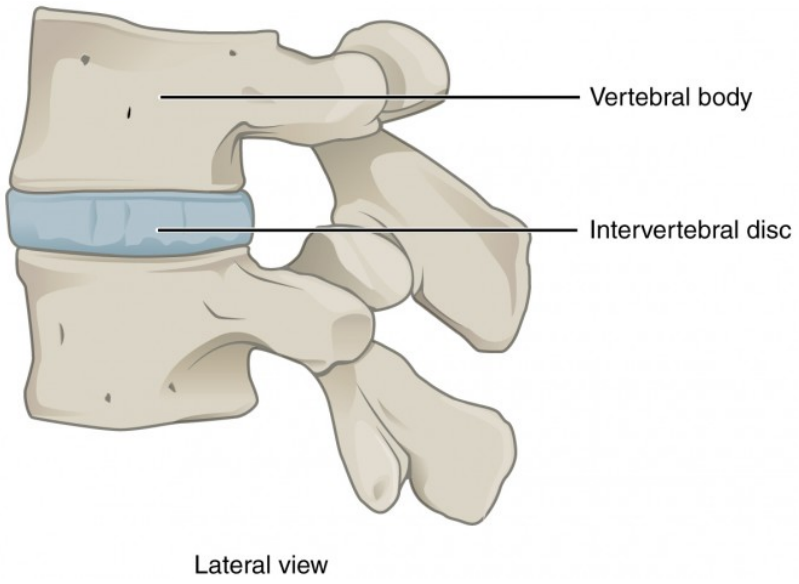


Figure 2. Intervertebral Disc. *An intervertebral disc unites the bodies of adjacent vertebrae within the vertebral column. Each disc allows for limited movement between the vertebrae and thus functionally forms an amphiarthrosis type of joint. Intervertebral discs are made of fibrocartilage and thereby structurally form a symphysis type of cartilaginous joint.*

Diarthrosis

A freely mobile joint is classified as a **diarthrosis**. These types of joints include all synovial joints of the body, which provide the majority of body movements. Most diarthrotic joints are found in the appendicular skeleton and thus give the limbs a wide range of motion. These joints are divided into three categories, based on the number of axes of motion provided by each. An axis in anatomy is described as the movements in reference to the three anatomical planes: transverse, frontal, and sagittal. Thus, diarthroses are classified as uniaxial (for movement in one plane), biaxial (for movement in two planes), or multiaxial joints (for movement in all three anatomical planes).

A **uniaxial joint** only allows for a motion in a single plane (around a single axis). The elbow joint, which only allows for bending or straightening, is an example of a uniaxial joint. A **biaxial joint** allows for motions within two planes. An example of a biaxial joint is a metacarpophalangeal joint (knuckle joint) of the hand. The joint allows for movement along one axis to produce bending or straightening of the finger, and movement along a second axis, which allows for spreading of the fingers away from each other and bringing them together. A joint that allows for the several directions of movement is called a **multiaxial joint** (polyaxial or triaxial joint). This type of diarthrotic joint allows for movement along three axes (Figure 3). The shoulder and hip joints are multiaxial joints. They allow the upper or lower limb to move in an anterior-posterior direction and a medial-lateral direction. In addition, the limb can also be rotated around its long axis. This third movement results in rotation of the limb so that its anterior surface is moved either toward or away from the midline of the body.

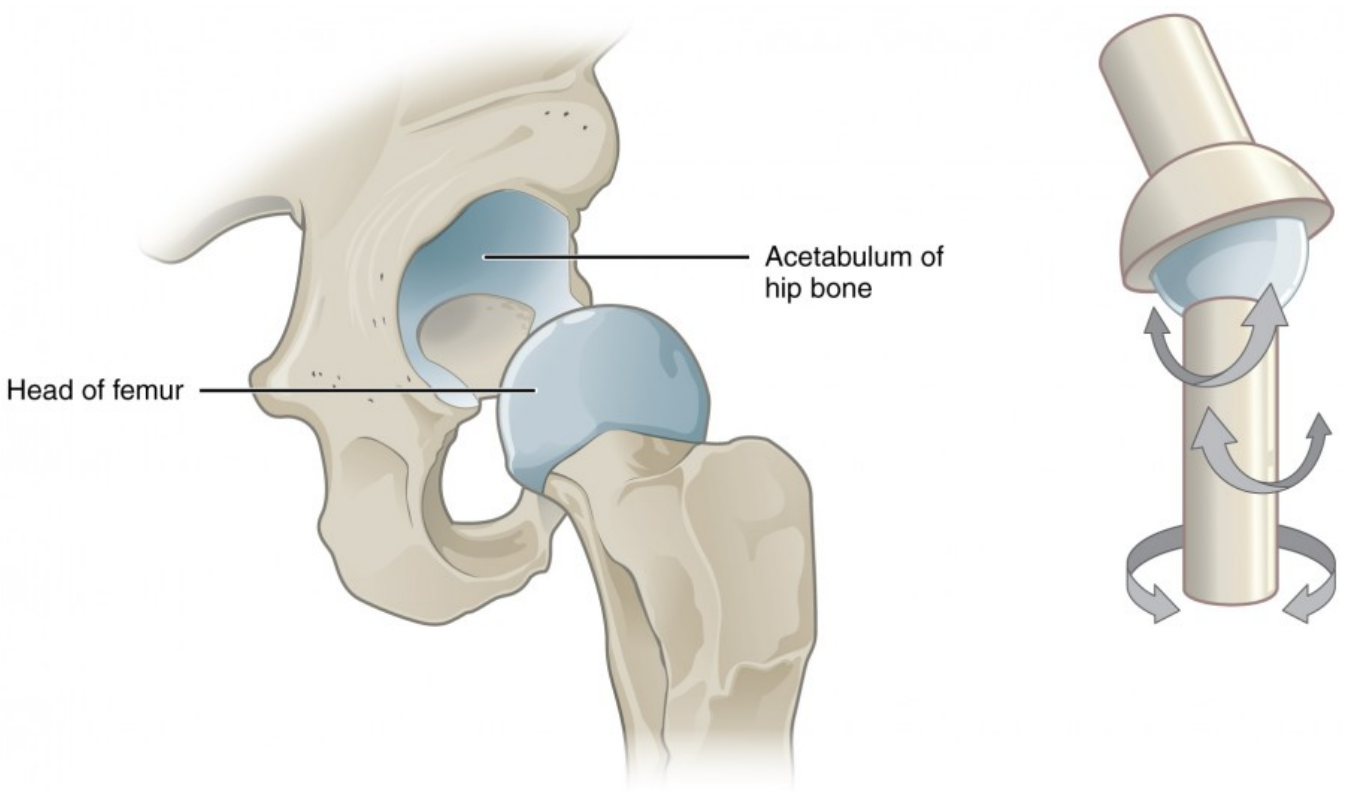


Figure 3. Multiaxial Joint. *A multiaxial joint, such as the hip joint, allows for three types of movement: anterior-posterior, medial-lateral, and rotational.*

Self-Check Questions

Visit your course online to take a quiz to check your understanding of the Classification of Joints:

FIBROUS JOINTS

Learning Objectives

- Describe the structural features of fibrous joints
- Distinguish between a suture, syndesmosis, and gomphosis
- Give an example of each type of fibrous joint

At a fibrous joint, the adjacent bones are directly connected to each other by fibrous connective tissue, and thus the bones do not have a joint cavity between them (Figure 1). The gap between the bones may be narrow or wide. There are three types of fibrous joints. A suture is the narrow fibrous joint found between most bones of the skull. At a syndesmosis joint, the bones are more widely separated but are held together by a narrow band of

fibrous connective tissue called a **ligament** or a wide sheet of connective tissue called an interosseous membrane. This type of fibrous joint is found between the shaft regions of the long bones in the forearm and in the leg. Lastly, a gomphosis is the narrow fibrous joint between the roots of a tooth and the bony socket in the jaw into which the tooth fits.

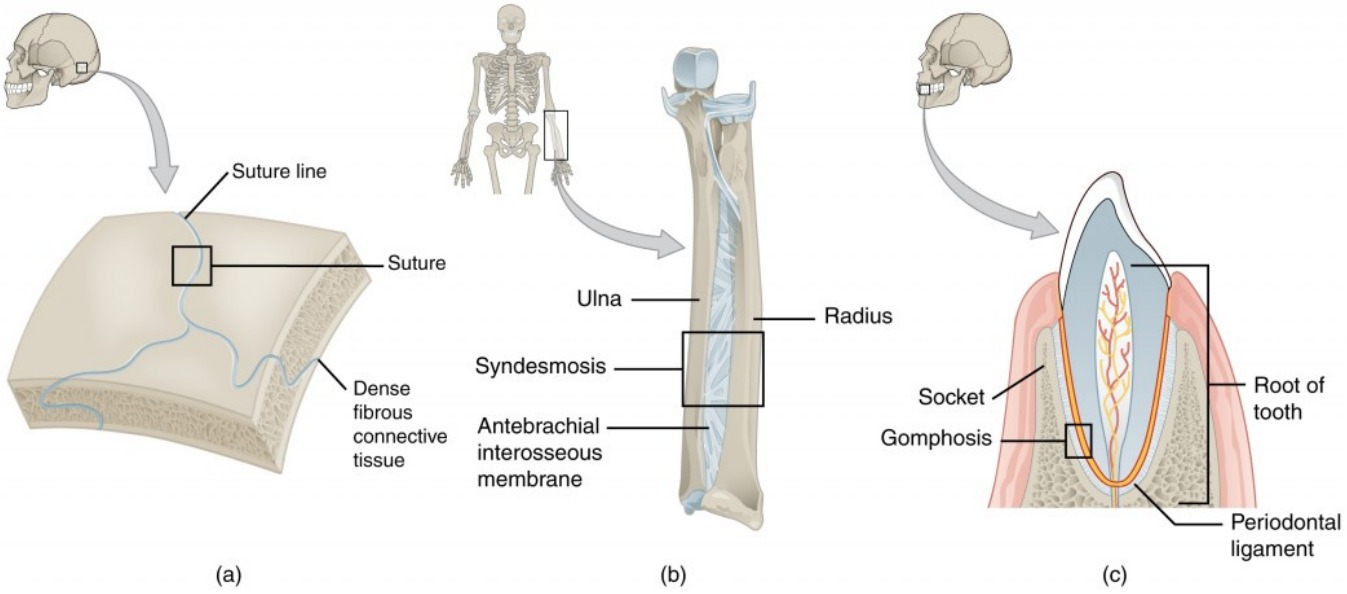


Figure 1. Fibrous Joints. *Fibrous joints form strong connections between bones. (a) Sutures join most bones of the skull. (b) An interosseous membrane forms a syndesmosis between the radius and ulna bones of the forearm. (c) A gomphosis is a specialized fibrous joint that anchors a tooth to its socket in the jaw.*

Suture

All the bones of the skull, except for the mandible, are joined to each other by a fibrous joint called a **suture**. The fibrous connective tissue found at a suture ("to bind or sew") strongly unites the adjacent skull bones and thus helps to protect the brain and form the face. In adults, the skull bones are closely opposed and fibrous connective tissue fills the narrow gap between the bones. The suture is frequently convoluted, forming a tight union that prevents most movement between the bones. (See Figure 1a.) Thus, skull sutures are functionally classified as a synarthrosis, although some sutures may allow for slight movements between the cranial bones.

In newborns and infants, the areas of connective tissue between the bones are much wider, especially in those areas on the top and sides of the skull that will become the sagittal, coronal, squamous, and lambdoid sutures. These broad areas of connective tissue are called **fontanelles** (Figure 2).

During birth, the fontanelles provide flexibility to the skull, allowing the bones to push closer together or to overlap slightly, thus aiding movement of the infant's head through the birth canal. After birth, these expanded regions of connective tissue allow for rapid growth of the skull and enlargement of the brain. The fontanelles greatly decrease in width during the first year after birth as the skull bones enlarge. When the connective tissue between the adjacent bones is

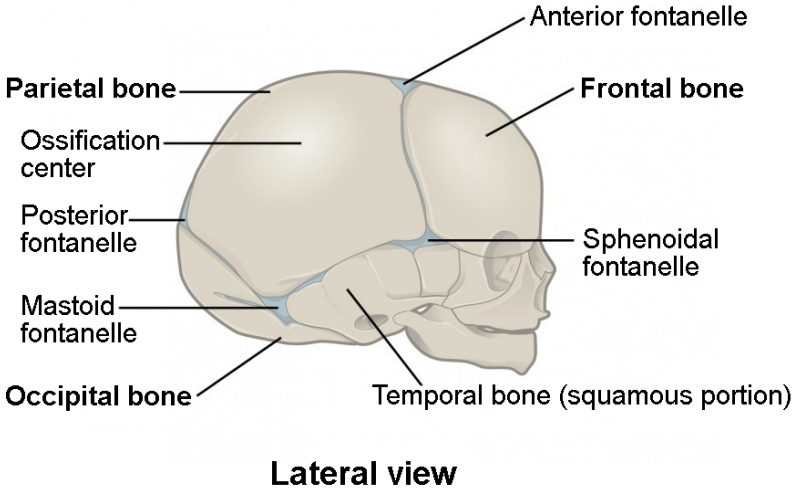


Figure 2. The Newborn Skull. *The fontanelles of a newborn's skull are broad areas of fibrous connective tissue that form fibrous joints between the bones of the skull.*

reduced to a narrow layer, these fibrous joints are now called sutures. At some sutures, the connective tissue will ossify and be converted into bone, causing the adjacent bones to fuse to each other. This fusion between bones is called a **synostosis** ("joined by bone"). Examples of synostosis fusions between cranial bones are found both early and late in life. At the time of birth, the frontal and maxillary bones consist of right and left halves joined together by sutures, which disappear by the eighth year as the halves fuse together to form a single bone. Late in life, the sagittal, coronal, and lambdoid sutures of the skull will begin to ossify and fuse, causing the suture line to gradually disappear.

Syndesmosis

A **syndesmosis** ("fastened with a band") is a type of fibrous joint in which two parallel bones are united to each other by fibrous connective tissue. The gap between the bones may be narrow, with the bones joined by ligaments, or the gap may be wide and filled in by a broad sheet of connective tissue called an **interosseous membrane**.

In the forearm, the wide gap between the shaft portions of the radius and ulna bones are strongly united by an interosseous membrane (see Figure 1b). Similarly, in the leg, the shafts of the tibia and fibula are also united by an interosseous membrane. In addition, at the distal tibiofibular joint, the articulating surfaces of the bones lack cartilage and the narrow gap between the bones is anchored by fibrous connective tissue and ligaments on both the anterior and posterior aspects of the joint. Together, the interosseous membrane and these ligaments form the tibiofibular syndesmosis.

The syndesmoses found in the forearm and leg serve to unite parallel bones and prevent their separation. However, a syndesmosis does not prevent all movement between the bones, and thus this type of fibrous joint is functionally classified as an amphiarthrosis. In the leg, the syndesmosis between the tibia and fibula strongly unites the bones, allows for little movement, and firmly locks the talus bone in place between the tibia and fibula at the ankle joint. This provides strength and stability to the leg and ankle, which are important during weight bearing. In the forearm, the interosseous membrane is flexible enough to allow for rotation of the radius bone during forearm movements. Thus in contrast to the stability provided by the tibiofibular syndesmosis, the flexibility of the antebrachial interosseous membrane allows for the much greater mobility of the forearm.

The interosseous membranes of the leg and forearm also provide areas for muscle attachment. Damage to a syndesmotic joint, which usually results from a fracture of the bone with an accompanying tear of the interosseous membrane, will produce pain, loss of stability of the bones, and may damage the muscles attached to the interosseous membrane. If the fracture site is not properly immobilized with a cast or splint, contractile activity by these muscles can cause improper alignment of the broken bones during healing.

Gomphosis

A **gomphosis** ("fastened with bolts") is the specialized fibrous joint that anchors the root of a tooth into its bony socket within the maxillary bone (upper jaw) or mandible bone (lower jaw) of the skull. A gomphosis is also known as a peg-and-socket joint. Spanning between the bony walls of the socket and the root of the tooth are numerous short bands of dense connective tissue, each of which is called a **periodontal ligament** (see Figure 1c). Due to the immobility of a gomphosis, this type of joint is functionally classified as a synarthrosis.

Self-Check Questions

Visit your course online to take a quiz to check your understanding of Fibrous Joints:

CARTILAGINOUS JOINTS

Learning Objectives

- Describe the structural features of cartilaginous joints
- Distinguish between a synchondrosis and symphysis
- Give an example of each type of cartilaginous joint

As the name indicates, at a cartilaginous joint, the adjacent bones are united by cartilage, a tough but flexible type of connective tissue. These types of joints lack a joint cavity and involve bones that are joined together by either hyaline cartilage or fibrocartilage (Figure 1). There are two types of cartilaginous joints. A synchondrosis is a cartilaginous joint where the bones are joined by hyaline cartilage. Also classified as a synchondrosis are places where bone is united to a cartilage structure, such as between the anterior end of a rib and the costal cartilage of the thoracic cage. The second type of cartilaginous joint is a symphysis, where the bones are joined by fibrocartilage.

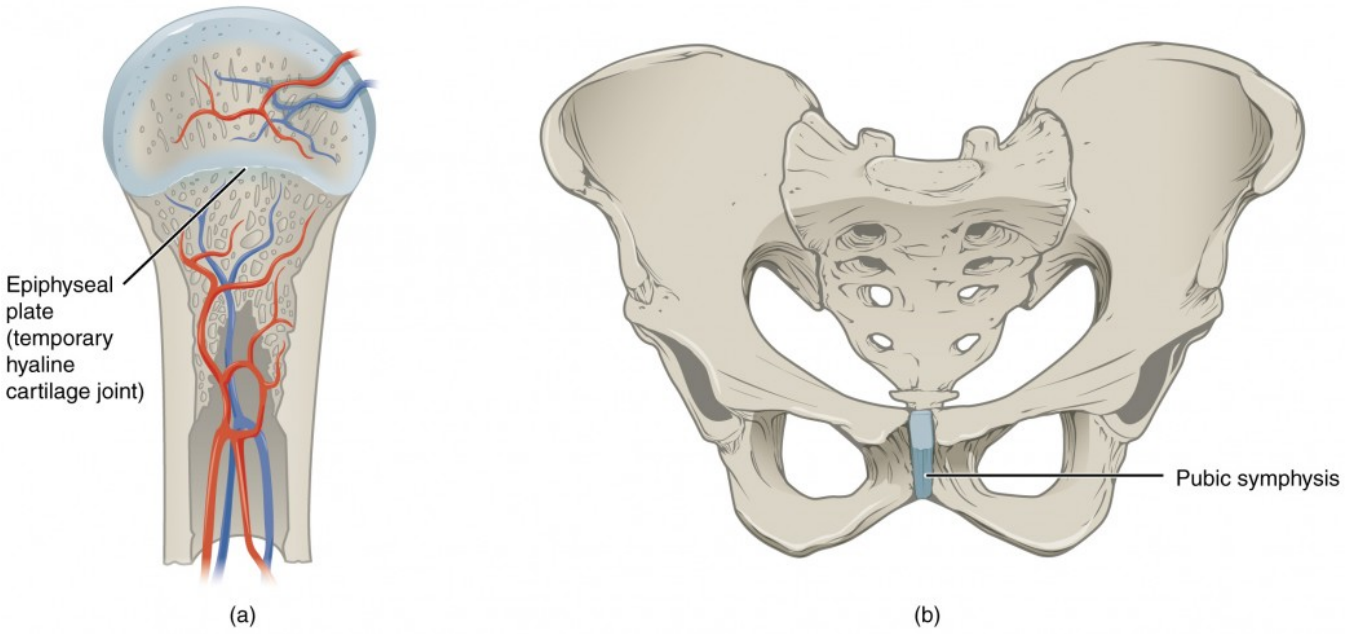


Figure 1. Cartiliginous Joints. *At cartilaginous joints, bones are united by hyaline cartilage to form a synchondrosis or by fibrocartilage to form a symphysis. (a) The hyaline cartilage of the epiphyseal plate (growth plate) forms a synchondrosis that unites the shaft (diaphysis) and end (epiphysis) of a long bone and allows the bone to grow in length. (b) The pubic portions of the right and left hip bones of the pelvis are joined together by fibrocartilage, forming the pubic symphysis.*

Synchondrosis

A **synchondrosis** (“joined by cartilage”) is a cartilaginous joint where bones are joined together by hyaline cartilage, or where bone is united to hyaline cartilage. A synchondrosis may be temporary or permanent. A temporary synchondrosis is the epiphyseal plate (growth plate) of a growing long bone. The epiphyseal plate is the region of growing hyaline cartilage that unites the diaphysis (shaft) of the bone to the epiphysis (end of the bone). Bone lengthening involves growth of the epiphyseal plate cartilage and its replacement by bone, which adds to the diaphysis. For many years during childhood growth, the rates of cartilage growth and bone formation

are equal and thus the epiphyseal plate does not change in overall thickness as the bone lengthens. During the late teens and early 20s, growth of the cartilage slows and eventually stops. The epiphyseal plate is then completely replaced by bone, and the diaphysis and epiphysis portions of the bone fuse together to form a single adult bone. This fusion of the diaphysis and epiphysis is a synostosis. Once this occurs, bone lengthening ceases. For this reason, the epiphyseal plate is considered to be a temporary synchondrosis. Because cartilage is softer than bone tissue, injury to a growing long bone can damage the epiphyseal plate cartilage, thus stopping bone growth and preventing additional bone lengthening.

Growing layers of cartilage also form synchondroses that join together the ilium, ischium, and pubic portions of the hip bone during childhood and adolescence. When body growth stops, the cartilage disappears and is replaced by bone, forming synostoses and fusing the bony components together into the single hip bone of the adult. Similarly, synostoses unite the sacral vertebrae that fuse together to form the adult sacrum.

Visit this website to view a radiograph (X-ray image) of a child's hand and wrist. The growing bones of child have an epiphyseal plate that forms a synchondrosis between the shaft and end of a long bone. Being less dense than bone, the area of epiphyseal cartilage is seen on this radiograph as the dark epiphyseal gaps located near the ends of the long bones, including the radius, ulna, metacarpal, and phalanx bones. Which of the bones in this image do not show an epiphyseal plate (epiphyseal gap)?

Examples of permanent synchondroses are found in the thoracic cage. One example is the first sternocostal joint, where the first rib is anchored to the manubrium by its costal cartilage. (The articulations of the remaining costal cartilages to the sternum are all synovial joints.) Additional synchondroses are formed where the anterior end of the other 11 ribs is joined to its costal cartilage. Unlike the temporary synchondroses of the epiphyseal plate, these permanent synchondroses retain their hyaline cartilage and thus do not ossify with age. Due to the lack of movement between the bone and cartilage, both temporary and permanent synchondroses are functionally classified as a synarthrosis.

Symphysis

A cartilaginous joint where the bones are joined by fibrocartilage is called a **symphysis** ("growing together"). Fibrocartilage is very strong because it contains numerous bundles of thick collagen fibers, thus giving it a much greater ability to resist pulling and bending forces when compared with hyaline cartilage. This gives symphyses the ability to strongly unite the adjacent bones, but can still allow for limited movement to occur. Thus, a symphysis is functionally classified as an amphiarthrosis.

The gap separating the bones at a symphysis may be narrow or wide. Examples in which the gap between the bones is narrow include the pubic symphysis and the manubriosternal joint. At the pubic symphysis, the pubic portions of the right and left hip bones of the pelvis are joined together by fibrocartilage across a narrow gap. Similarly, at the manubriosternal joint, fibrocartilage unites the manubrium and body portions of the sternum.

The intervertebral symphysis is a wide symphysis located between the bodies of adjacent vertebrae of the vertebral column. Here a thick pad of fibrocartilage called an intervertebral disc strongly unites the adjacent vertebrae by filling the gap between them. The width of the intervertebral symphysis is important because it allows for small movements between the adjacent vertebrae. In addition, the thick intervertebral disc provides cushioning between the vertebrae, which is important when carrying heavy objects or during high-impact activities such as running or jumping.

Self-Check Questions

Visit your course online to take a quiz to check your understanding of Cartilaginous Joints:

SYNOVIAL JOINTS

Learning Objectives

- Describe the structural features of a synovial joint
- Discuss the function of additional structures associated with synovial joints
- List the six types of synovial joints and give an example of each

Synovial joints are the most common type of joint in the body (Figure 1). A key structural characteristic for a synovial joint that is not seen at fibrous or cartilaginous joints is the presence of a joint cavity. This fluid-filled space is the site at which the articulating surfaces of the bones contact each other. Also unlike fibrous or cartilaginous joints, the articulating bone surfaces at a synovial joint are not directly connected to each other with fibrous connective tissue or cartilage. This gives the bones of a synovial joint the ability to move smoothly against each other, allowing for increased joint mobility.

Structural Features of Synovial Joints

Synovial joints are characterized by the presence of a joint cavity. The walls of this space are formed by the **articular capsule**, a fibrous connective tissue structure that is attached to each bone just outside the area of the bone's articulating surface. The bones of the joint articulate with each other within the joint cavity.

Friction between the bones at a synovial joint is prevented by the presence of the **articular cartilage**, a thin layer of hyaline cartilage that covers the entire articulating surface of each bone. However, unlike at a cartilaginous joint, the articular cartilages of each bone are not continuous with each other. Instead, the articular cartilage acts like a Teflon® coating over the bone surface, allowing the articulating bones to move smoothly against each other without damaging the underlying bone tissue. Lining the inner surface of the articular capsule is a thin **synovial membrane**. The cells of this membrane secrete **synovial fluid** (synovia = "a thick fluid"), a thick, slimy fluid that provides lubrication to further reduce friction between the bones of the joint. This fluid also provides nourishment to the articular cartilage, which does not contain blood vessels. The ability of the bones to move smoothly against each other within the joint cavity, and the freedom of joint movement this provides, means that each synovial joint is functionally classified as a diarthrosis.

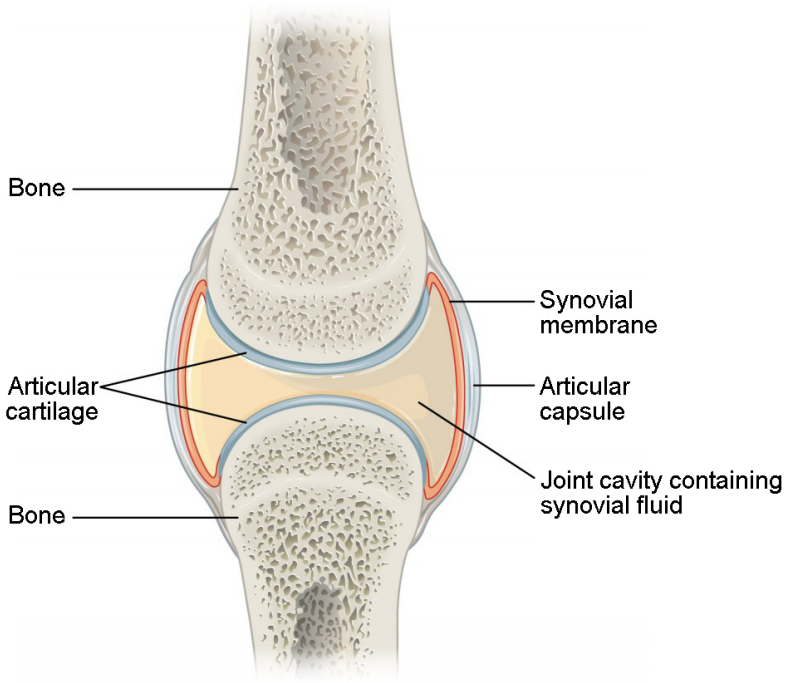


Figure 1. Synovial Joints. *Synovial joints allow for smooth movements between the adjacent bones. The joint is surrounded by an articular capsule that defines a joint cavity filled with synovial fluid. The articulating surfaces of the bones are covered by a thin layer of articular cartilage. Ligaments support the joint by holding the bones together and resisting excess or abnormal joint motions.*

Outside of their articulating surfaces, the bones are connected together by ligaments, which are strong bands of fibrous connective tissue. These strengthen and support the joint by anchoring the bones together and preventing their separation. Ligaments allow for normal movements at a joint, but limit the range of these motions, thus preventing excessive or abnormal joint movements. Ligaments are classified based on their relationship to the fibrous articular capsule. An **extrinsic ligament** is located outside of the articular capsule, an **intrinsic ligament** is fused to or incorporated into the wall of the articular capsule, and an **intracapsular ligament** is located inside of the articular capsule.

At many synovial joints, additional support is provided by the muscles and their tendons that act across the joint. A **tendon** is the dense connective tissue structure that attaches a muscle to bone. As forces acting on a joint increase, the body will automatically increase the overall strength of contraction of the muscles crossing that joint, thus allowing the muscle and its tendon to serve as a "dynamic ligament" to resist forces and support the joint. This type of indirect support by muscles is very important at the shoulder joint, for example, where the ligaments are relatively weak.

Additional Structures Associated with Synovial Joints

A few synovial joints of the body have a fibrocartilage structure located between the articulating bones. This is called an **articular disc**, which is generally small and oval-shaped, or a **meniscus**, which is larger and C-shaped. These structures can serve several functions, depending on the specific joint. In some places, an articular disc may act to strongly unite the bones of the joint to each other. Examples of this include the articular discs found at the sternoclavicular joint or between the distal ends of the radius and ulna bones. At other synovial joints, the disc can provide shock absorption and cushioning between the bones, which is the function of each meniscus within the knee joint. Finally, an articular disc can serve to smooth the movements between the articulating bones, as seen at the temporomandibular joint. Some synovial joints also have a fat pad, which can serve as a cushion between the bones.

Additional structures located outside of a synovial joint serve to prevent friction between the bones of the joint and the overlying muscle tendons or skin. A **bursa** (plural = bursae) is a thin connective tissue sac filled with lubricating liquid. They are located in regions where skin, ligaments, muscles, or muscle tendons can rub against each other, usually near a body joint (Figure 2). Bursae reduce friction by separating the adjacent structures, preventing them from rubbing directly against each other. Bursae are classified by their location. A **subcutaneous bursa** is located between the skin and an underlying bone. It allows skin to move smoothly over the bone. Examples include the prepatellar bursa located over the kneecap and the olecranon bursa at the tip of the elbow. A **submuscular bursa** is found between a muscle and an underlying bone, or between adjacent muscles. These prevent rubbing of the muscle during movements. A large submuscular bursa, the trochanteric bursa, is found at the lateral hip, between the greater trochanter of the femur and the overlying gluteus maximus muscle. A **subtendinous bursa** is found between a tendon and a bone. Examples include the subacromial bursa that protects the tendon of shoulder muscle as it passes under the acromion of the scapula, and the suprapatellar bursa that separates the tendon of the large anterior thigh muscle from the distal femur just above the knee.

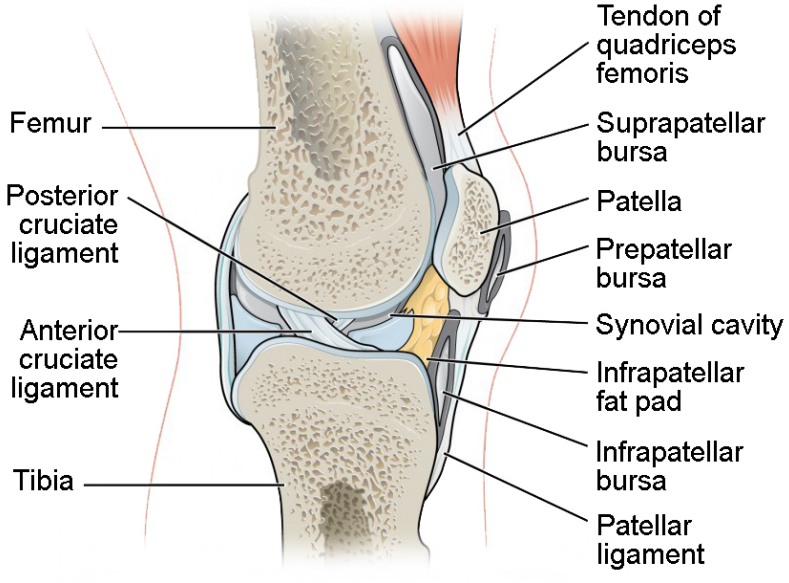


Figure 2. Bursae. *Bursae are fluid-filled sacs that serve to prevent friction between skin, muscle, or tendon and an underlying bone. Three major bursae and a fat pad are part of the complex joint that unites the femur and tibia of the leg.*

A **tendon sheath** is similar in structure to a bursa, but smaller. It is a connective tissue sac that surrounds a muscle tendon at places where the tendon crosses a joint. It contains a lubricating fluid that allows for smooth motions of the tendon during muscle contraction and joint movements.

Homeostatic Imbalances: Bursitis

Bursitis is the inflammation of a bursa near a joint. This will cause pain, swelling, or tenderness of the bursa and surrounding area, and may also result in joint stiffness. Bursitis is most commonly associated with the bursae found at or near the shoulder, hip, knee, or elbow joints. At the shoulder, subacromial bursitis may occur in the bursa that separates the acromion of the scapula from the tendon of a shoulder muscle as it passes deep to the acromion. In the hip region, trochanteric bursitis can occur in the bursa that overlies the greater trochanter of the femur, just below the lateral side of the hip. Ischial bursitis occurs in the bursa that separates the skin from the ischial tuberosity of the pelvis, the bony structure that is weight bearing when sitting. At the knee, inflammation and swelling of the bursa located between the skin and patella bone is prepatellar bursitis ("housemaid's knee"), a condition more commonly seen today in roofers or floor and carpet installers who do not use knee pads. At the elbow, olecranon bursitis is inflammation of the bursa between the skin and olecranon process of the ulna. The olecranon forms the bony tip of the elbow, and bursitis here is also known as "student's elbow."

Bursitis can be either acute (lasting only a few days) or chronic. It can arise from muscle overuse, trauma, excessive or prolonged pressure on the skin, rheumatoid arthritis, gout, or infection of the joint. Repeated acute episodes of bursitis can result in a chronic condition. Treatments for the disorder include antibiotics if the bursitis is caused by an infection, or anti-inflammatory agents, such as nonsteroidal anti-inflammatory drugs (NSAIDs) or corticosteroids if the bursitis is due to trauma or overuse. Chronic bursitis may require that fluid be drained, but additional surgery is usually not required.

Types of Synovial Joints

Synovial joints are subdivided based on the shapes of the articulating surfaces of the bones that form each joint. The six types of synovial joints are pivot, hinge, condyloid, saddle, plane, and ball-and socket-joints (Figure 3).

Pivot Joint

At a **pivot joint**, a rounded portion of a bone is enclosed within a ring formed partially by the articulation with another bone and partially by a ligament (see Figure 3a). The bone rotates within this ring. Since the rotation is around a single axis, pivot joints are functionally classified as a uniaxial diarthrosis type of joint. An example of a pivot joint is the atlantoaxial joint, found between the C1 (atlas) and C2 (axis) vertebrae. Here, the upward projecting dens of the axis articulates with the inner aspect of the atlas, where it is held in place by a ligament. Rotation at this joint allows you to turn your head from side to side. A second pivot joint is found at the **proximal radioulnar joint**. Here, the head of the radius is largely encircled by a ligament that holds it in place as it articulates with the radial notch of the ulna. Rotation of the radius allows for forearm movements.

Hinge Joint

In a **hinge joint**, the convex end of one bone articulates with the concave end of the adjoining bone (see Figure 3b). This type of joint allows only for bending and straightening motions along a single axis, and thus hinge joints are functionally classified as uniaxial joints. A good example is the elbow joint, with the articulation between the trochlea of the humerus and the trochlear notch of the ulna. Other hinge joints of the body include the knee, ankle, and interphalangeal joints between the phalanx bones of the fingers and toes.

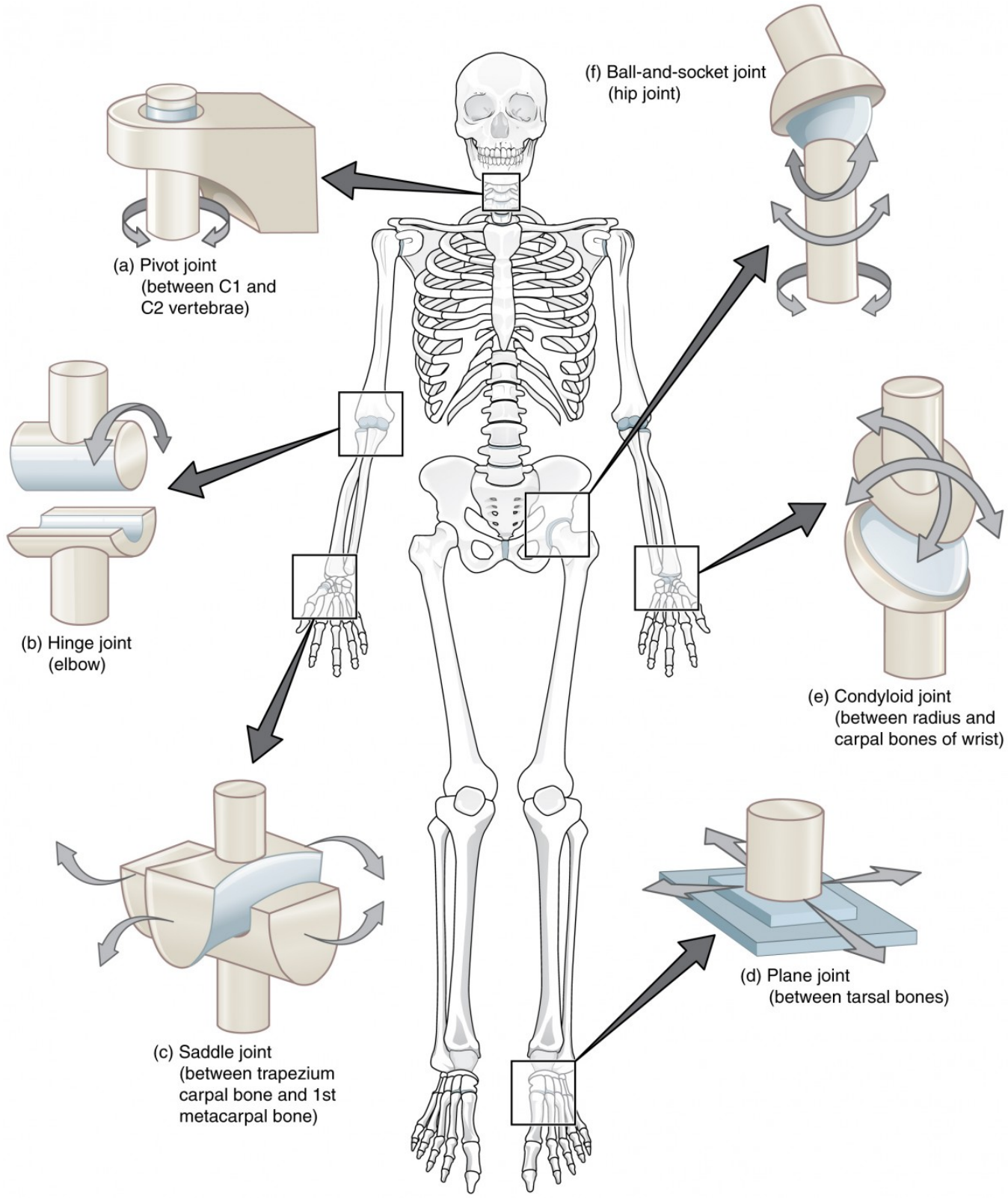


Figure 3. Types of Synovial Joints. *The six types of synovial joints allow the body to move in a variety of ways. (a) Pivot joints allow for rotation around an axis, such as between the first and second cervical vertebrae, which allows for side-to-side rotation of the head. (b) The hinge joint of the elbow works like a door hinge. (c) The articulation between the trapezium carpal bone and the first metacarpal bone at the base of the thumb is a saddle joint. (d) Plane joints, such as those between the tarsal bones of the foot, allow for limited gliding movements between bones. (e) The radiocarpal joint of the wrist is a condyloid joint. (f) The hip and shoulder joints are the only ball-and-socket joints of the body.*

Saddle Joint

At a **saddle joint**, both of the articulating surfaces for the bones have a saddle shape, which is concave in one direction and convex in the other (see Figure 3c). This allows the two bones to fit together like a rider sitting on a saddle. Saddle joints are functionally classified as biaxial joints. The primary example is the first carpometacarpal joint, between the trapezium (a carpal bone) and the first metacarpal bone at the base of the thumb. This joint provides the thumb the ability to move away from the palm of the hand along two planes. Thus, the thumb can move within the same plane as the palm of the hand, or it can jut out anteriorly, perpendicular to the palm. This movement of the first carpometacarpal joint is what gives humans their distinctive “opposable” thumbs. The sternoclavicular joint is also classified as a saddle joint.

Plane Joint

At a **plane joint** (gliding joint), the articulating surfaces of the bones are flat or slightly curved and of approximately the same size, which allows the bones to slide against each other (see Figure 3d). The motion at this type of joint is usually small and tightly constrained by surrounding ligaments. Based only on their shape, plane joints can allow multiple movements, including rotation. Thus plane joints can be functionally classified as a multiaxial joint. However, not all of these movements are available to every plane joint due to limitations placed on it by ligaments or neighboring bones. Thus, depending upon the specific joint of the body, a plane joint may exhibit only a single type of movement or several movements. Plane joints are found between the carpal bones (intercarpal joints) of the wrist or tarsal bones (intertarsal joints) of the foot, between the clavicle and acromion of the scapula (acromioclavicular joint), and between the superior and inferior articular processes of adjacent vertebrae (zygapophysial joints).

Condyloid Joint

At a **condyloid joint** (ellipsoid joint), the shallow depression at the end of one bone articulates with a rounded structure from an adjacent bone or bones (see Figure 3e). The knuckle (metacarpophalangeal) joints of the hand between the distal end of a metacarpal bone and the proximal phalanx bone are condyloid joints. Another example is the radiocarpal joint of the wrist, between the shallow depression at the distal end of the radius bone and the rounded scaphoid, lunate, and triquetrum carpal bones. In this case, the articulation area has a more oval (elliptical) shape. Functionally, condyloid joints are biaxial joints that allow for two planes of movement. One movement involves the bending and straightening of the fingers or the anterior-posterior movements of the hand. The second movement is a side-to-side movement, which allows you to spread your fingers apart and bring them together, or to move your hand in a medial-going or lateral-going direction.

Ball-and-Socket Joint

The joint with the greatest range of motion is the **ball-and-socket joint**. At these joints, the rounded head of one bone (the ball) fits into the concave articulation (the socket) of the adjacent bone (see Figure 3f). The hip joint and the glenohumeral (shoulder) joint are the only ball-and-socket joints of the body. At the hip joint, the head of the femur articulates with the acetabulum of the hip bone, and at the shoulder joint, the head of the humerus articulates with the glenoid cavity of the scapula.

Ball-and-socket joints are classified functionally as multiaxial joints. The femur and the humerus are able to move in both anterior-posterior and medial-lateral directions and they can also rotate around their long axis. The shallow socket formed by the glenoid cavity allows the shoulder joint an extensive range of motion. In contrast, the deep socket of the acetabulum and the strong supporting ligaments of the hip joint serve to constrain movements of the femur, reflecting the need for stability and weight-bearing ability at the hip.

Watch this video to see an animation of synovial joints in action. Synovial joints are places where bones articulate with each other inside of a joint cavity. The different types of synovial joints are the ball-and-socket joint (shoulder joint), hinge joint (knee), pivot joint (atlantoaxial joint, between C1 and C2 vertebrae of the neck), condyloid joint (radiocarpal joint of the wrist), saddle joint (first carpometacarpal joint, between the trapezium carpal bone and the first metacarpal bone, at the base of the thumb), and plane joint (facet joints of

vertebral column, between superior and inferior articular processes). Which type of synovial joint allows for the widest range of motion?

Watch this video online: https://youtu.be/VNbrvU7MgY0

Aging and the Joints

Arthritis is a common disorder of synovial joints that involves inflammation of the joint. This often results in significant joint pain, along with swelling, stiffness, and reduced joint mobility. There are more than 100 different forms of arthritis. Arthritis may arise from aging, damage to the articular cartilage, autoimmune diseases, bacterial or viral infections, or unknown (probably genetic) causes.

The most common type of arthritis is osteoarthritis, which is associated with aging and "wear and tear" of the articular cartilage (Figure 4). Risk factors that may lead to osteoarthritis later in life include injury to a joint; jobs that involve physical labor; sports with running, twisting, or throwing actions; and being overweight. These factors put stress on the articular cartilage that covers the surfaces of bones at synovial joints, causing the cartilage to gradually become thinner. As the articular cartilage layer wears down, more pressure is placed on the bones. The joint responds by increasing production of the lubricating synovial fluid, but this can lead to swelling of the joint cavity, causing pain and joint stiffness as the articular capsule is stretched. The bone tissue underlying the damaged articular cartilage also responds by thickening, producing irregularities and causing the articulating surface of the bone to become rough or bumpy. Joint movement then results in pain and inflammation. In its early stages, symptoms of osteoarthritis may be reduced by mild activity that "warms up" the joint, but the symptoms may worsen following exercise. In individuals with more advanced osteoarthritis, the affected joints can become more painful and therefore are difficult to use effectively, resulting in increased immobility. There is no cure for osteoarthritis, but several treatments can help alleviate the pain. Treatments may include lifestyle changes, such as weight loss and low-impact exercise, and over-the-counter or prescription medications that help to alleviate the pain and inflammation. For severe cases, joint replacement surgery (arthroplasty) may be required.

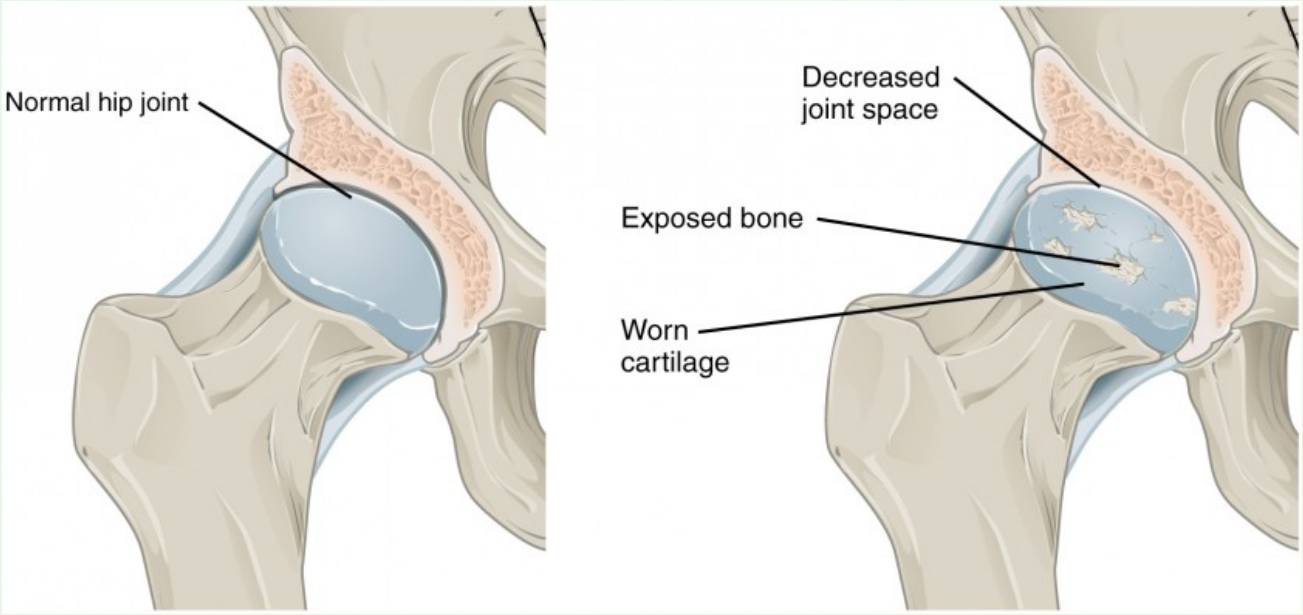


Figure 4. Osteoarthritis. *Osteoarthritis of a synovial joint results from aging or prolonged joint wear and tear. These cause erosion and loss of the articular cartilage covering the surfaces of the bones, resulting in inflammation that causes joint stiffness and pain.*

Joint replacement is a very invasive procedure, so other treatments are always tried before surgery. However arthroplasty can provide relief from chronic pain and can enhance mobility within a few months following the surgery. This type of surgery involves replacing the articular surfaces of the bones with prosthesis (artificial components). For example, in hip arthroplasty, the worn or damaged parts of the hip joint, including the head

and neck of the femur and the acetabulum of the pelvis, are removed and replaced with artificial joint components. The replacement head for the femur consists of a rounded ball attached to the end of a shaft that is inserted inside the diaphysis of the femur. The acetabulum of the pelvis is reshaped and a replacement socket is fitted into its place. The parts, which are always built in advance of the surgery, are sometimes custom made to produce the best possible fit for a patient.

Gout is a form of arthritis that results from the deposition of uric acid crystals within a body joint. Usually only one or a few joints are affected, such as the big toe, knee, or ankle. The attack may only last a few days, but may return to the same or another joint. Gout occurs when the body makes too much uric acid or the kidneys do not properly excrete it. A diet with excessive fructose has been implicated in raising the chances of a susceptible individual developing gout.

Other forms of arthritis are associated with various autoimmune diseases, bacterial infections of the joint, or unknown genetic causes. Autoimmune diseases, including rheumatoid arthritis, scleroderma, or systemic lupus erythematosus, produce arthritis because the immune system of the body attacks the body joints. In rheumatoid arthritis, the joint capsule and synovial membrane become inflamed. As the disease progresses, the articular cartilage is severely damaged or destroyed, resulting in joint deformation, loss of movement, and severe disability. The most commonly involved joints are the hands, feet, and cervical spine, with corresponding joints on both sides of the body usually affected, though not always to the same extent. Rheumatoid arthritis is also associated with lung fibrosis, vasculitis (inflammation of blood vessels), coronary heart disease, and premature mortality. With no known cure, treatments are aimed at alleviating symptoms. Exercise, anti-inflammatory and pain medications, various specific disease-modifying anti-rheumatic drugs, or surgery are used to treat rheumatoid arthritis.

Visit this website to learn about a patient who arrives at the hospital with joint pain and weakness in his legs. What caused this patient's weakness?

Watch this animation to observe hip replacement surgery (total hip arthroplasty), which can be used to alleviate the pain and loss of joint mobility associated with osteoarthritis of the hip joint. What is the most common cause of hip disability?

Watch this video to learn about the symptoms and treatments for rheumatoid arthritis. Which system of the body malfunctions in rheumatoid arthritis and what does this cause?

Self-Check Questions

Visit your course online to take a quiz to check your understanding of Synovial Joints:

TYPES OF BODY MOVEMENTS

Learning Objectives

- Define the different types of body movements
- Identify the joints that allow for these motions

Synovial joints allow the body a tremendous range of movements. Each movement at a synovial joint results from the contraction or relaxation of the muscles that are attached to the bones on either side of the articulation. The type of movement that can be produced at a synovial joint is determined by its structural type. While the ball-and-socket joint gives the greatest range of movement at an individual joint, in other regions of the body, several joints may work together to produce a particular movement. Overall, each type of synovial joint is necessary to provide the body with its great flexibility and mobility. There are many types of movement that can occur at synovial joints (Table 1). Movement types are generally paired, with one being the opposite of the other. Body movements are always described in relation to the anatomical position of the body: upright stance, with upper limbs to the side of body and palms facing forward.

Watch this video to learn about anatomical motions. What motions involve increasing or decreasing the angle of the foot at the ankle?

Watch this video online: https://youtu.be/5YcNAPzDxDg

Flexion and Extension

Flexion and **extension** are movements that take place within the sagittal plane and involve anterior or posterior movements of the body or limbs. For the vertebral column, flexion (anterior flexion) is an anterior (forward) bending of the neck or body, while extension involves a posterior-directed motion, such as straightening from a flexed position or bending backward. **Lateral flexion** is the bending of the neck or body toward the right or left side. These movements of the vertebral column involve both the symphysis joint formed by each intervertebral disc, as well as the plane type of synovial joint formed between the inferior articular processes of one vertebra and the superior articular processes of the next lower vertebra.

In the limbs, flexion decreases the angle between the bones (bending of the joint), while extension increases the angle and straightens the joint. For the upper limb, all anterior-going motions are flexion and all posterior-going motions are extension. These include anterior-posterior movements of the arm at the shoulder, the forearm at the elbow, the hand at the wrist, and the fingers at the metacarpophalangeal and interphalangeal joints. For the thumb, extension moves the thumb away from the palm of the hand, within the same plane as the palm, while flexion brings the thumb back against the index finger or into the palm. These motions take place at the first carpometacarpal joint. In the lower limb, bringing the thigh forward and upward is flexion at the hip joint, while any posterior-going motion of the thigh is extension. Note that extension of the thigh beyond the anatomical (standing) position is greatly limited by the ligaments that support the hip joint. Knee flexion is the bending of the knee to bring the foot toward the posterior thigh, and extension is the straightening of the knee. Flexion and extension movements are seen at the hinge, condyloid, saddle, and ball-and-socket joints of the limbs (see Figure 1).

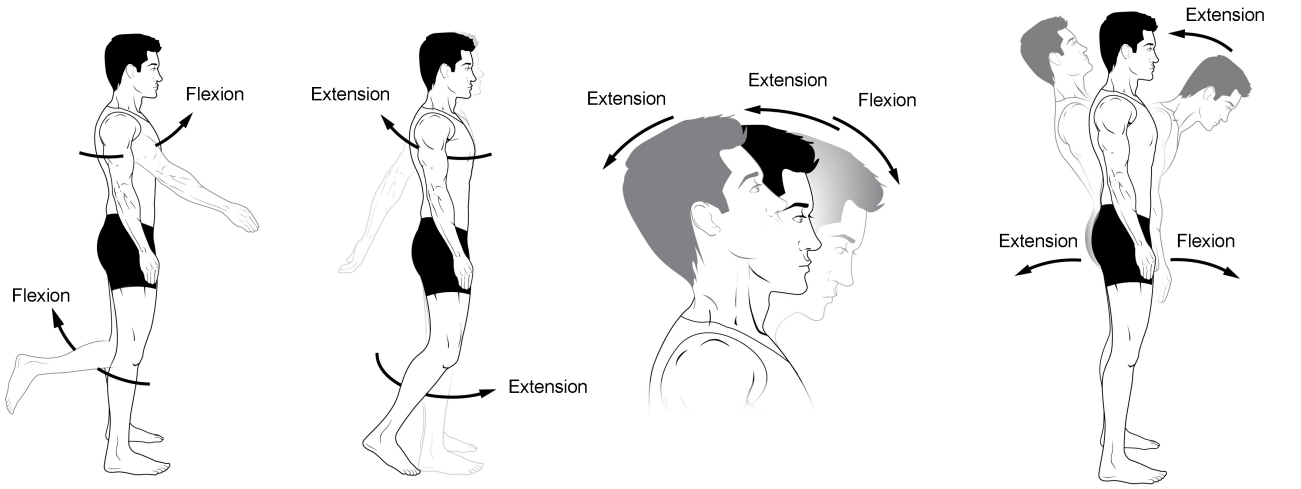


Figure 1. Flexion and extension. *(a)–(b) Flexion and extension motions are in the sagittal (anterior–posterior) plane of motion. These movements take place at the shoulder, hip, elbow, knee, wrist, metacarpophalangeal, metatarsophalangeal, and*

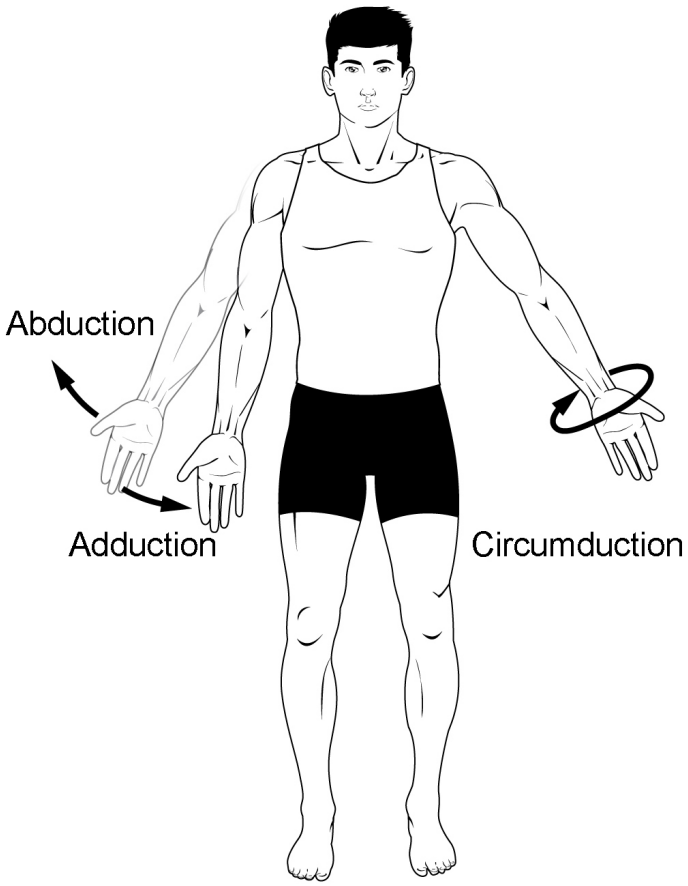
interphalangeal joints. (c)–(d) Anterior bending of the head or vertebral column is flexion, while any posterior-going movement is extension.

Hyperextension is the abnormal or excessive extension of a joint beyond its normal range of motion, thus resulting in injury. Similarly, **hyperflexion** is excessive flexion at a joint. Hyperextension injuries are common at hinge joints such as the knee or elbow. In cases of "whiplash" in which the head is suddenly moved backward and then forward, a patient may experience both hyperextension and hyperflexion of the cervical region.

Abduction, Adduction, and Circumduction

Abduction and adduction are motions of the limbs, hand, fingers, or toes in the coronal (medial–lateral) plane of movement. Moving the limb or hand laterally away from the body, or spreading the fingers or toes, is abduction. Adduction brings the limb or hand toward or across the midline of the body, or brings the fingers or toes together. Circumduction is the movement of the limb, hand, or fingers in a circular pattern, using the sequential combination of flexion, adduction, extension, and abduction motions.

Adduction, abduction, and circumduction take place at the shoulder, hip, wrist, metacarpophalangeal, and metatarsophalangeal joints.



Angular movements: abduction, adduction, and circumduction of the upper limb at the shoulder

Figure 2. Abduction, adduction, and circumduction.

Abduction and Adduction

Abduction and **adduction** motions occur within the coronal plane and involve medial-lateral motions of the limbs, fingers, toes, or thumb. Abduction moves the limb laterally away from the midline of the body, while adduction is the opposing movement that brings the limb toward the body or across the midline. For example, abduction is raising the arm at the shoulder joint, moving it laterally away from the body, while adduction brings the arm down to the side of the body. Similarly, abduction and adduction at the wrist moves the hand away from or toward the midline of the body. Spreading the fingers or toes apart is also abduction, while bringing the fingers or toes together is adduction. For the thumb, abduction is the anterior movement that brings the thumb to a 90° perpendicular position, pointing straight out from the palm. Adduction moves the thumb back to the anatomical position, next to the index finger. Abduction and adduction movements are seen at condyloid, saddle, and ball-and-socket joints (see Figure 2).

Circumduction

Circumduction is the movement of a body region in a circular manner, in which one end of the body region being moved stays relatively stationary while the other end describes a circle. It involves the sequential combination of flexion, adduction, extension, and abduction at a joint. This type of motion is found at biaxial condyloid and saddle joints, and at multiaxial ball-and-sockets joints (see Figure 2).

Rotation

Rotation can occur within the vertebral column, at a pivot joint, or at a ball-and-socket joint. Rotation of the neck or body is the twisting movement produced by the summation of the small rotational movements available between adjacent vertebrae. At a pivot joint, one bone rotates in relation to another bone. This is a uniaxial joint, and thus rotation is the only motion allowed at a pivot joint. For example, at the atlantoaxial joint, the first cervical (C1) vertebra (atlas) rotates around the dens, the upward projection from the second cervical (C2) vertebra (axis). This allows the head to rotate from side to side as when shaking the head "no." The proximal radioulnar joint is a pivot joint formed by the head of the radius and its articulation with the ulna. This joint allows for the radius to rotate along its length during pronation and supination movements of the forearm.

Rotation can also occur at the ball-and-socket joints of the shoulder and hip. Here, the humerus and femur rotate around their long axis, which moves the anterior surface of the arm or thigh either toward or away from the midline of the body. Movement that brings the anterior surface of the limb toward the midline of the body is called **medial (internal) rotation**. Conversely, rotation of the limb so that the anterior surface moves away from the midline is **lateral (external) rotation** (see Figure 3). Be sure to distinguish medial and lateral rotation, which can only occur at the multiaxial shoulder and hip joints, from circumduction, which can occur at either biaxial or multiaxial joints.

Turning of the head side to side or twisting of the body is rotation. Medial and lateral rotation of the upper limb at the shoulder or lower limb at the hip involves turning the anterior surface of the limb toward the midline of the body (medial or internal rotation) or away from the midline (lateral or external rotation).

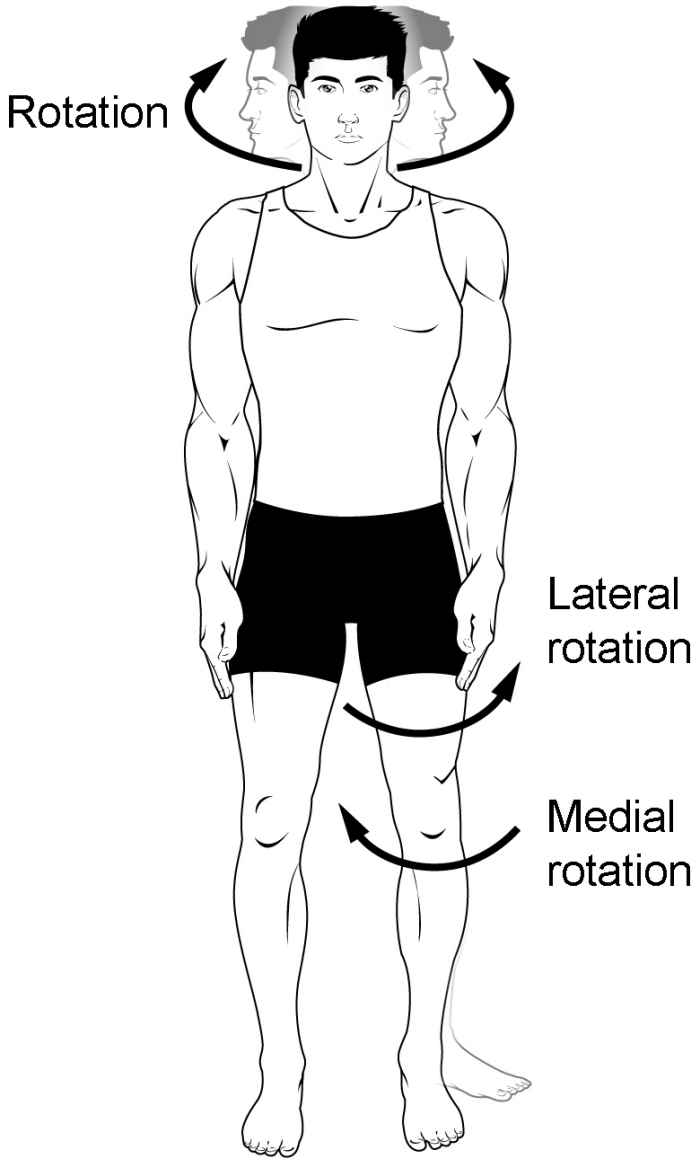


Figure 3. Rotation.

Supination and Pronation

Supination and pronation are movements of the forearm. In the anatomical position, the upper limb is held next to the body with the palm facing forward. This is the **supinated position** of the forearm. In this position, the radius and ulna are parallel to each other. When the palm of the hand faces backward, the forearm is in the **pronated position**, and the radius and ulna form an X-shape.

Supination and pronation are the movements of the forearm that go between these two positions. **Pronation** is the motion that moves the forearm from the supinated (anatomical) position to the pronated (palm backward) position. This motion is produced by rotation of the radius at the proximal radioulnar joint, accompanied by movement of the radius at the distal radioulnar joint. The proximal radioulnar joint is a pivot joint that allows for rotation of the head of the radius. Because of the slight curvature of the shaft of the radius, this rotation causes the distal end of

the radius to cross over the distal ulna at the distal radioulnar joint. This crossing over brings the radius and ulna into an X-shape position. **Supination** is the opposite motion, in which rotation of the radius returns the bones to their parallel positions and moves the palm to the anterior facing (supinated) position. It helps to remember that supination is the motion you use when scooping up soup with a spoon (see Figure 4).

Dorsiflexion and Plantar Flexion

Dorsiflexion and **plantar flexion** are movements at the ankle joint, which is a hinge joint. Lifting the front of the foot, so that the top of the foot moves toward the anterior leg is dorsiflexion, while lifting the heel of the foot from the ground or pointing the toes downward is plantar flexion. These are the only movements available at the ankle joint (see Figure 4).

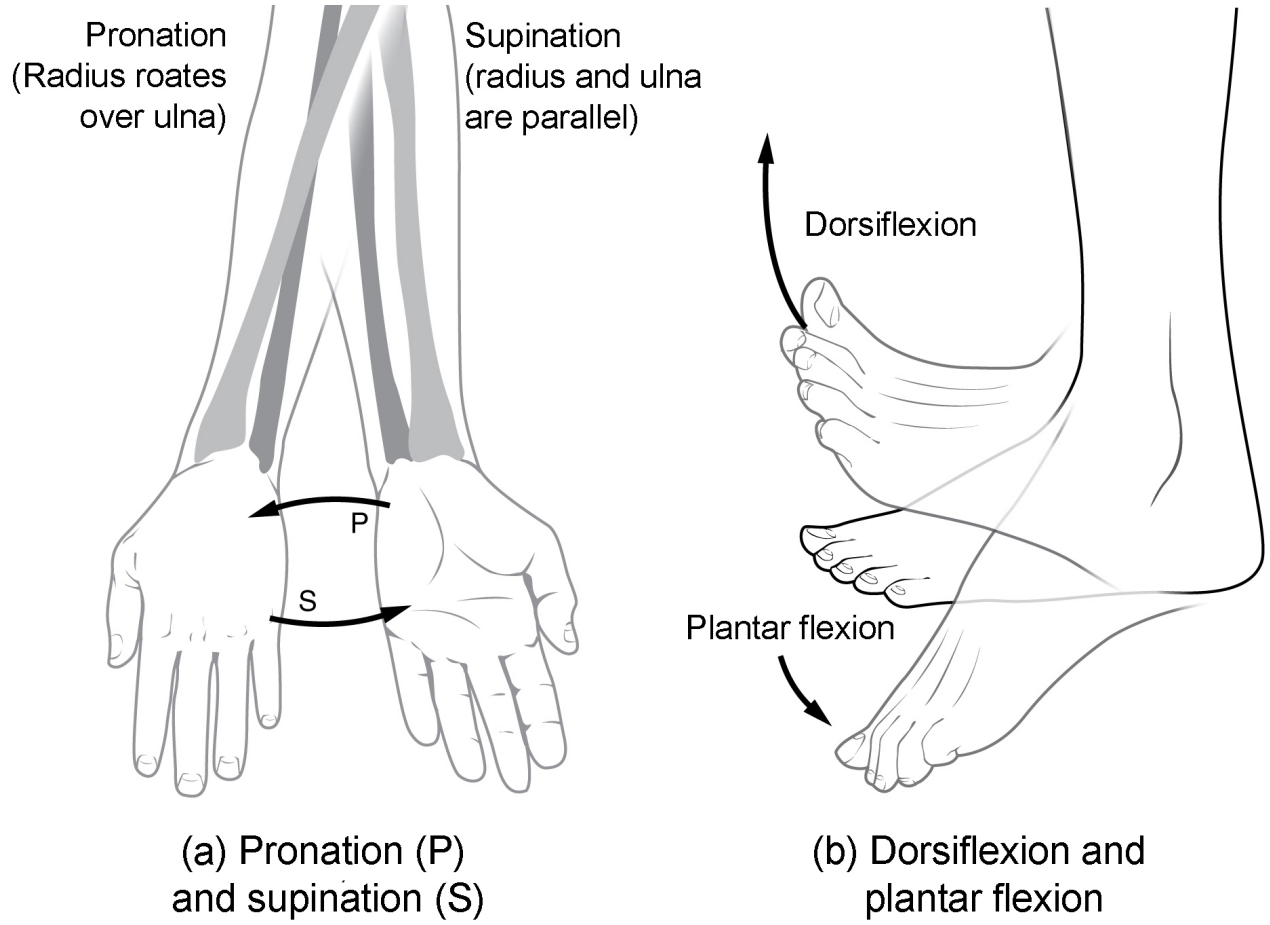


Figure 4. Supination and pronation. *(a) Supination of the forearm turns the hand to the palm forward position in which the radius and ulna are parallel, while forearm pronation turns the hand to the palm backward position in which the radius crosses over the ulna to form an "X." (b) Dorsiflexion of the foot at the ankle joint moves the top of the foot toward the leg, while plantar flexion lifts the heel and points the toes.*

Inversion and Eversion

Inversion and eversion are complex movements that involve the multiple plane joints among the tarsal bones of the posterior foot (intertarsal joints) and thus are not motions that take place at the ankle joint. **Inversion** is the turning of the foot to angle the bottom of the foot toward the midline, while **eversion** turns the bottom of the foot away from the midline. The foot has a greater range of inversion than eversion motion. These are important motions that help to stabilize the foot when walking or running on an uneven surface and aid in the quick side-to-side changes in direction used during active sports such as basketball, racquetball, or soccer (see Figure 5).

Protraction and Retraction

Protraction and **retraction** are anterior-posterior movements of the scapula or mandible. Protraction of the scapula occurs when the shoulder is moved forward, as when pushing against something or throwing a ball. Retraction is the opposite motion, with the scapula being pulled posteriorly and medially, toward the vertebral column. For the mandible, protraction occurs when the lower jaw is pushed forward, to stick out the chin, while retraction pulls the lower jaw backward. (See Figure 5.)

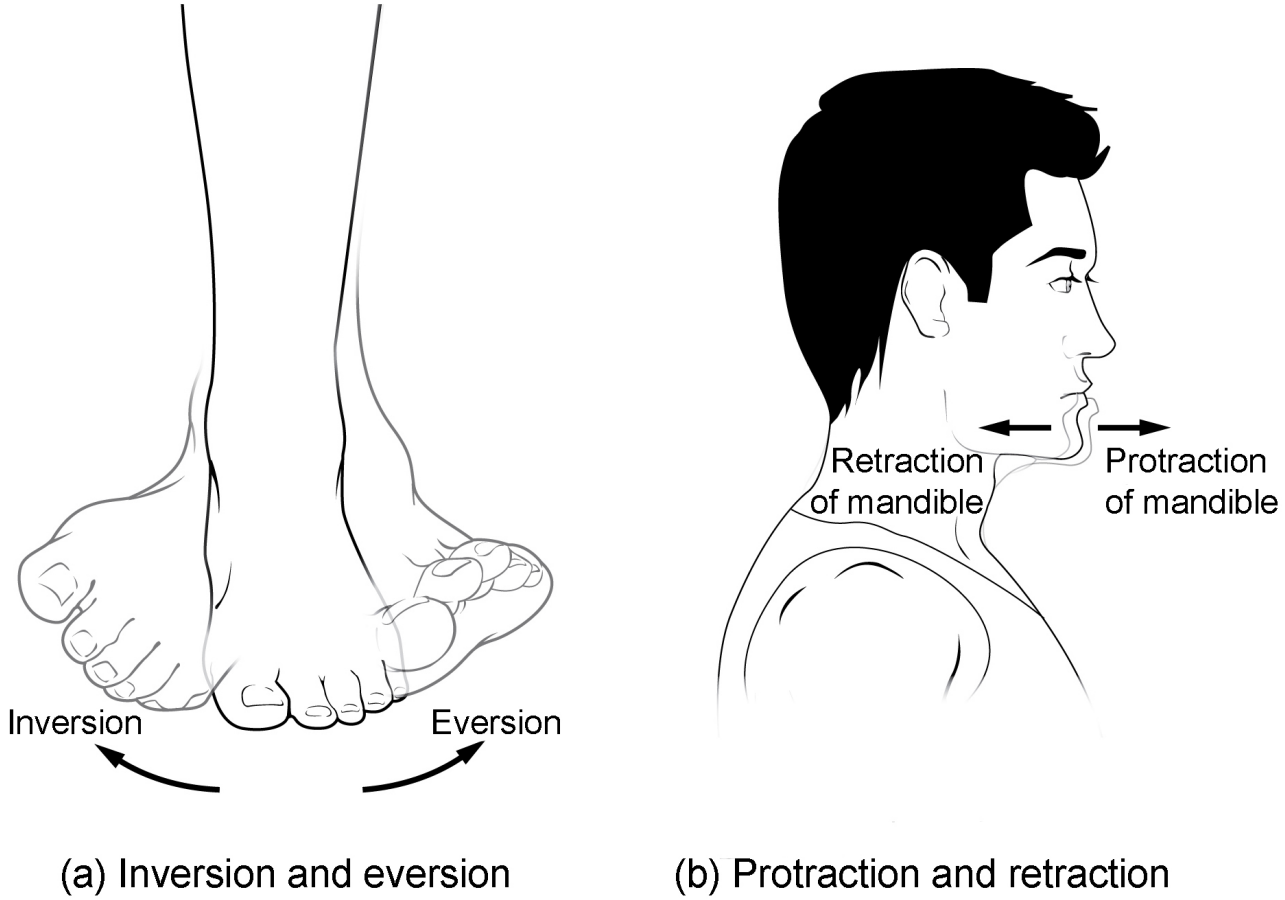


Figure 5. Inversion, eversion, protraction, and retraction. *(a) Eversion of the foot moves the bottom (sole) of the foot away from the midline of the body, while foot inversion faces the sole toward the midline. (b) Protraction of the mandible pushes the chin forward, and retraction pulls the chin back.*

Depression and Elevation

Depression and **elevation** are downward and upward movements of the scapula or mandible. The upward movement of the scapula and shoulder is elevation, while a downward movement is depression. These movements are used to shrug your shoulders. Similarly, elevation of the mandible is the upward movement of the lower jaw used to close the mouth or bite on something, and depression is the downward movement that produces opening of the mouth (see Figure 6).

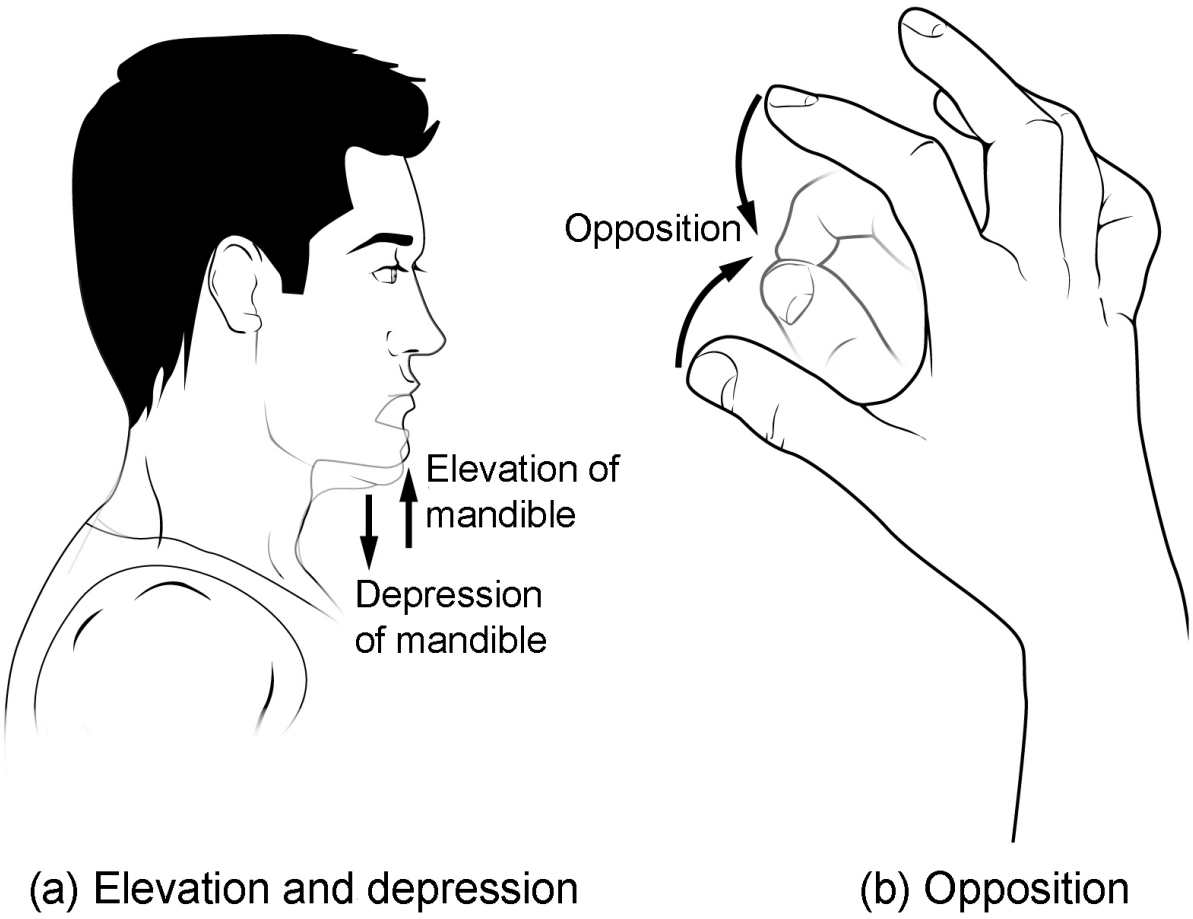


Figure 6. Depression, elevation, and opposition. *(a) Depression of the mandible opens the mouth, while elevation closes it. (b) Opposition of the thumb brings the tip of the thumb into contact with the tip of the fingers of the same hand and reposition brings the thumb back next to the index finger.*

Excursion

Excursion is the side to side movement of the mandible. **Lateral excursion** moves the mandible away from the midline, toward either the right or left side. **Medial excursion** returns the mandible to its resting position at the midline.

Superior Rotation and Inferior Rotation

Superior and inferior rotation are movements of the scapula and are defined by the direction of movement of the glenoid cavity. These motions involve rotation of the scapula around a point inferior to the scapular spine and are produced by combinations of muscles acting on the scapula. During **superior rotation**, the glenoid cavity moves upward as the medial end of the scapular spine moves downward. This is a very important motion that contributes to upper limb abduction. Without superior rotation of the scapula, the greater tubercle of the humerus would hit the acromion of the scapula, thus preventing any abduction of the arm above shoulder height. Superior rotation of the scapula is thus required for full abduction of the upper limb. Superior rotation is also used without arm abduction when carrying a heavy load with your hand or on your shoulder. You can feel this rotation when you pick up a load, such as a heavy book bag and carry it on only one shoulder. To increase its weight-bearing support for the bag, the shoulder lifts as the scapula superiorly rotates. **Inferior rotation** occurs during limb adduction and involves the downward motion of the glenoid cavity with upward movement of the medial end of the scapular spine.

Opposition and Reposition

Opposition is the thumb movement that brings the tip of the thumb in contact with the tip of a finger. This movement is produced at the first carpometacarpal joint, which is a saddle joint formed between the trapezium carpal bone and the first metacarpal bone. Thumb opposition is produced by a combination of flexion and abduction of the thumb at this joint. Returning the thumb to its anatomical position next to the index finger is called **reposition** (see Figure 6).

Table 1. Movements of the Joints

Type of Joint	Movement	Example
Pivot	Uniaxial joint; allows rotational movement	Atlantoaxial joint (C1–C2 vertebrae articulation); proximal radioulnar joint
Hinge	Uniaxial joint; allows flexion/extension movements	Knee; elbow; ankle; interphalangeal joints of fingers and toes
Condyloid	Biaxial joint; allows flexion/extension, abduction/adduction, and circumduction movements	Metacarpophalangeal (knuckle) joints of fingers; radiocarpal joint of wrist; metatarsophalangeal joints for toes
Saddle	Biaxial joint; allows flexion/extension, abduction/adduction, and circumduction movements	First carpometacarpal joint of the thumb; sternoclavicular joint
Plane	Multiaxial joint; allows inversion and eversion of foot, or flexion, extension, and lateral flexion of the vertebral column	Intertarsal joints of foot; superior-inferior articular process articulations between vertebrae
Ball-and-socket	Multiaxial joint; allows flexion/extension, abduction/adduction, circumduction, and medial/lateral rotation movements	Shoulder and hip joints

ANATOMY OF SELECTED SYNOVIAL JOINTS

Learning Objectives

- Describe the bones that articulate together to form selected synovial joints
- Discuss the movements available at each joint
- Describe the structures that support and prevent excess movements at each joint

Each synovial joint of the body is specialized to perform certain movements. The movements that are allowed are determined by the structural classification for each joint. For example, a multiaxial ball-and-socket joint has much more mobility than a uniaxial hinge joint. However, the ligaments and muscles that support a joint may place restrictions on the total range of motion available. Thus, the ball-and-socket joint of the shoulder has little in the way of ligament support, which gives the shoulder a very large range of motion. In contrast, movements at the hip joint are restricted by strong ligaments, which reduce its range of motion but confer stability during standing and weight bearing.

This section will examine the anatomy of selected synovial joints of the body. Anatomical names for most joints are derived from the names of the bones that articulate at that joint, although some joints, such as the elbow, hip, and knee joints are exceptions to this general naming scheme.

Articulations of the Vertebral Column

In addition to being held together by the intervertebral discs, adjacent vertebrae also articulate with each other at synovial joints formed between the superior and inferior articular processes called **zygapophysial joints** (facet joints). These are plane joints that provide for only limited motions between the vertebrae. The orientation of the articular processes at these joints varies in different regions of the vertebral column and serves to determine the types of motions available in each vertebral region. The cervical and lumbar regions have the greatest ranges of motions.

In the neck, the articular processes of cervical vertebrae are flattened and generally face upward or downward. This orientation provides the cervical vertebral column with extensive ranges of motion for flexion, extension, lateral flexion, and rotation. In the thoracic region, the downward projecting and overlapping spinous processes, along with the attached thoracic cage, greatly limit flexion, extension, and lateral flexion. However, the flattened and vertically positioned thoracic articular processes allow for the greatest range of rotation within the vertebral column. The lumbar region allows for considerable extension, flexion, and lateral flexion, but the orientation of the articular processes largely prohibits rotation.

The articulations formed between the skull, the atlas (C1 vertebra), and the axis (C2 vertebra) differ from the articulations in other vertebral areas and play important roles in movement of the head. The **atlanto-occipital joint** is formed by the articulations between the superior articular processes of the atlas and the occipital condyles on the base of the skull. This articulation has a pronounced U-shaped curvature, oriented along the anterior-posterior axis. This allows the skull to rock forward and backward, producing flexion and extension of the head. This moves the head up and down, as when shaking your head “yes.”

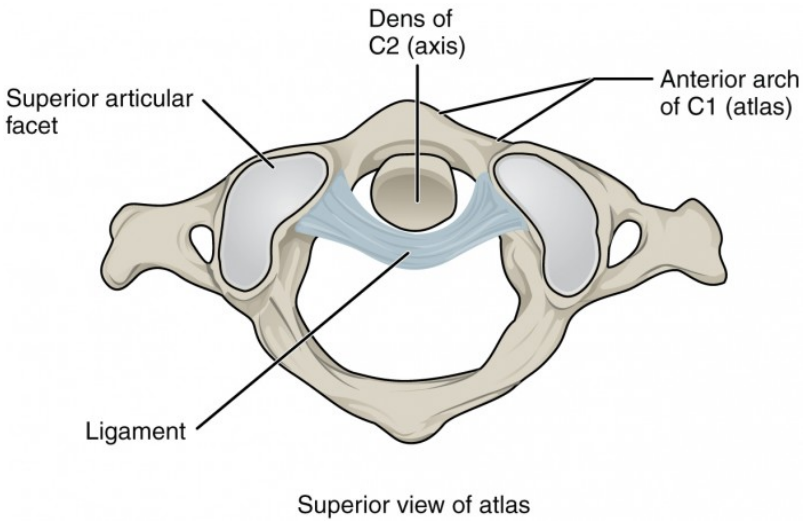


Figure 1. Atlantoaxial Joint*. The atlantoaxial joint is a pivot type of joint between the dens portion of the axis (C2 vertebra) and the anterior arch of the atlas (C1 vertebra), with the dens held in place by a ligament. The atlantoaxial joint is a pivot type of joint between the dens portion of the axis (C2 vertebra) and the anterior arch of the atlas (C1 vertebra), with the dens held in place by a ligament.*

The **atlantoaxial joint**, between the atlas and axis, consists of three articulations. The paired superior articular processes of the axis articulate with the inferior articular processes of the atlas. These articulating surfaces are relatively flat and oriented horizontally. The third articulation is the pivot joint formed between the dens, which projects upward from the body of the axis, and the inner aspect of the anterior arch of the atlas (Figure 1). A strong ligament passes posterior to the dens to hold it in position against the anterior arch. These articulations allow the atlas to rotate on top of the axis, moving the head toward the right or left, as when shaking your head “no.”

Temporomandibular Joint

The **temporomandibular joint (TMJ)** is the joint that allows for opening (mandibular depression) and closing (mandibular elevation) of the mouth, as well as side-to-side and protraction/retraction motions of the lower jaw. This joint involves the articulation between the mandibular fossa and articular tubercle of the temporal bone, with the condyle (head) of the mandible. Located between these bony structures, filling the gap between the skull and mandible, is a flexible articular disc (Figure 2). This disc serves to smooth the movements between the temporal bone and mandibular condyle.

Movement at the TMJ during opening and closing of the mouth involves both gliding and hinge motions of the mandible. With the mouth closed, the mandibular condyle and articular disc are located within the mandibular fossa of the temporal bone. During opening of the mouth, the mandible hinges downward and at the same time is pulled anteriorly, causing both the condyle and the articular disc to glide forward from the mandibular fossa onto the downward projecting articular tubercle. The net result is a forward and downward motion of the condyle and mandibular depression. The temporomandibular joint is supported by an extrinsic ligament that anchors the mandible to the skull. This ligament spans the distance between the base of the skull and the lingula on the medial side of the mandibular ramus.

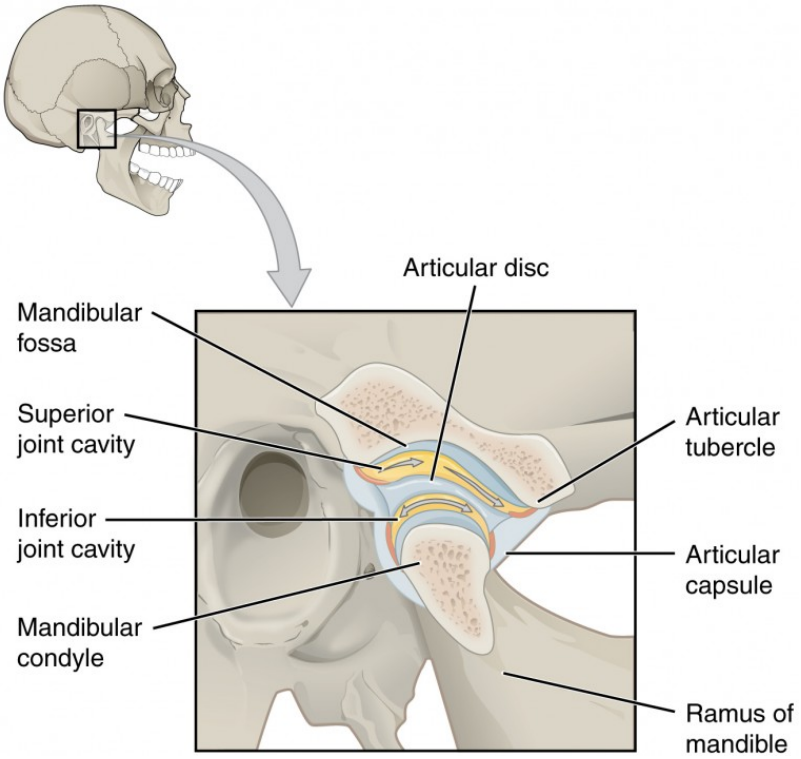


Figure 2. Temporomandibular Joint. *The temporomandibular joint is the articulation between the temporal bone of the skull and the condyle of the mandible, with an articular disc located between these bones. During depression of the mandible (opening of the mouth), the mandibular condyle moves both forward and hinges downward as it travels from the mandibular fossa onto the articular tubercle.*

Dislocation of the TMJ may occur when opening the mouth too wide (such as when taking a large bite) or following a blow to the jaw, resulting in the mandibular condyle moving beyond (anterior to) the articular tubercle. In this case, the individual would not be able to close his or her mouth. Temporomandibular joint disorder is a painful condition that may arise due to arthritis, wearing of the articular cartilage covering the bony surfaces of the joint, muscle fatigue from overuse or grinding of the teeth, damage to the articular disc within the joint, or jaw injury. Temporomandibular joint disorders can also cause headache, difficulty chewing, or even the inability to move the jaw (lock jaw). Pharmacologic agents for pain or other therapies, including bite guards, are used as treatments.

Watch this video to learn about TMJ. Opening of the mouth requires the combination of two motions at the temporomandibular joint, an anterior gliding motion of the articular disc and mandible and the downward hinging of the mandible. What is the initial movement of the mandible during opening and how much mouth opening does this produce?

Watch this video online: https://youtu.be/8MKx5c0BRrQ

Shoulder Joint

The shoulder joint is called the **glenohumeral joint**. This is a ball-and-socket joint formed by the articulation between the head of the humerus and the glenoid cavity of the scapula (Figure 3). This joint has the largest range

of motion of any joint in the body. However, this freedom of movement is due to the lack of structural support and thus the enhanced mobility is offset by a loss of stability.

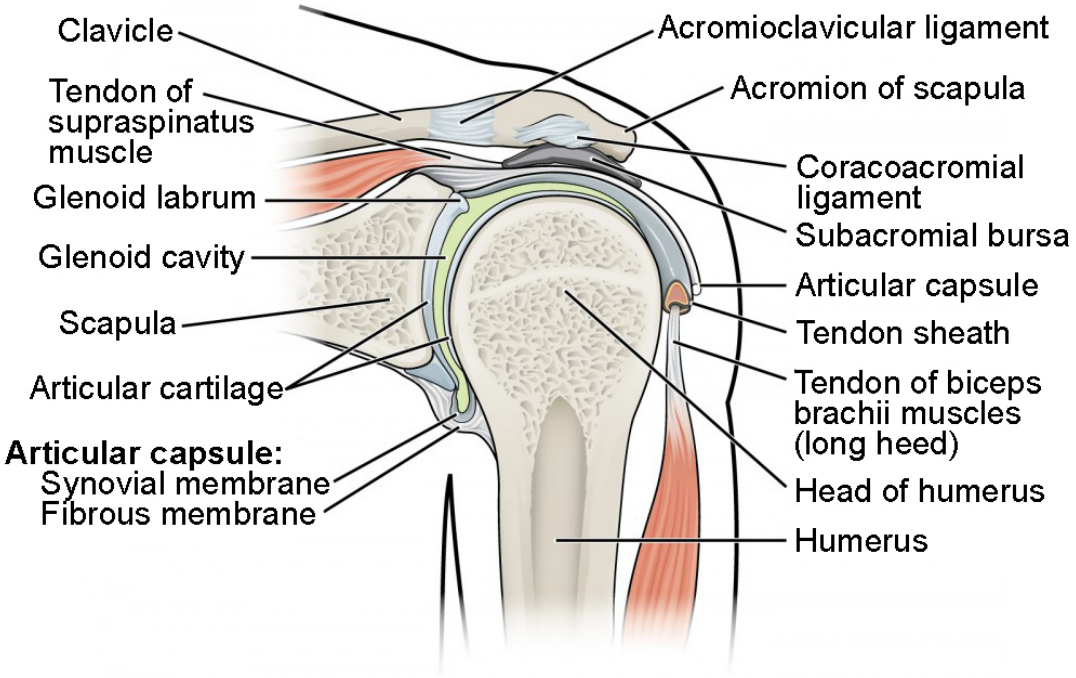


Figure 3. Glenohumeral Joint. *The glenohumeral (shoulder) joint is a ball-and-socket joint that provides the widest range of motions. It has a loose articular capsule and is supported by ligaments and the rotator cuff muscles.*

The large range of motions at the shoulder joint is provided by the articulation of the large, rounded humeral head with the small and shallow glenoid cavity, which is only about one third of the size of the humeral head. The socket formed by the glenoid cavity is deepened slightly by a small lip of fibrocartilage called the **glenoid labrum**, which extends around the outer margin of the cavity. The articular capsule that surrounds the glenohumeral joint is relatively thin and loose to allow for large motions of the upper limb. Some structural support for the joint is provided by thickenings of the articular capsule wall that form weak intrinsic ligaments. These include the **coracohumeral ligament**, running from the coracoid process of the scapula to the anterior humerus, and three ligaments, each called a **glenohumeral ligament**, located on the anterior side of the articular capsule. These ligaments help to strengthen the superior and anterior capsule walls.

However, the primary support for the shoulder joint is provided by muscles crossing the joint, particularly the four rotator cuff muscles. These muscles (supraspinatus, infraspinatus, teres minor, and subscapularis) arise from the scapula and attach to the greater or lesser tubercles of the humerus. As these muscles cross the shoulder joint, their tendons encircle the head of the humerus and become fused to the anterior, superior, and posterior walls of the articular capsule. The thickening of the capsule formed by the fusion of these four muscle tendons is called the **rotator cuff**. Two bursae, the **subacromial bursa** and the **subscapular bursa**, help to prevent friction between the rotator cuff muscle tendons and the scapula as these tendons cross the glenohumeral joint. In addition to their individual actions of moving the upper limb, the rotator cuff muscles also serve to hold the head of the humerus in position within the glenoid cavity. By constantly adjusting their strength of contraction to resist forces acting on the shoulder, these muscles serve as “dynamic ligaments” and thus provide the primary structural support for the glenohumeral joint.

Injuries to the shoulder joint are common. Repetitive use of the upper limb, particularly in abduction such as during throwing, swimming, or racquet sports, may lead to acute or chronic inflammation of the bursa or muscle tendons, a tear of the glenoid labrum, or degeneration or tears of the rotator cuff. Because the humeral head is strongly supported by muscles and ligaments around its anterior, superior, and posterior aspects, most dislocations of the humerus occur in an inferior direction. This can occur when force is applied to the humerus when the upper limb is fully abducted, as when diving to catch a baseball and landing on your hand or elbow. Inflammatory responses to any shoulder injury can lead to the formation of scar tissue between the articular

capsule and surrounding structures, thus reducing shoulder mobility, a condition called adhesive capsulitis (“frozen shoulder”).

Watch this video for a tutorial on the anatomy of the shoulder joint. What movements are available at the shoulder joint?

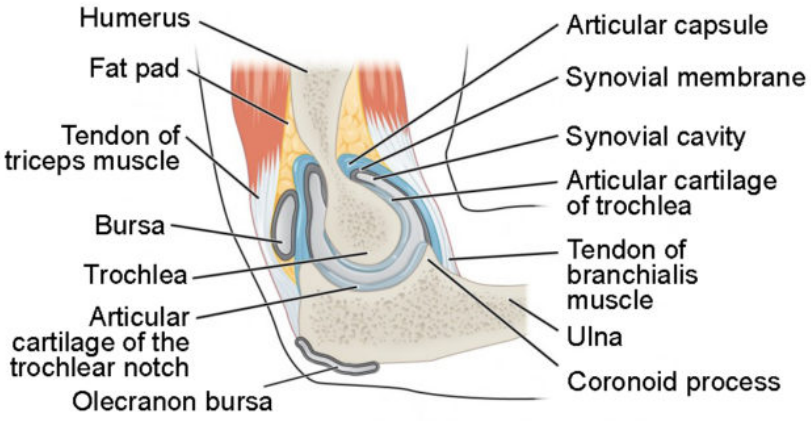
Watch this video online: https://youtu.be/vG1XQkj3Yx0

Watch this video to learn more about the anatomy of the shoulder joint, including bones, joints, muscles, nerves, and blood vessels. What is the shape of the glenoid labrum in cross-section, and what is the importance of this shape?

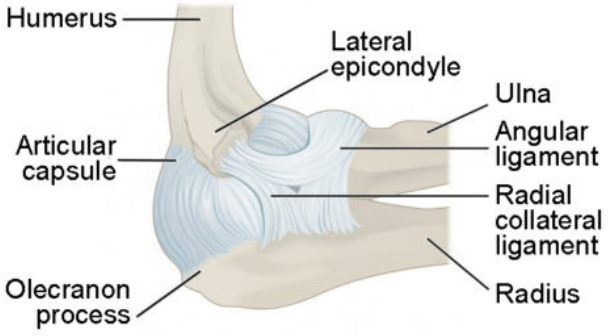
Watch this video online: https://youtu.be/D3GVKjeY1FM

Elbow Joint

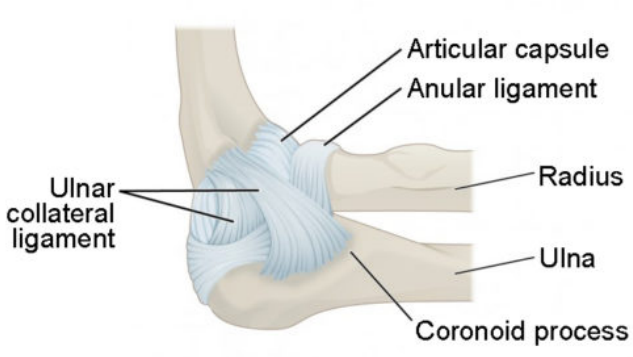
The **elbow joint** is a uniaxial hinge joint formed by the **humeroulnar joint**, the articulation between the trochlea of the humerus and the trochlear notch of the ulna. Also associated with the elbow are the **humeroradial joint** and the proximal radioulnar joint. All three of these joints are enclosed within a single articular capsule (Figure 4).



(a) Medial sagittal section through right elbow (lateral view)



(b) Lateral view of right elbow joint



(c) Medial view of right elbow joint

Figure 4. Elbow Joint. *(a) The elbow is a hinge joint that allows only for flexion and extension of the forearm. (b) It is supported by the ulnar and radial collateral ligaments. (c) The annular ligament supports the head of the radius at the proximal radioulnar joint, the pivot joint that allows for rotation of the radius.*

The articular capsule of the elbow is thin on its anterior and posterior aspects, but is thickened along its outside margins by strong intrinsic ligaments. These ligaments prevent side-to-side movements and hyperextension. On the medial side is the triangular **ulnar collateral ligament**. This arises from the medial epicondyle of the humerus and attaches to the medial side of the proximal ulna. The strongest part of this ligament is the anterior portion, which resists hyperextension of the elbow. The ulnar collateral ligament may be injured by frequent, forceful extensions of the forearm, as is seen in baseball pitchers. Reconstructive surgical repair of this ligament is referred to as Tommy John surgery, named for the former major league pitcher who was the first person to have this treatment.

The lateral side of the elbow is supported by the **radial collateral ligament**. This arises from the lateral epicondyle of the humerus and then blends into the lateral side of the annular ligament. The **annular ligament** encircles the head of the radius. This ligament supports the head of the radius as it articulates with the radial notch of the ulna at the proximal radioulnar joint. This is a pivot joint that allows for rotation of the radius during supination and pronation of the forearm.

Watch this animation to learn more about the anatomy of the elbow joint. Which structures provide the main stability for the elbow?

Watch this video online: https://youtu.be/VEg2rReyM6k

Watch this video to learn more about the anatomy of the elbow joint, including bones, joints, muscles, nerves, and blood vessels. What are the functions of the articular cartilage?

Watch this video online: https://youtu.be/3l3-5Ij3JZ8

Hip Joint

The hip joint is a multiaxial ball-and-socket joint between the head of the femur and the acetabulum of the hip bone (Figure 5). The hip carries the weight of the body and thus requires strength and stability during standing and walking. For these reasons, its range of motion is more limited than at the shoulder joint.

The acetabulum is the socket portion of the hip joint. This space is deep and has a large articulation area for the femoral head, thus giving stability and weight bearing ability to the joint. The acetabulum is further deepened by the **acetabular labrum**, a fibrocartilage lip attached to the outer margin of the acetabulum. The surrounding articular capsule is strong, with several thickened areas forming intrinsic ligaments. These ligaments arise from the hip bone, at the margins of the acetabulum, and attach to the femur at the base of the neck. The ligaments are the **iliofemoral ligament**,**pubofemoral ligament**, and **ischiofemoral ligament**, all of which spiral around the head and neck of the femur. The ligaments are tightened by extension at the hip, thus pulling the head of the femur tightly into the acetabulum when in the upright, standing position. Very little additional extension of the thigh is permitted beyond this vertical position. These ligaments thus stabilize the hip joint and allow you to maintain an upright standing position with only minimal muscle contraction. Inside of the articular capsule, the **ligament of the head of the femur** (ligamentum teres) spans between the acetabulum and femoral head. This intracapsular ligament is normally slack and does not provide any significant joint support, but it does provide a pathway for an important artery that supplies the head of the femur.

The hip is prone to osteoarthritis, and thus was the first joint for which a replacement prosthesis was developed. A common injury in elderly individuals, particularly those with weakened bones due to osteoporosis, is a “broken hip,” which is actually a fracture of the femoral neck. This may result from a fall, or it may cause the fall. This can happen as one lower limb is taking a step and all of the body weight is placed on the other limb, causing the femoral neck to break and producing a fall. Any accompanying disruption of the blood supply to the femoral neck or head can lead to necrosis of these areas, resulting in bone and cartilage death. Femoral fractures usually require surgical treatment, after which the patient will need mobility assistance for a prolonged period, either from family members or in a long-term care facility. Consequentially, the associated health care costs of “broken hips” are substantial. In addition, hip fractures are associated with increased rates of morbidity (incidences of disease)

and mortality (death). Surgery for a hip fracture followed by prolonged bed rest may lead to life-threatening complications, including pneumonia, infection of pressure ulcers (bedsores), and thrombophlebitis (deep vein thrombosis; blood clot formation) that can result in a pulmonary embolism (blood clot within the lung).

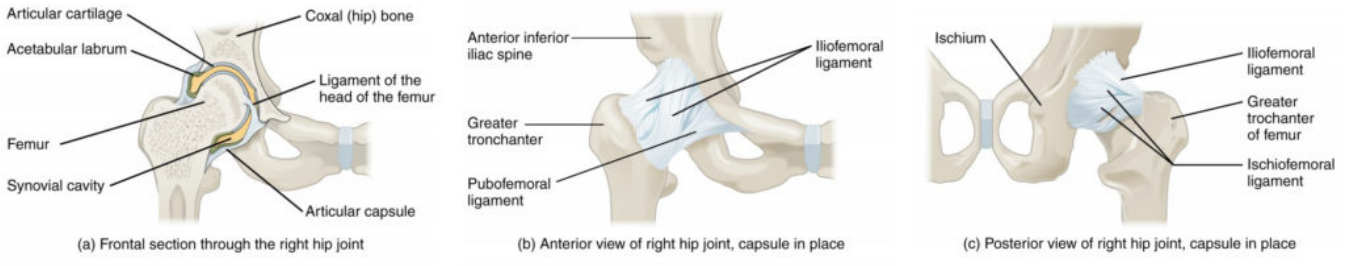


Figure 5. Hip Joint. *Click for a larger image. (a) The ball-and-socket joint of the hip is a multiaxial joint that provides both stability and a wide range of motion. (b–c) When standing, the supporting ligaments are tight, pulling the head of the femur into the acetabulum.*

Watch this video for a tutorial on the anatomy of the hip joint. What is a possible consequence following a fracture of the femoral neck within the capsule of the hip joint?

Watch this video online: https://youtu.be/ZWcdMj8wRos

Watch this video to learn more about the anatomy of the hip joint, including bones, joints, muscles, nerves, and blood vessels. Where is the articular cartilage thickest within the hip joint?

Watch this video online: https://youtu.be/qlCvKEOZtpo

Knee Joint

The knee joint is the largest joint of the body (Figure 6). It actually consists of three articulations. The **femoropatellar joint** is found between the patella and the distal femur. The **medial tibiofemoral joint** and **lateral tibiofemoral joint** are located between the medial and lateral condyles of the femur and the medial and lateral condyles of the tibia. All of these articulations are enclosed within a single articular capsule. The knee functions as a hinge joint, allowing flexion and extension of the leg. This action is generated by both rolling and gliding motions of the femur on the tibia. In addition, some rotation of the leg is available when the knee is flexed, but not when extended. The knee is well constructed for weight bearing in its extended position, but is vulnerable to injuries associated with hyperextension, twisting, or blows to the medial or lateral side of the joint, particularly while weight bearing.

At the femoropatellar joint, the patella slides vertically within a groove on the distal femur. The patella is a sesamoid bone incorporated into the tendon of the quadriceps femoris muscle, the large muscle of the anterior thigh. The patella serves to protect the quadriceps tendon from friction against the distal femur. Continuing from the patella to the anterior tibia just below the knee is the **patellar ligament**. Acting via the patella and patellar ligament, the quadriceps femoris is a powerful muscle that acts to extend the leg at the knee. It also serves as a “dynamic ligament” to provide very important support and stabilization for the knee joint.

The medial and lateral tibiofemoral joints are the articulations between the rounded condyles of the femur and the relatively flat condyles of the tibia. During flexion and extension motions, the condyles of the femur both roll and glide over the surfaces of the tibia. The rolling action produces flexion or extension, while the gliding action serves to maintain the femoral condyles centered over the tibial condyles, thus ensuring maximal bony, weight-bearing support for the femur in all knee positions. As the knee comes into full extension, the femur undergoes a slight medial rotation in relation to tibia. The rotation results because the lateral condyle of the femur is slightly smaller than the medial condyle. Thus, the lateral condyle finishes its rolling motion first, followed by the medial condyle. The resulting small medial rotation of the femur serves to “lock” the knee into its fully extended and most stable position. Flexion of the knee is initiated by a slight lateral rotation of the femur on the tibia, which “unlocks” the knee. This lateral rotation motion is produced by the popliteus muscle of the posterior leg.

Located between the articulating surfaces of the femur and tibia are two articular discs, the **medial meniscus** and **lateral meniscus** (see Figure 6b). Each is a C-shaped fibrocartilage structure that is thin along its inside margin and thick along the outer margin. They are attached to their tibial condyles, but do not attach to the femur. While both menisci are free to move during knee motions, the medial meniscus shows less movement because it is anchored at its outer margin to the articular capsule and tibial collateral ligament. The menisci provide padding between the bones and help to fill the gap between the round femoral condyles and flattened tibial condyles. Some areas of each meniscus lack an arterial blood supply and thus these areas heal poorly if damaged.

The knee joint has multiple ligaments that provide support, particularly in the extended position (see Figure 6c). Outside of the articular capsule, located at the sides of the knee, are two extrinsic ligaments. The **fibular collateral ligament** (lateral collateral ligament) is on the lateral side and spans from the lateral epicondyle of the femur to the head of the fibula. The **tibial collateral ligament** (medial collateral ligament) of the medial knee runs from the medial epicondyle of the femur to the medial tibia. As it crosses the knee, the tibial collateral ligament is firmly attached on its deep side to the articular capsule and to the medial meniscus, an important factor when considering knee injuries. In the fully extended knee position, both collateral ligaments are taut (tight), thus serving to stabilize and support the extended knee and preventing side-to-side or rotational motions between the femur and tibia.

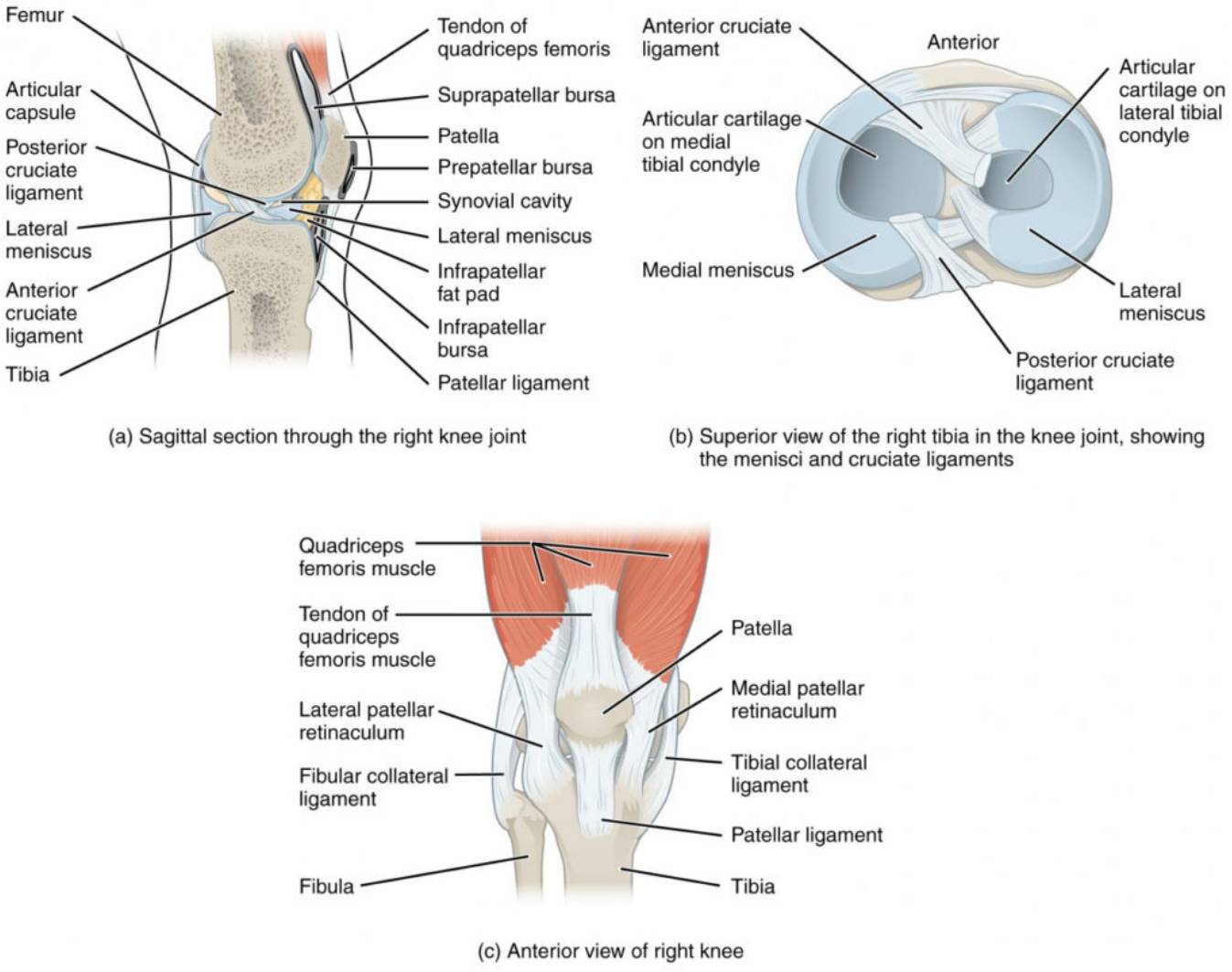


Figure 6. Knee Joint. *(a) The knee joint is the largest joint of the body. (b)–(c) It is supported by the tibial and fibular collateral ligaments located on the sides of the knee outside of the articular capsule, and the anterior and posterior cruciate ligaments found inside the capsule. The medial and lateral menisci provide padding and support between the femoral condyles and tibial condyles.*

The articular capsule of the posterior knee is thickened by intrinsic ligaments that help to resist knee hyperextension. Inside the knee are two intracapsular ligaments, the **anterior cruciate ligament** and **posterior cruciate ligament**. These ligaments are anchored inferiorly to the tibia at the intercondylar eminence, the roughened area between the tibial condyles. The cruciate ligaments are named for whether they are attached anteriorly or posteriorly to this tibial region. Each ligament runs diagonally upward to attach to the inner aspect of a femoral condyle. The cruciate ligaments are named for the X-shape formed as they pass each other (cruciate means “cross”). The posterior cruciate ligament is the stronger ligament. It serves to support the knee when it is flexed and weight bearing, as when walking downhill. In this position, the posterior cruciate ligament prevents the femur from sliding anteriorly off the top of the tibia. The anterior cruciate ligament becomes tight when the knee is extended, and thus resists hyperextension.

Watch this video to learn more about the flexion and extension of the knee, as the femur both rolls and glides on the tibia to maintain stable contact between the bones in all knee positions. The patella glides along a groove on the anterior side of the distal femur. The collateral ligaments on the sides of the knee become tight in the fully extended position to help stabilize the knee. The posterior cruciate ligament supports the knee when flexed and the anterior cruciate ligament becomes tight when the knee comes into full extension to resist hyperextension. What are the ligaments that support the knee joint?

Watch this video online: https://youtu.be/H3YgbJLbIXk

Watch this video to learn more about the anatomy of the knee joint, including bones, joints, muscles, nerves, and blood vessels. Which ligament of the knee keeps the tibia from sliding too far forward in relation to the femur and which ligament keeps the tibia from sliding too far backward?

Watch this video online: https://youtu.be/_q-Jxj5sT0g

Disorders of the Joints

Injuries to the knee are common. Since this joint is primarily supported by muscles and ligaments, injuries to any of these structures will result in pain or knee instability. Injury to the posterior cruciate ligament occurs when the knee is flexed and the tibia is driven posteriorly, such as falling and landing on the tibial tuberosity or hitting the tibia on the dashboard when not wearing a seatbelt during an automobile accident. More commonly, injuries occur when forces are applied to the extended knee, particularly when the foot is planted and unable to move. Anterior cruciate ligament injuries can result with a forceful blow to the anterior knee, producing hyperextension, or when a runner makes a quick change of direction that produces both twisting and hyperextension of the knee.

A worse combination of injuries can occur with a hit to the lateral side of the extended knee (Figure 7). A moderate blow to the lateral knee will cause the medial side of the joint to open, resulting in stretching or damage to the tibial collateral ligament. Because the medial meniscus is attached to the tibial collateral ligament, a stronger blow can tear the ligament and also damage the medial meniscus. This is one reason that the medial meniscus is 20 times more likely to be injured than the lateral meniscus. A powerful blow to the lateral knee produces a “terrible triad” injury, in which there is a sequential injury to the tibial collateral ligament, medial meniscus, and anterior cruciate ligament.

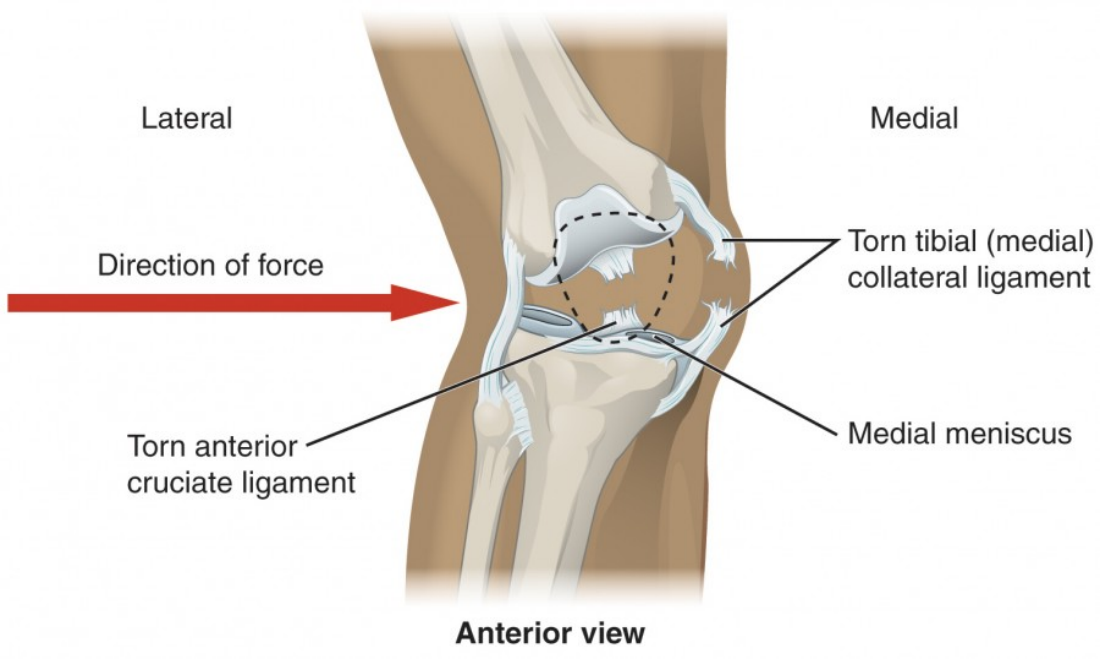


Figure 7. Knee Injury. *A strong blow to the lateral side of the extended knee will cause three injuries, in sequence: tearing of the tibial collateral ligament, damage to the medial meniscus, and rupture of the anterior cruciate ligament.*

Arthroscopic surgery has greatly improved the surgical treatment of knee injuries and reduced subsequent recovery times. This procedure involves a small incision and the insertion into the joint of an arthroscope, a pencil-thin instrument that allows for visualization of the joint interior. Small surgical instruments are also inserted via additional incisions. These tools allow a surgeon to remove or repair a torn meniscus or to reconstruct a ruptured cruciate ligament. The current method for anterior cruciate ligament replacement involves using a portion of the patellar ligament. Holes are drilled into the cruciate ligament attachment points on the tibia and femur, and the patellar ligament graft, with small areas of attached bone still intact at each end, is inserted into these holes. The bone-to-bone sites at each end of the graft heal rapidly and strongly, thus enabling a rapid recovery.

Watch this video to learn more about different knee injuries and diagnostic testing of the knee. What are the most common causes of anterior cruciate ligament injury?

Watch this video online: https://youtu.be/SnfEmezg7eY

Ankle and Foot Joints

The ankle is formed by the **talocrural joint** (Figure 8). It consists of the articulations between the talus bone of the foot and the distal ends of the tibia and fibula of the leg (crural = “leg”). The superior aspect of the talus bone is square-shaped and has three areas of articulation. The top of the talus articulates with the inferior tibia. This is the portion of the ankle joint that carries the body weight between the leg and foot. The sides of the talus are firmly held in position by the articulations with the medial malleolus of the tibia and the lateral malleolus of the fibula, which prevent any side-to-side motion of the talus. The ankle is thus a uniaxial hinge joint that allows only for dorsiflexion and plantar flexion of the foot.

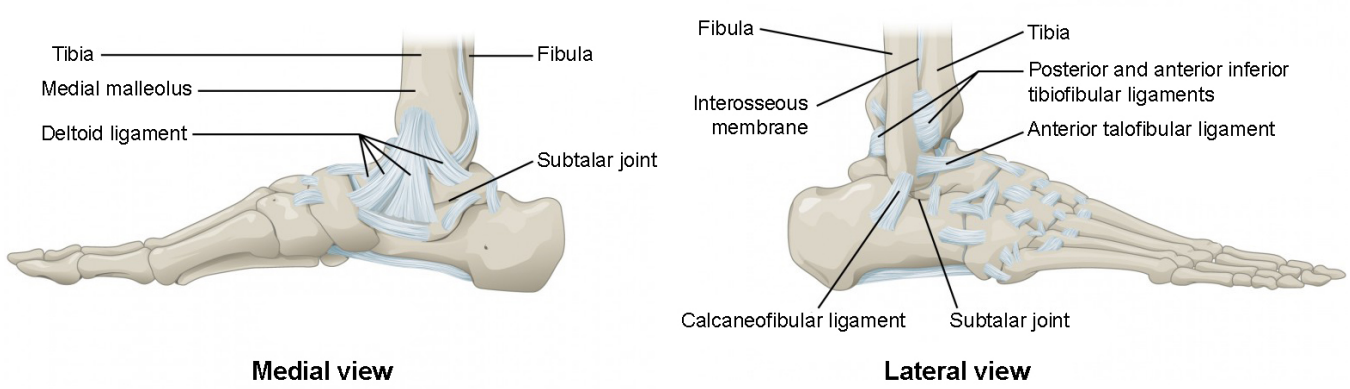


Figure 8. Ankle Joint. *The talocrural (ankle) joint is a uniaxial hinge joint that only allows for dorsiflexion or plantar flexion of the foot. Movements at the subtalar joint, between the talus and calcaneus bones, combined with motions at other intertarsal joints, enables eversion/inversion movements of the foot. Ligaments that unite the medial or lateral malleolus with the talus and calcaneus bones serve to support the talocrural joint and to resist excess eversion or inversion of the foot.*

Additional joints between the tarsal bones of the posterior foot allow for the movements of foot inversion and eversion. Most important for these movements is the **subtalar joint**, located between the talus and calcaneus bones. The joints between the talus and navicular bones and the calcaneus and cuboid bones are also important contributors to these movements. All of the joints between tarsal bones are plane joints. Together, the small motions that take place at these joints all contribute to the production of inversion and eversion foot motions.

Like the hinge joints of the elbow and knee, the talocrural joint of the ankle is supported by several strong ligaments located on the sides of the joint. These ligaments extend from the medial malleolus of the tibia or lateral malleolus of the fibula and anchor to the talus and calcaneus bones. Since they are located on the sides of the ankle joint, they allow for dorsiflexion and plantar flexion of the foot. They also prevent abnormal side-to-side and twisting movements of the talus and calcaneus bones during eversion and inversion of the foot. On the medial side is the broad **deltoid ligament**. The deltoid ligament supports the ankle joint and also resists excessive eversion of the foot. The lateral side of the ankle has several smaller ligaments. These include the **anterior talofibular ligament** and the **posterior talofibular ligament**, both of which span between the talus bone and the lateral malleolus of the fibula, and the **calcaneofibular ligament**, located between the calcaneus bone and fibula. These ligaments support the ankle and also resist excess inversion of the foot.

Watch this video for a tutorial on the anatomy of the ankle joint. What are the three ligaments found on the lateral side of the ankle joint?

Watch this video online: https://youtu.be/lPLdoFQlZXQ

Watch this video to learn more about the anatomy of the ankle joint, including bones, joints, muscles, nerves, and blood vessels. Which type of joint used in woodworking does the ankle joint resemble?

Watch this video online: https://youtu.be/4hCS1O2LP_c

Disorders of the Joints

The ankle is the most frequently injured joint in the body, with the most common injury being an inversion ankle sprain. A sprain is the stretching or tearing of the supporting ligaments. Excess inversion causes the talus bone to tilt laterally, thus damaging the ligaments on the lateral side of the ankle. The anterior talofibular ligament is most commonly injured, followed by the calcaneofibular ligament. In severe inversion injuries, the forceful lateral movement of the talus not only ruptures the lateral ankle ligaments, but also fractures the distal fibula.

Less common are eversion sprains of the ankle, which involve stretching of the deltoid ligament on the medial side of the ankle. Forcible eversion of the foot, for example, with an awkward landing from a jump or when a

football player has a foot planted and is hit on the lateral ankle, can result in a Pott's fracture and dislocation of the ankle joint. In this injury, the very strong deltoid ligament does not tear, but instead shears off the medial malleolus of the tibia. This frees the talus, which moves laterally and fractures the distal fibula. In extreme cases, the posterior margin of the tibia may also be sheared off.

Above the ankle, the distal ends of the tibia and fibula are united by a strong syndesmosis formed by the interosseous membrane and ligaments at the distal tibiofibular joint. These connections prevent separation between the distal ends of the tibia and fibula and maintain the talus locked into position between the medial malleolus and lateral malleolus. Injuries that produce a lateral twisting of the leg on top of the planted foot can result in stretching or tearing of the tibiofibular ligaments, producing a syndesmotic ankle sprain or "high ankle sprain."

Most ankle sprains can be treated using the RICE technique: Rest, Ice, Compression, and Elevation. Reducing joint mobility using a brace or cast may be required for a period of time. More severe injuries involving ligament tears or bone fractures may require surgery.

Watch this video to learn more about the ligaments of the ankle joint, ankle sprains, and treatment. During an inversion ankle sprain injury, all three ligaments that resist excessive inversion of the foot may be injured. What is the sequence in which these three ligaments are injured?

Watch this video online: https://youtu.be/B0-n-ndTAX0

VIDEO TUTORIALS: SYNOVIAL JOINTS

Watch the following videos for a tour of the ankle, knee, hip, shoulder, and elbow joints. Watching these videos will help you better visualize the way joints work in the body.

The Shoulder Joint

Watch this video online: https://youtu.be/vG1XQkj3Yx0

The Elbow Joint

Watch this video online: https://youtu.be/S1Jo3Asc68g

The Hip Joint

Watch this video online: https://youtu.be/ZWcdMj8wRos

The Knee Joint

Watch this video online: https://youtu.be/ve448qTT_-4

Watch this video online: https://youtu.be/58g4nWqbHAc

The Ankle Joint

Watch this video online: https://youtu.be/lPLdoFQlZXQ

DEVELOPMENT OF JOINTS

Learning Objectives

- Describe the two processes by which mesenchyme can give rise to bone
- Discuss the process by which joints of the limbs are formed

Joints form during embryonic development in conjunction with the formation and growth of the associated bones. The embryonic tissue that gives rise to all bones, cartilages, and connective tissues of the body is called mesenchyme. In the head, mesenchyme will accumulate at those areas that will become the bones that form the top and sides of the skull. The mesenchyme in these areas will develop directly into bone through the process of intramembranous ossification, in which mesenchymal cells differentiate into bone-producing cells that then generate bone tissue. The mesenchyme between the areas of bone production will become the fibrous connective tissue that fills the spaces between the developing bones. Initially, the connective tissue-filled gaps between the bones are wide, and are called fontanelles. After birth, as the skull bones grow and enlarge, the gaps between them decrease in width and the fontanelles are reduced to suture joints in which the bones are united by a narrow layer of fibrous connective tissue.

The bones that form the base and facial regions of the skull develop through the process of endochondral ossification. In this process, mesenchyme accumulates and differentiates into hyaline cartilage, which forms a model of the future bone. The hyaline cartilage model is then gradually, over a period of many years, displaced by bone. The mesenchyme between these developing bones becomes the fibrous connective tissue of the suture joints between the bones in these regions of the skull.

A similar process of endochondral ossification gives rises to the bones and joints of the limbs. The limbs initially develop as small limb buds that appear on the sides of the embryo around the end of the fourth week of development. Starting during the sixth week, as each limb bud continues to grow and elongate, areas of mesenchyme within the bud begin to differentiate into the hyaline cartilage that will form models for of each of the future bones. The synovial joints will form between the adjacent cartilage models, in an area called the **joint interzone**. Cells at the center of this interzone region undergo cell death to form the joint cavity, while surrounding mesenchyme cells will form the articular capsule and supporting ligaments. The process of endochondral ossification, which converts the cartilage models into bone, begins by the twelfth week of embryonic development. At birth, ossification of much of the bone has occurred, but the hyaline cartilage of the epiphyseal plate will remain throughout childhood and adolescence to allow for bone lengthening. Hyaline cartilage is also retained as the articular cartilage that covers the surfaces of the bones at synovial joints.

ARTICULAR SYSTEM REVIEW GAMES

You can practice your understanding of the articular system by playing the review games on Anatomy Arcade.

GLOSSARY: JOINTS

abduction: movement in the coronal plane that moves a limb laterally away from the body; spreading of the fingers

acetabular labrum: lip of fibrocartilage that surrounds outer margin of the acetabulum on the hip bone

adduction: movement in the coronal plane that moves a limb medially toward or across the midline of the body; bringing fingers together

amphiarthrosis: slightly mobile joint

annular ligament: intrinsic ligament of the elbow articular capsule that surrounds and supports the head of the radius at the proximal radioulnar joint

anterior cruciate ligament: intracapsular ligament of the knee; extends from anterior, superior surface of the tibia to the inner aspect of the lateral condyle of the femur; resists hyperextension of knee

anterior talofibular ligament: intrinsic ligament located on the lateral side of the ankle joint, between talus bone and lateral malleolus of fibula; supports talus at the talocrural joint and resists excess inversion of the foot

articular capsule: connective tissue structure that encloses the joint cavity of a synovial joint

articular cartilage: thin layer of hyaline cartilage that covers the articulating surfaces of bones at a synovial joint

articular disc: meniscus; a fibrocartilage structure found between the bones of some synovial joints; provides padding or smooths movements between the bones; strongly unites the bones together

articulation: joint of the body

atlanto-occipital joint: articulation between the occipital condyles of the skull and the superior articular processes of the atlas (C1 vertebra)

atlantoaxial joint: series of three articulations between the atlas (C1) vertebra and the axis (C2) vertebra, consisting of the joints between the inferior articular processes of C1 and the superior articular processes of C2, and the articulation between the dens of C2 and the anterior arch of C1

ball-and-socket joint: synovial joint formed between the spherical end of one bone (the ball) that fits into the depression of a second bone (the socket); found at the hip and shoulder joints; functionally classified as a multiaxial joint

biaxial joint: type of diarthrosis; a joint that allows for movements within two planes (two axes)

bursa: connective tissue sac containing lubricating fluid that prevents friction between adjacent structures, such as skin and bone, tendons and bone, or between muscles

calcaneofibular ligament: intrinsic ligament located on the lateral side of the ankle joint, between the calcaneus bone and lateral malleolus of the fibula; supports the talus bone at the ankle joint and resists excess inversion of the foot

cartilaginous joint: joint at which the bones are united by hyaline cartilage (synchondrosis) or fibrocartilage (symphysis)

circumduction: circular motion of the arm, thigh, hand, thumb, or finger that is produced by the sequential combination of flexion, abduction, extension, and adduction

condyloid joint: synovial joint in which the shallow depression at the end of one bone receives a rounded end from a second bone or a rounded structure formed by two bones; found at the metacarpophalangeal joints of the fingers or the radiocarpal joint of the wrist; functionally classified as a biaxial joint

coracohumeral ligament: intrinsic ligament of the shoulder joint; runs from the coracoid process of the scapula to the anterior humerus

deltoid ligament: broad intrinsic ligament located on the medial side of the ankle joint; supports the talus at the talocrural joint and resists excess eversion of the foot

depression: downward (inferior) motion of the scapula or mandible

diarthrosis: freely mobile joint

dorsiflexion: movement at the ankle that brings the top of the foot toward the anterior leg

elbow joint: humeroulnar joint

elevation: upward (superior) motion of the scapula or mandible

eversion: foot movement involving the intertarsal joints of the foot in which the bottom of the foot is turned laterally, away from the midline

extension: movement in the sagittal plane that increases the angle of a joint (straightens the joint); motion involving posterior bending of the vertebral column or returning to the upright position from a flexed position

extrinsic ligament: ligament located outside of the articular capsule of a synovial joint

femoropatellar joint: portion of the knee joint consisting of the articulation between the distal femur and the patella

fibrous joint: joint where the articulating areas of the adjacent bones are connected by fibrous connective tissue

fibular collateral ligament: extrinsic ligament of the knee joint that spans from the lateral epicondyle of the femur to the head of the fibula; resists hyperextension and rotation of the extended knee

flexion: movement in the sagittal plane that decreases the angle of a joint (bends the joint); motion involving anterior bending of the vertebral column

fontanelles: expanded areas of fibrous connective tissue that separate the braincase bones of the skull prior to birth and during the first year after birth

glenohumeral joint: shoulder joint; articulation between the glenoid cavity of the scapula and head of the humerus; multiaxial ball-and-socket joint that allows for flexion/extension, abduction/adduction, circumduction, and medial/lateral rotation of the humerus

glenohumeral ligament: one of the three intrinsic ligaments of the shoulder joint that strengthen the anterior articular capsule

glenoid labrum: lip of fibrocartilage located around the outside margin of the glenoid cavity of the scapula

gomphosis: type of fibrous joint in which the root of a tooth is anchored into its bony jaw socket by strong periodontal ligaments

hinge joint: synovial joint at which the convex surface of one bone articulates with the concave surface of a second bone; includes the elbow, knee, ankle, and interphalangeal joints; functionally classified as a uniaxial joint

humeroradial joint: articulation between the capitulum of the humerus and head of the radius

humeroulnar joint: articulation between the trochlea of humerus and the trochlear notch of the ulna; uniaxial hinge joint that allows for flexion/extension of the forearm

hyperextension: excessive extension of joint, beyond the normal range of movement

hyperflexion: excessive flexion of joint, beyond the normal range of movement

iliofemoral ligament: intrinsic ligament spanning from the ilium of the hip bone to the femur, on the superior-anterior aspect of the hip joint

inferior rotation: movement of the scapula during upper limb adduction in which the glenoid cavity of the scapula moves in a downward direction as the medial end of the scapular spine moves in an upward direction

interosseous membrane: wide sheet of fibrous connective tissue that fills the gap between two parallel bones, forming a syndesmosis; found between the radius and ulna of the forearm and between the tibia and fibula of the leg

intracapsular ligament: ligament that is located within the articular capsule of a synovial joint

intrinsic ligament: ligament that is fused to or incorporated into the wall of the articular capsule of a synovial joint

inversion: foot movement involving the intertarsal joints of the foot in which the bottom of the foot is turned toward the midline

ischiofemoral ligament: intrinsic ligament spanning from the ischium of the hip bone to the femur, on the posterior aspect of the hip joint

joint cavity: space enclosed by the articular capsule of a synovial joint that is filled with synovial fluid and contains the articulating surfaces of the adjacent bones

joint interzone: site within a growing embryonic limb bud that will become a synovial joint

joint: site at which two or more bones or bone and cartilage come together (articulate)

lateral (external) rotation: movement of the arm at the shoulder joint or the thigh at the hip joint that moves the anterior surface of the limb away from the midline of the body

lateral excursion: side-to-side movement of the mandible away from the midline, toward either the right or left side

lateral flexion: bending of the neck or body toward the right or left side

lateral meniscus: C-shaped fibrocartilage articular disc located at the knee, between the lateral condyle of the femur and the lateral condyle of the tibia

lateral tibiofemoral joint: portion of the knee consisting of the articulation between the lateral condyle of the tibia and the lateral condyle of the femur; allows for flexion/extension at the knee

ligament of the head of the femur: intracapsular ligament that runs from the acetabulum of the hip bone to the head of the femur

ligament: strong band of dense connective tissue spanning between bones

medial (internal) rotation: movement of the arm at the shoulder joint or the thigh at the hip joint that brings the anterior surface of the limb toward the midline of the body

medial excursion: side-to-side movement that returns the mandible to the midline

medial meniscus: C-shaped fibrocartilage articular disc located at the knee, between the medial condyle of the femur and medial condyle of the tibia

medial tibiofemoral joint: portion of the knee consisting of the articulation between the medial condyle of the tibia and the medial condyle of the femur; allows for flexion/extension at the knee

meniscus: articular disc

multiaxial joint: type of diarthrosis; a joint that allows for movements within three planes (three axes)

opposition: thumb movement that brings the tip of the thumb in contact with the tip of a finger

patellar ligament: ligament spanning from the patella to the anterior tibia; serves as the final attachment for the quadriceps femoris muscle

periodontal ligament: band of dense connective tissue that anchors the root of a tooth into the bony jaw socket

pivot joint: synovial joint at which the rounded portion of a bone rotates within a ring formed by a ligament and an articulating bone; functionally classified as uniaxial joint

plane joint: synovial joint formed between the flattened articulating surfaces of adjacent bones; functionally classified as a multiaxial joint

plantar flexion: foot movement at the ankle in which the heel is lifted off of the ground

posterior cruciate ligament: intracapsular ligament of the knee; extends from the posterior, superior surface of the tibia to the inner aspect of the medial condyle of the femur; prevents anterior displacement of the femur when the knee is flexed and weight bearing

posterior talofibular ligament: intrinsic ligament located on the lateral side of the ankle joint, between the talus bone and lateral malleolus of the fibula; supports the talus at the talocrural joint and resists excess inversion of the foot

pronated position: forearm position in which the palm faces backward

pronation: forearm motion that moves the palm of the hand from the palm forward to the palm backward position

protraction: anterior motion of the scapula or mandible

proximal radioulnar joint: articulation between head of radius and radial notch of ulna; uniaxial pivot joint that allows for rotation of radius during pronation/supination of forearm

pubofemoral ligament: intrinsic ligament spanning from the pubis of the hip bone to the femur, on the anterior-inferior aspect of the hip joint

radial collateral ligament: intrinsic ligament on the lateral side of the elbow joint; runs from the lateral epicondyle of humerus to merge with the annular ligament

reposition: movement of the thumb from opposition back to the anatomical position (next to index finger)

retraction: posterior motion of the scapula or mandible

rotation: movement of a bone around a central axis (atlantoaxial joint) or around its long axis (proximal radioulnar joint; shoulder or hip joint); twisting of the vertebral column resulting from the summation of small motions between adjacent vertebrae

rotator cuff: strong connective tissue structure formed by the fusion of four rotator cuff muscle tendons to the articular capsule of the shoulder joint; surrounds and supports superior, anterior, lateral, and posterior sides of the humeral head

saddle joint: synovial joint in which the articulating ends of both bones are convex and concave in shape, such as at the first carpometacarpal joint at the base of the thumb; functionally classified as a biaxial joint

subacromial bursa: bursa that protects the supraspinatus muscle tendon and superior end of the humerus from rubbing against the acromion of the scapula

subcutaneous bursa: bursa that prevents friction between skin and an underlying bone

submuscular bursa: bursa that prevents friction between bone and a muscle or between adjacent muscles

subscapular bursa: bursa that prevents rubbing of the subscapularis muscle tendon against the scapula

subtalar joint: articulation between the talus and calcaneus bones of the foot; allows motions that contribute to inversion/eversion of the foot

subtendinous bursa: bursa that prevents friction between bone and a muscle tendon

superior rotation: movement of the scapula during upper limb abduction in which the glenoid cavity of the scapula moves in an upward direction as the medial end of the scapular spine moves in a downward direction

supinated position: forearm position in which the palm faces anteriorly (anatomical position)

supination: forearm motion that moves the palm of the hand from the palm backward to the palm forward position

suture: fibrous joint that connects the bones of the skull (except the mandible); an immobile joint (synarthrosis)

symphysis: type of cartilaginous joint where the bones are joined by fibrocartilage

synarthrosis: immobile or nearly immobile joint

synchondrosis: type of cartilaginous joint where the bones are joined by hyaline cartilage

syndesmosis: type of fibrous joint in which two separated, parallel bones are connected by an interosseous membrane

synostosis: site at which adjacent bones or bony components have fused together

synovial fluid: thick, lubricating fluid that fills the interior of a synovial joint

synovial joint: joint at which the articulating surfaces of the bones are located within a joint cavity formed by an articular capsule

synovial membrane: thin layer that lines the inner surface of the joint cavity at a synovial joint; produces the synovial fluid

talocrural joint: ankle joint; articulation between the talus bone of the foot and medial malleolus of the tibia, distal tibia, and lateral malleolus of the fibula; a uniaxial hinge joint that allows only for dorsiflexion and plantar flexion of the foot

temporomandibular joint (TMJ): articulation between the condyle of the mandible and the mandibular fossa and articular tubercle of the temporal bone of the skull; allows for depression/elevation (opening/closing of mouth), protraction/retraction, and side-to-side motions of the mandible

tendon sheath: connective tissue that surrounds a tendon at places where the tendon crosses a joint; contains a lubricating fluid to prevent friction and allow smooth movements of the tendon

tendon: dense connective tissue structure that anchors a muscle to bone

tibial collateral ligament: extrinsic ligament of knee joint that spans from the medial epicondyle of the femur to the medial tibia; resists hyperextension and rotation of extended knee

ulnar collateral ligament: intrinsic ligament on the medial side of the elbow joint; spans from the medial epicondyle of the humerus to the medial ulna

uniaxial joint: type of diarthrosis; joint that allows for motion within only one plane (one axis)

zygapophysial joints: facet joints; plane joints between the superior and inferior articular processes of adjacent vertebrae that provide for only limited motions between the vertebrae

PRACTICE TEST: JOINTS

Review the material from this module by completing the practice in course online.

JOINTS AND MOVEMENT WORKSHEET

Access the Joints and Movement Worksheet here: http://provihod.wikispaces.com/file/view/Joints+%26+Movement+Worksheet.pdf

MODULE 11: MUSCLE TISSUE

INTRODUCTION TO MUSCLE TISSUE

Learning Objectives

- Explain the organization of muscle tissue
- Describe the function and structure of skeletal, cardiac muscle, and smooth muscle
- Explain how muscles work with tendons to move the body
- Describe how muscles contract and relax
- Define the process of muscle metabolism
- Explain how the nervous system controls muscle tension
- Relate the connections between exercise and muscle performance
- Explain the development and regeneration of muscle tissue

When most people think of muscles, they think of the muscles that are visible just under the skin, particularly of the limbs. These are skeletal muscles, so-named because most of them move the skeleton. But there are two other types of muscle in the body, with distinctly different jobs.

Cardiac muscle, found in the heart, is concerned with pumping blood through the circulatory system. Smooth muscle is concerned with various involuntary movements, such as having one's hair stand on end when cold or frightened, or moving food through the digestive system. This chapter will examine the structure and function of these three types of muscles.

Figure 1. Tennis Player. *Athletes rely on toned skeletal muscles to supply the force required for movement. (credit: Emmanuel Huybrechts/flickr)*

TYPES OF MUSCLE TISSUES

Learning Objectives

- Describe the different types of muscle
- Explain contractibility and extensibility

Muscle is one of the four primary tissue types of the body, and the body contains three types of muscle tissue: skeletal muscle, cardiac muscle, and smooth muscle (Figure 1). All three muscle tissues have some properties in common; they all exhibit a quality called **excitability** as their plasma membranes can change their electrical states (from polarized to depolarized) and send an electrical wave called an action potential along the entire length of the membrane. While the nervous system can influence the excitability of cardiac and smooth muscle to some degree, skeletal muscle completely depends on signaling from the nervous system to work properly. On the other hand, both cardiac muscle and smooth muscle can respond to other stimuli, such as hormones and local stimuli.

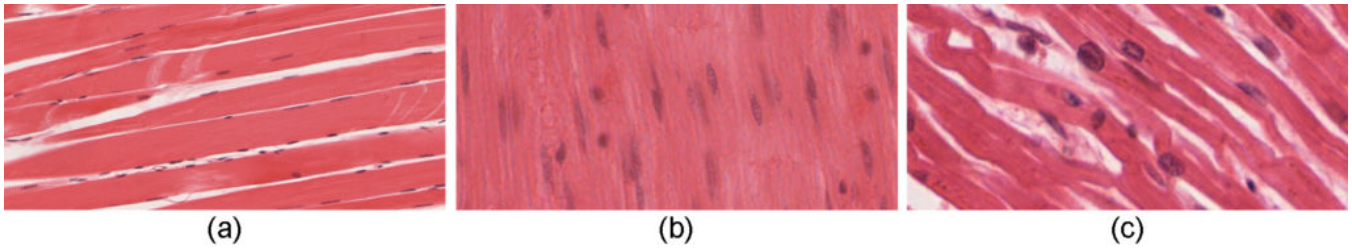


Figure 1. The Three Types of Muscle Tissue. *The body contains three types of muscle tissue: (a) skeletal muscle, (b) smooth muscle, and (c) cardiac muscle. From top, LM × 1600, LM × 1600, LM × 1600. (Micrographs provided by the Regents of University of Michigan Medical School © 2012)*

The muscles all begin the actual process of contracting (shortening) when a protein called actin is pulled by a protein called myosin. This occurs in striated muscle (skeletal and cardiac) after specific binding sites on the actin have been exposed in response to the interaction between calcium ions (Ca^{++}) and proteins (troponin and tropomyosin) that "shield" the actin-binding sites. Ca^{++} also is required for the contraction of smooth muscle, although its role is different: here Ca^{++} activates enzymes, which in turn activate myosin heads. All muscles require adenosine triphosphate (ATP) to continue the process of contracting, and they all relax when the Ca^{++} is removed and the actin-binding sites are re-shielded.

A muscle can return to its original length when relaxed due to a quality of muscle tissue called **elasticity**. It can recoil back to its original length due to elastic fibers. Muscle tissue also has the quality of **extensibility**; it can stretch or extend. **Contractility** allows muscle tissue to pull on its attachment points and shorten with force.

Differences among the three muscle types include the microscopic organization of their contractile proteins—actin and myosin. The actin and myosin proteins are arranged very regularly in the cytoplasm of individual muscle cells (referred to as fibers) in both skeletal muscle and cardiac muscle, which creates a pattern, or stripes, called striations. The striations are visible with a light microscope under high magnification (see Figure 1). **Skeletal muscle** fibers are multinucleated structures that compose the skeletal muscle. **Cardiac muscle** fibers each have one to two nuclei and are physically and electrically connected to each other so that the entire heart contracts as one unit (called a syncytium).

Because the actin and myosin are not arranged in such regular fashion in **smooth muscle**, the cytoplasm of a smooth muscle fiber (which has only a single nucleus) has a uniform, nonstriated appearance (resulting in the name smooth muscle). However, the less organized appearance of smooth muscle should not be interpreted as less efficient. Smooth muscle in the walls of arteries is a critical component that regulates blood pressure

necessary to push blood through the circulatory system; and smooth muscle in the skin, visceral organs, and internal passageways is essential for moving all materials through the body.

SKELETAL MUSCLE

Learning Objectives

- Describe the layers of connective tissues packaging skeletal muscle
- Explain how muscles work with tendons to move the body
- Identify areas of the skeletal muscle fibers
- Describe excitation-contraction coupling

The best-known feature of skeletal muscle is its ability to contract and cause movement. Skeletal muscles act not only to produce movement but also to stop movement, such as resisting gravity to maintain posture. Small, constant adjustments of the skeletal muscles are needed to hold a body upright or balanced in any position. Muscles also prevent excess movement of the bones and joints, maintaining skeletal stability and preventing skeletal structure damage or deformation. Joints can become misaligned or dislocated entirely by pulling on the associated bones; muscles work to keep joints stable. Skeletal muscles are located throughout the body at the openings of internal tracts to control the movement of various substances. These muscles allow functions, such as swallowing, urination, and defecation, to be under voluntary control. Skeletal muscles also protect internal organs (particularly abdominal and pelvic organs) by acting as an external barrier or shield to external trauma and by supporting the weight of the organs.

Skeletal muscles contribute to the maintenance of homeostasis in the body by generating heat. Muscle contraction requires energy, and when ATP is broken down, heat is produced. This heat is very noticeable during exercise, when sustained muscle movement causes body temperature to rise, and in cases of extreme cold, when shivering produces random skeletal muscle contractions to generate heat.

Each skeletal muscle is an organ that consists of various integrated tissues. These tissues include the skeletal muscle fibers, blood vessels, nerve fibers, and connective tissue. Each skeletal muscle has three layers of connective tissue (called “mysia”) that enclose it and provide structure to the muscle as a whole, and also compartmentalize the muscle fibers within the muscle (Figure 1). Each muscle is wrapped in a sheath of dense, irregular connective tissue called the **epimysium**, which allows a muscle to contract and move powerfully while maintaining its structural integrity. The epimysium also separates muscle from other tissues and organs in the area, allowing the muscle to move independently.

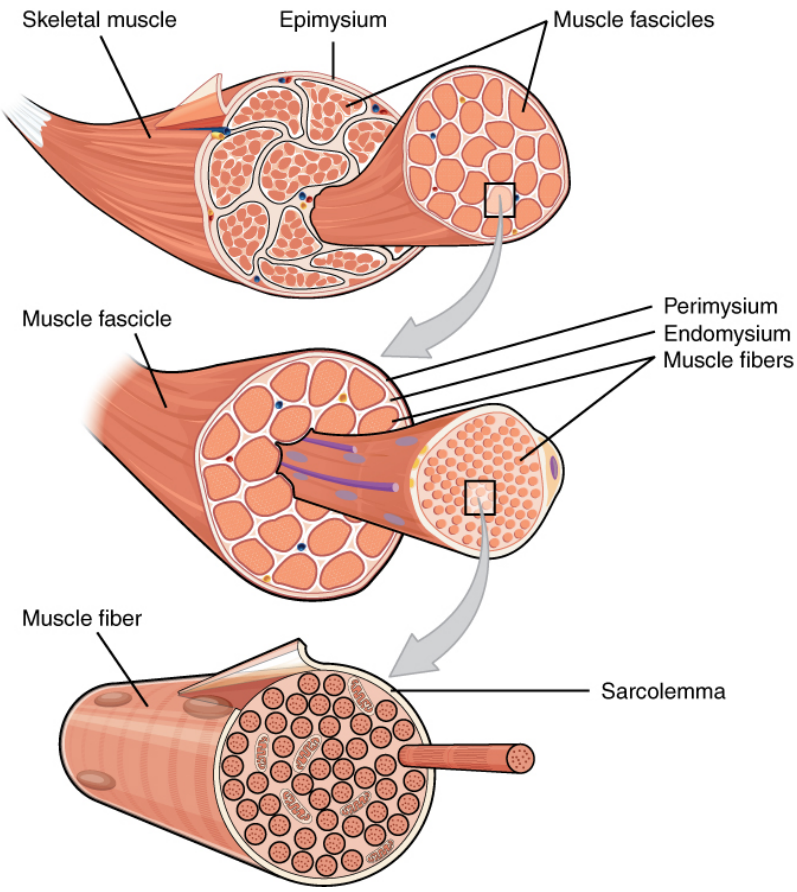


Figure 1. The Three Connective Tissue Layers. *Bundles of muscle fibers, called fascicles, are covered by the perimysium. Muscle fibers are covered by the endomysium.*

Inside each skeletal muscle, muscle fibers are organized into individual bundles, each called a **fascicle**, by a middle layer of connective tissue called the **perimysium**. This fascicular organization is common in muscles of the limbs; it allows the nervous system to trigger a specific movement of a muscle by activating a subset of muscle fibers within a bundle, or fascicle of the muscle. Inside each fascicle, each muscle fiber is encased in a thin connective tissue layer of collagen and reticular fibers called the **endomysium**. The endomysium contains the extracellular fluid and nutrients to support the muscle fiber. These nutrients are supplied via blood to the muscle tissue.

In skeletal muscles that work with tendons to pull on bones, the collagen in the three tissue layers (the mysia) intertwines with the collagen of a tendon. At the other end of the tendon, it fuses with the periosteum coating the bone. The tension created by contraction of the muscle fibers is then transferred though the mysia, to the tendon, and then to the periosteum to pull on the bone for movement of the skeleton. In other places, the mysia may fuse with a broad, tendon-like sheet called an **aponeurosis**, or to fascia, the connective tissue between skin and bones. The broad sheet of connective tissue in the lower back that the latissimus dorsi muscles (the “lats”) fuse into is an example of an aponeurosis.

Every skeletal muscle is also richly supplied by blood vessels for nourishment, oxygen delivery, and waste removal. In addition, every muscle fiber in a skeletal muscle is supplied by the axon branch of a somatic motor neuron, which signals the fiber to contract. Unlike cardiac and smooth muscle, the only way to functionally contract a skeletal muscle is through signaling from the nervous system.

Skeletal Muscle Fibers

Because skeletal muscle cells are long and cylindrical, they are commonly referred to as muscle fibers. Skeletal muscle fibers can be quite large for human cells, with diameters up to 100 μm and lengths up to 30 cm (11.8 in) in the Sartorius of the upper leg. During early development, embryonic myoblasts, each with its own nucleus, fuse with up to hundreds of other myoblasts to form the multinucleated skeletal muscle fibers. Multiple nuclei mean multiple copies of genes, permitting the production of the large amounts of proteins and enzymes needed for muscle contraction.

Some other terminology associated with muscle fibers is rooted in the Greek *sarco*, which means "flesh." The plasma membrane of muscle fibers is called the **sarcolemma**, the cytoplasm is referred to as **sarcoplasm**, and the specialized smooth endoplasmic reticulum, which stores, releases, and retrieves calcium ions (Ca^{++}) is called the **sarcoplasmic reticulum (SR)** (Figure 2). As will soon be described, the functional unit of a skeletal muscle fiber is the sarcomere, a highly organized arrangement of the contractile myofilaments **actin** (thin filament) and **myosin** (thick filament), along with other support proteins.

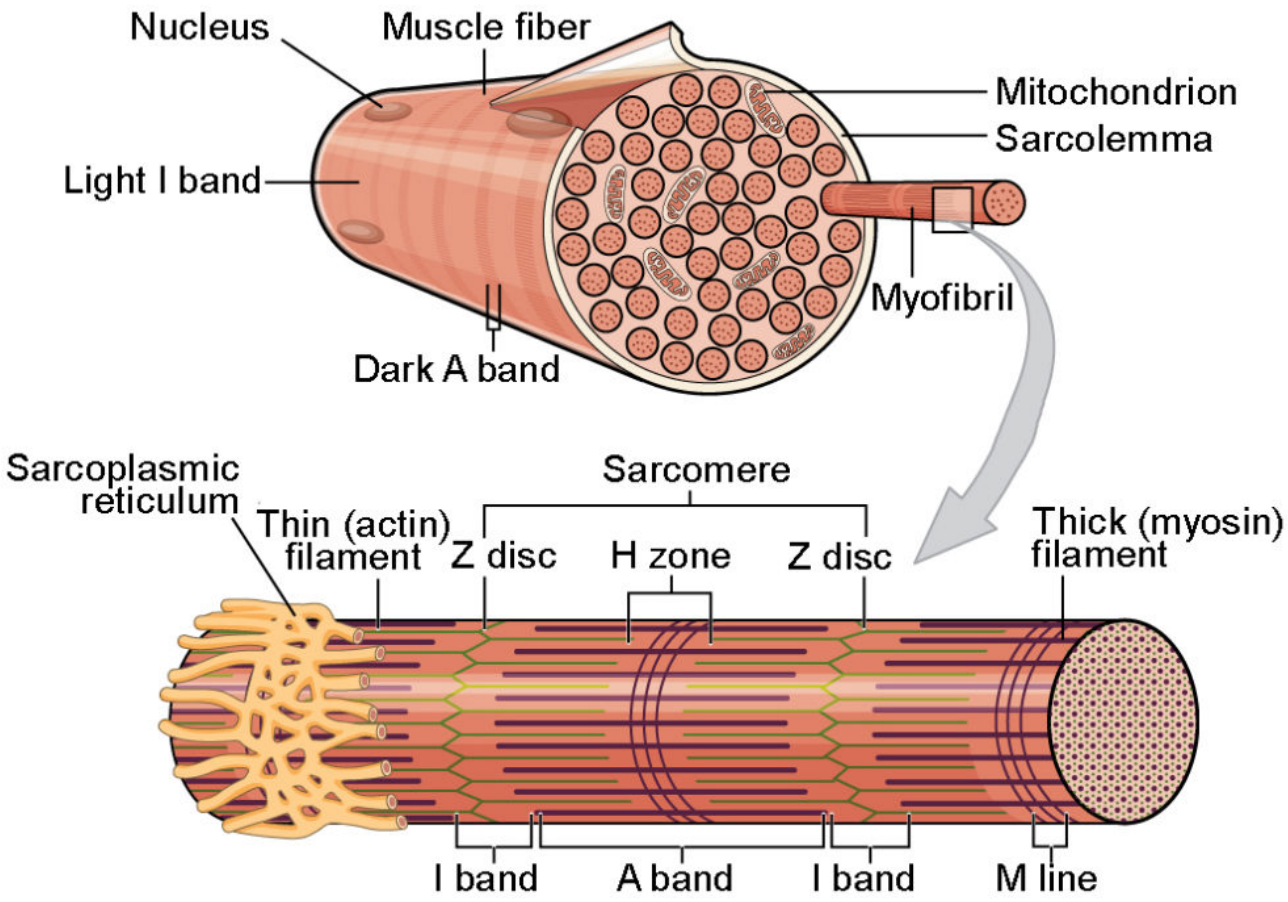


Figure 2. Muscle Fiber. *A skeletal muscle fiber is surrounded by a plasma membrane called the sarcolemma, which contains sarcoplasm, the cytoplasm of muscle cells. A muscle fiber is composed of many fibrils, which give the cell its striated appearance.*

The Sarcomere

The striated appearance of skeletal muscle fibers is due to the arrangement of the myofilaments of actin and myosin in sequential order from one end of the muscle fiber to the other. Each packet of these microfilaments and their regulatory proteins, **troponin** and **tropomyosin** (along with other proteins) is called a **sarcomere**.

> Watch this video to learn more about macro- and microstructures of skeletal muscles. (a) What are the names of the "junction points" between sarcomeres? (b) What are the names of the "subunits" within the myofibrils that run the length of skeletal muscle fibers? (c) What is the "double strand of pearls" described in the video? (d) What gives a skeletal muscle fiber its striated appearance?

The sarcomere is the functional unit of the muscle fiber. The sarcomere itself is bundled within the myofibril that runs the entire length of the muscle fiber and attaches to the sarcolemma at its end. As myofibrils contract, the entire muscle cell contracts. Because myofibrils are only approximately 1.2 μm in diameter, hundreds to thousands (each with thousands of sarcomeres) can be found inside one muscle fiber. Each sarcomere is approximately 2 μm in length with a three-dimensional cylinder-like arrangement and is bordered by structures

called Z-discs (also called Z-lines, because pictures are two-dimensional), to which the actin myofilaments are anchored (Figure 3). Because the actin and its troponin-tropomyosin complex (projecting from the Z-discs toward the center of the sarcomere) form strands that are thinner than the myosin, it is called the **thin filament** of the sarcomere. Likewise, because the myosin strands and their multiple heads (projecting from the center of the sarcomere, toward but not all to way to, the Z-discs) have more mass and are thicker, they are called the **thick filament** of the sarcomere.

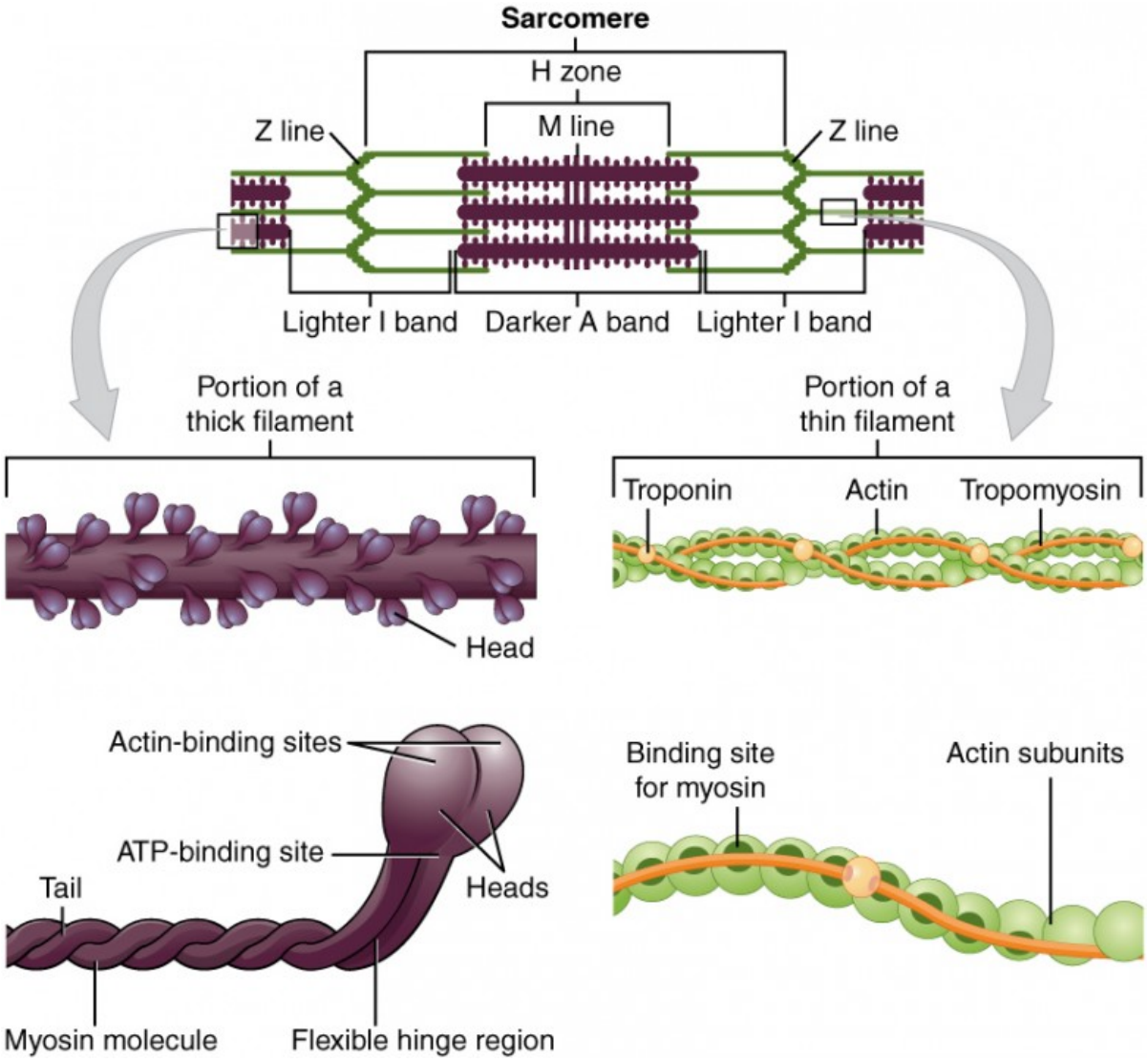


Figure 3. The Sarcomere. *The sarcomere, the region from one Z-line to the next Z-line, is the functional unit of a skeletal muscle fiber.*

The Neuromuscular Junction

Another specialization of the skeletal muscle is the site where a motor neuron's terminal meets the muscle fiber—called the **neuromuscular junction (NMJ)**. This is where the muscle fiber first responds to signaling by the motor neuron. Every skeletal muscle fiber in every skeletal muscle is innervated by a motor neuron at the NMJ. Excitation signals from the neuron are the only way to functionally activate the fiber to contract.

Every skeletal muscle fiber is supplied by a motor neuron at the NMJ. Watch this video to learn more about what happens at the NMJ. (a) What is the definition of a motor unit? (b) What is the structural and functional difference between a large motor unit and a small motor unit? (c) Can you give an example of each? (d) Why is the neurotransmitter acetylcholine degraded after binding to its receptor?

Excitation-Contraction Coupling

All living cells have membrane potentials, or electrical gradients across their membranes. The inside of the membrane is usually around -60 to -90 mV, relative to the outside. This is referred to as a cell's membrane potential. Neurons and muscle cells can use their membrane potentials to generate electrical signals. They do this by controlling the movement of charged particles, called ions, across their membranes to create electrical currents. This is achieved by opening and closing specialized proteins in the membrane called ion channels. Although the currents generated by ions moving through these channel proteins are very small, they form the basis of both neural signaling and muscle contraction.

Both neurons and skeletal muscle cells are electrically excitable, meaning that they are able to generate action potentials. An action potential is a special type of electrical signal that can travel along a cell membrane as a wave. This allows a signal to be transmitted quickly and faithfully over long distances.

Although the term **excitation-contraction coupling** confuses or scares some students, it comes down to this: for a skeletal muscle fiber to contract, its membrane must first be "excited"—in other words, it must be stimulated to fire an action potential. The muscle fiber action potential, which sweeps along the sarcolemma as a wave, is "coupled" to the actual contraction through the release of calcium ions (Ca^{++}) from the SR. Once released, the Ca^{++} interacts with the shielding proteins, forcing them to move aside so that the actin-binding sites are available for attachment by myosin heads. The myosin then pulls the actin filaments toward the center, shortening the muscle fiber.

In skeletal muscle, this sequence begins with signals from the somatic motor division of the nervous system. In other words, the "excitation" step in skeletal muscles is always triggered by signaling from the nervous system (Figure 4).

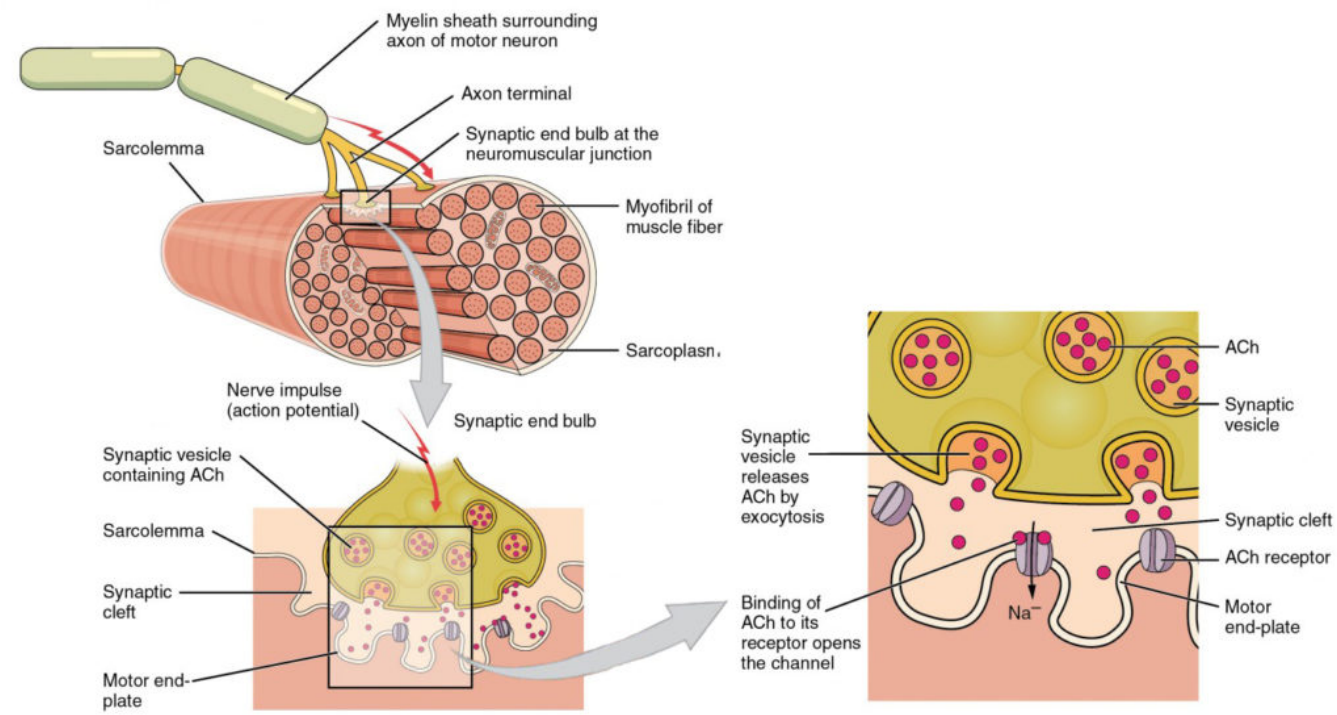


Figure 4. Motor End-Plate and Innervation. *At the NMJ, the axon terminal releases ACh. The motor end-plate is the location of the ACh-receptors in the muscle fiber sarcolemma. When ACh molecules are released, they diffuse across a minute space called the synaptic cleft and bind to the receptors.*

The motor neurons that tell the skeletal muscle fibers to contract originate in the spinal cord, with a smaller number located in the brainstem for activation of skeletal muscles of the face, head, and neck. These neurons have long processes, called axons, which are specialized to transmit action potentials long distances— in this

case, all the way from the spinal cord to the muscle itself (which may be up to three feet away). The axons of multiple neurons bundle together to form nerves, like wires bundled together in a cable.

Signaling begins when a neuronal **action potential** travels along the axon of a motor neuron, and then along the individual branches to terminate at the NMJ. At the NMJ, the axon terminal releases a chemical messenger, or **neurotransmitter**, called **acetylcholine (ACh)**. The ACh molecules diffuse across a minute space called the **synaptic cleft** and bind to ACh receptors located within the **motor end-plate** of the sarcolemma on the other side of the synapse. Once ACh binds, a channel in the ACh receptor opens and positively charged ions can pass through into the muscle fiber, causing it to **depolarize**, meaning that the membrane potential of the muscle fiber becomes less negative (closer to zero.)

As the membrane depolarizes, another set of ion channels called **voltage-gated sodium channels** are triggered to open. Sodium ions enter the muscle fiber, and an action potential rapidly spreads (or "fires") along the entire membrane to initiate excitation-contraction coupling.

Things happen very quickly in the world of excitable membranes (just think about how quickly you can snap your fingers as soon as you decide to do it). Immediately following depolarization of the membrane, it repolarizes, re-establishing the negative membrane potential. Meanwhile, the ACh in the synaptic cleft is degraded by the enzyme acetylcholinesterase (AChE) so that the ACh cannot rebind to a receptor and reopen its channel, which would cause unwanted extended muscle excitation and contraction.

Propagation of an action potential along the sarcolemma is the excitation portion of excitation-contraction coupling. Recall that this excitation actually triggers the release of calcium ions (Ca^{++}) from its storage in the cell's SR. For the action potential to reach the membrane of the SR, there are periodic invaginations in the sarcolemma, called **T-tubules** ("T" stands for "transverse"). You will recall that the diameter of a muscle fiber can be up to 100 μm, so these T-tubules ensure that the membrane can get close to the SR in the sarcoplasm. The arrangement of a T-tubule with the membranes of SR on either side is called a **triad** (Figure 5). The triad surrounds the cylindrical structure called a **myofibril**, which contains actin and myosin.

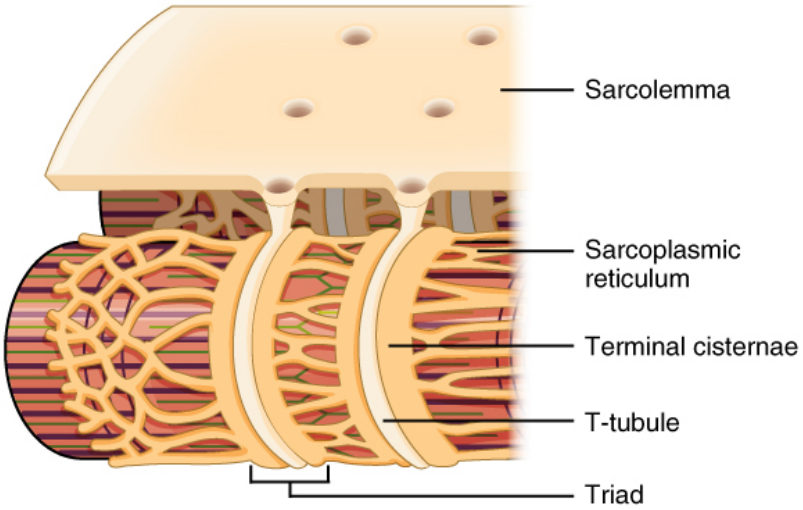


Figure 5. The T-tubule. *Narrow T-tubules permit the conduction of electrical impulses. The SR functions to regulate intracellular levels of calcium. Two terminal cisternae (where enlarged SR connects to the T-tubule) and one T-tubule comprise a triad—a "threesome" of membranes, with those of SR on two sides and the T-tubule sandwiched between them.*

The T-tubules carry the action potential into the interior of the cell, which triggers the opening of calcium channels in the membrane of the adjacent SR, causing Ca^{++} to diffuse out of the SR and into the sarcoplasm. It is the arrival of Ca^{++} in the sarcoplasm that initiates contraction of the muscle fiber by its contractile units, or sarcomeres.

MUSCLE FIBER CONTRACTION AND RELAXATION

Learning Objectives

- Describe the components involved in a muscle contraction
- Explain how muscles contract and relax
- Describe the sliding filament model of muscle contraction

The sequence of events that result in the contraction of an individual muscle fiber begins with a signal—the neurotransmitter, ACh—from the motor neuron innervating that fiber. The local membrane of the fiber will depolarize as positively charged sodium ions (Na^+) enter, triggering an action potential that spreads to the rest of the membrane will depolarize, including the T-tubules. This triggers the release of calcium ions (Ca^{++}) from storage in the sarcoplasmic reticulum (SR). The Ca^{++} then initiates contraction, which is sustained by ATP (Figure 1). As long as Ca^{++} ions remain in the sarcoplasm to bind to troponin, which keeps the actin-binding sites "unshielded," and as long as ATP is available to drive the cross-bridge cycling and the pulling of actin strands by myosin, the muscle fiber will continue to shorten to an anatomical limit.

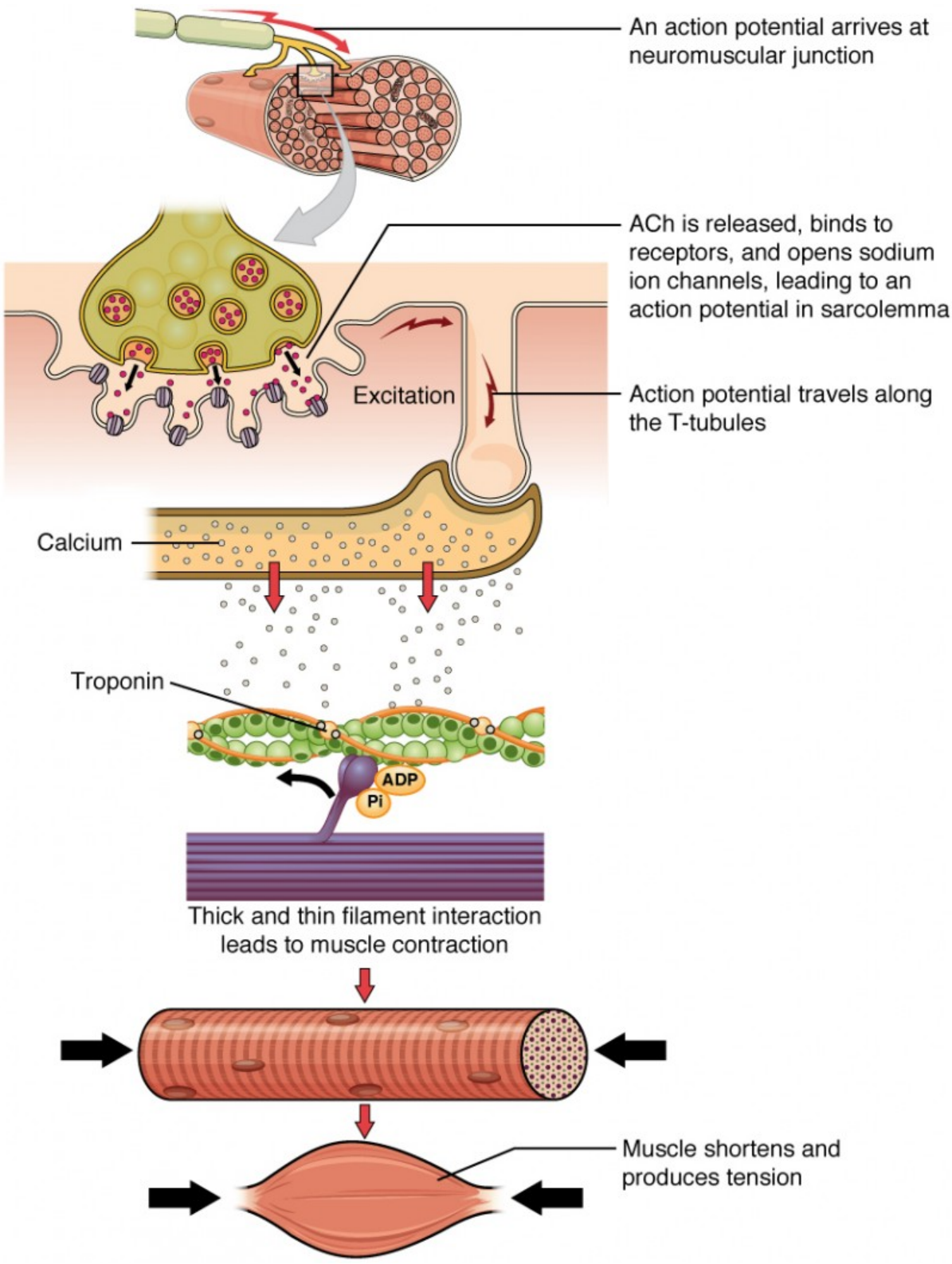


Figure 1. Contraction of a Muscle Fiber*. A cross-bridge forms between actin and the myosin heads triggering contraction. As long as Ca^{++} ions remain in the sarcoplasm to bind to troponin, and as long as ATP is available, the muscle fiber will continue to shorten.*

Muscle contraction usually stops when signaling from the motor neuron ends, which repolarizes the sarcolemma and T-tubules, and closes the voltage-gated calcium channels in the SR. Ca^{++} ions are then pumped back into

the SR, which causes the tropomyosin to reshield (or re-cover) the binding sites on the actin strands. A muscle also can stop contracting when it runs out of ATP and becomes fatigued (Figure 2).

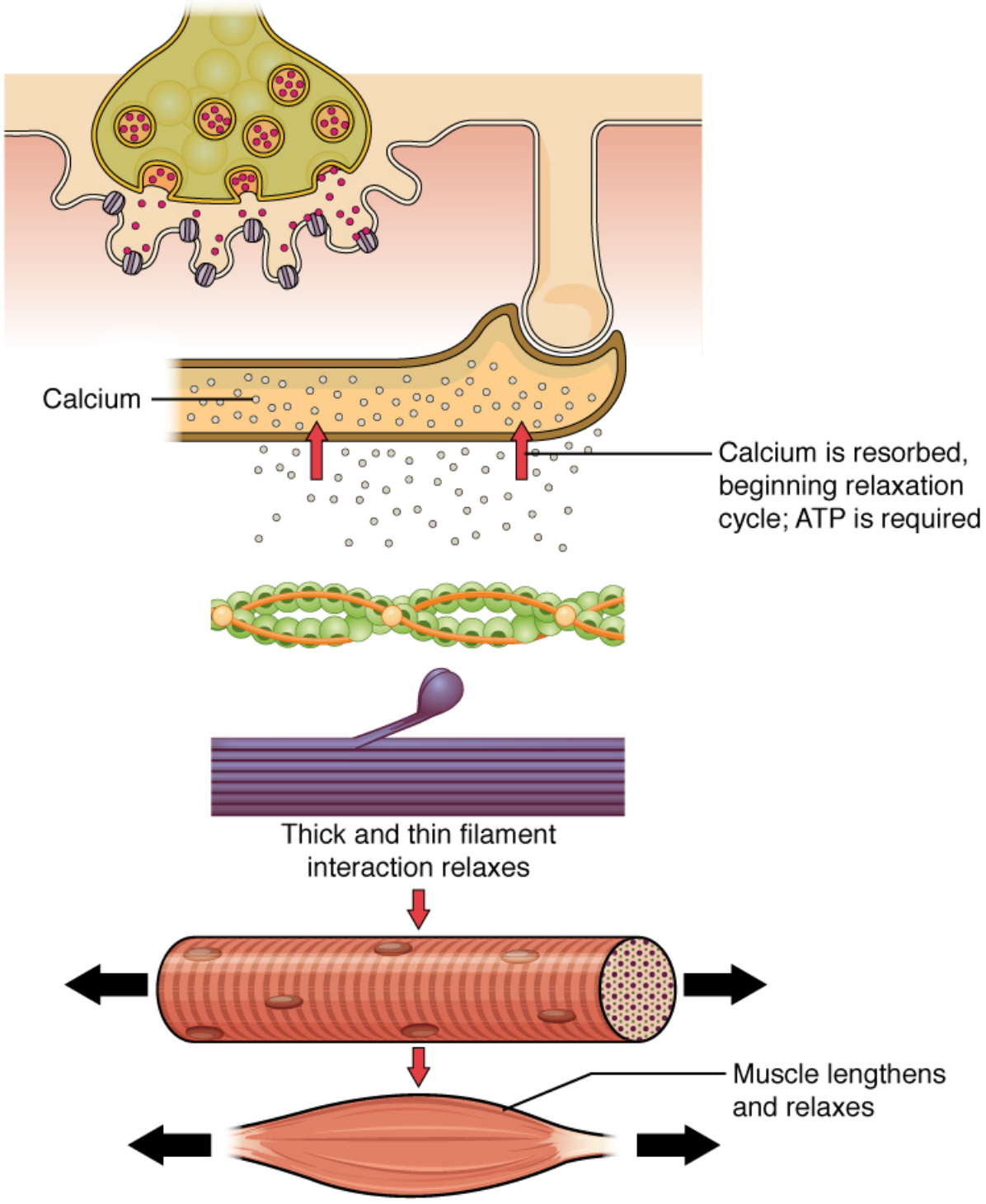


Figure 2. Relaxation of a Muscle Fiber. *Ca^{++} ions are pumped back into the SR, which causes the tropomyosin to reshield the binding sites on the actin strands. A muscle may also stop contracting when it runs out of ATP and becomes fatigued.*

The release of calcium ions initiates muscle contractions. Watch this video to learn more about the role of calcium. (a) What are “T-tubules” and what is their role? (b) Please describe how actin-binding sites are made available for cross-bridging with myosin heads during contraction.

The molecular events of muscle fiber shortening occur within the fiber's sarcomeres (see Figure 3). The contraction of a striated muscle fiber occurs as the sarcomeres, linearly arranged within myofibrils, shorten as myosin heads pull on the actin filaments.

The region where thick and thin filaments overlap has a dense appearance, as there is little space between the filaments. This zone where thin and thick filaments overlap is very important to muscle contraction, as it is the site where filament movement starts. Thin filaments, anchored at their ends by the Z-discs, do not extend completely into the central region that only contains thick filaments, anchored at their bases at a spot called the M-line. A myofibril is composed of many sarcomeres running along its length; thus, myofibrils and muscle cells contract as the sarcomeres contract.

The Sliding Filament Model of Contraction

When signaled by a motor neuron, a skeletal muscle fiber contracts as the thin filaments are pulled and then slide past the thick filaments within the fiber's sarcomeres. This process is known as the sliding filament model of muscle contraction (Figure 3). The sliding can only occur when myosin-binding sites on the actin filaments are exposed by a series of steps that begins with Ca^{++} entry into the sarcoplasm.

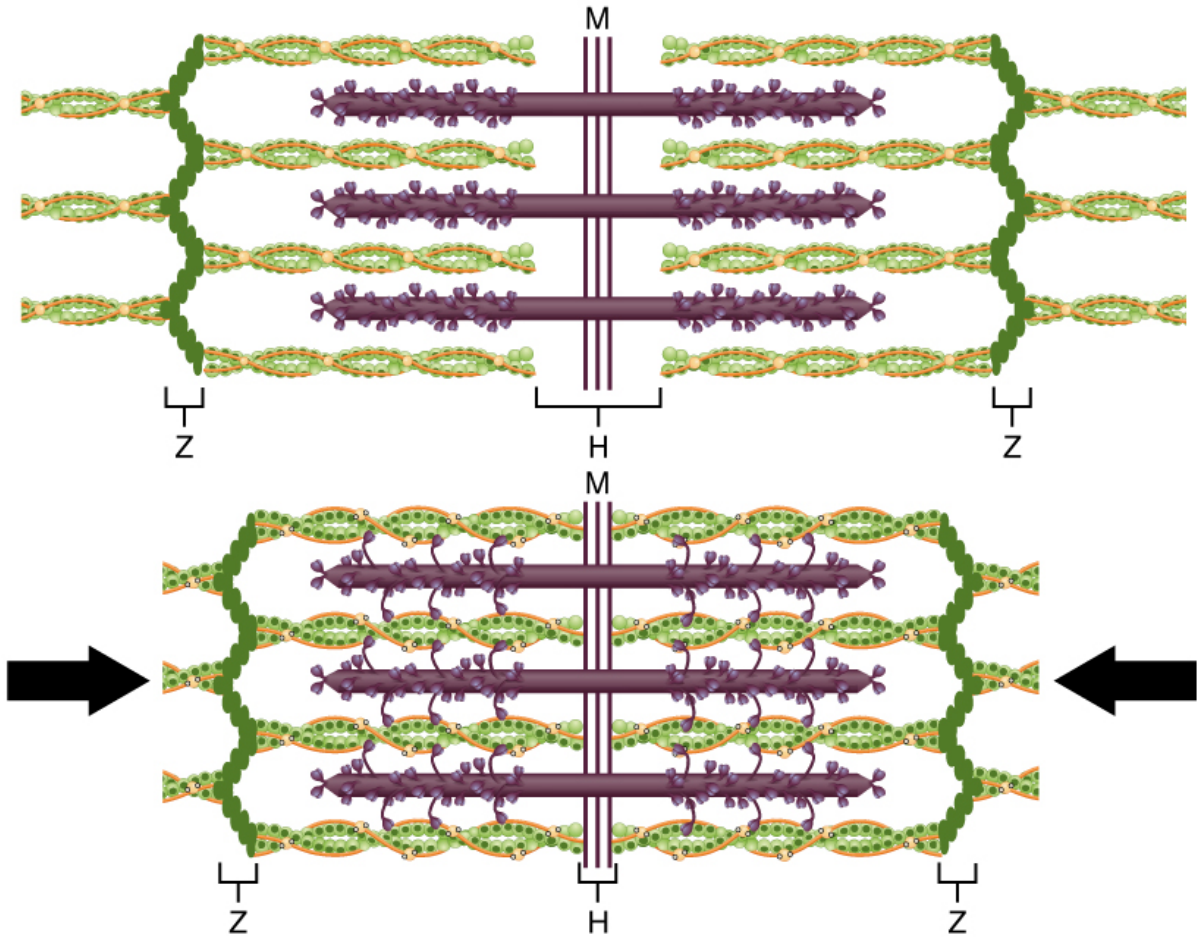


Figure 3. The Sliding Filament Model of Muscle Contraction. *When a sarcomere contracts, the Z lines move closer together, and the I band becomes smaller. The A band stays the same width. At full contraction, the thin and thick filaments overlap.*

Tropomyosin is a protein that winds around the chains of the actin filament and covers the myosin-binding sites to prevent actin from binding to myosin. Tropomyosin binds to troponin to form a troponin-tropomyosin complex. The troponin-tropomyosin complex prevents the myosin "heads" from binding to the active sites on the actin microfilaments. Troponin also has a binding site for Ca^{++} ions.

To initiate muscle contraction, tropomyosin has to expose the myosin-binding site on an actin filament to allow cross-bridge formation between the actin and myosin microfilaments. The first step in the process of contraction is for Ca^{++} to bind to troponin so that tropomyosin can slide away from the binding sites on the actin strands. This allows the myosin heads to bind to these exposed binding sites and form cross-bridges. The thin filaments are then pulled by the myosin heads to slide past the thick filaments toward the center of the sarcomere. But each head can only pull a very short distance before it has reached its limit and must be “re-cocked” before it can pull again, a step that requires ATP.

ATP and Muscle Contraction

For thin filaments to continue to slide past thick filaments during muscle contraction, myosin heads must pull the actin at the binding sites, detach, re-cock, attach to more binding sites, pull, detach, re-cock, etc. This repeated movement is known as the cross-bridge cycle. This motion of the myosin heads is similar to the oars when an individual rows a boat: The paddle of the oars (the myosin heads) pull, are lifted from the water (detach), repositioned (re-cocked) and then immersed again to pull (Figure 4). Each cycle requires energy, and the action of the myosin heads in the sarcomeres repetitively pulling on the thin filaments also requires energy, which is provided by ATP.

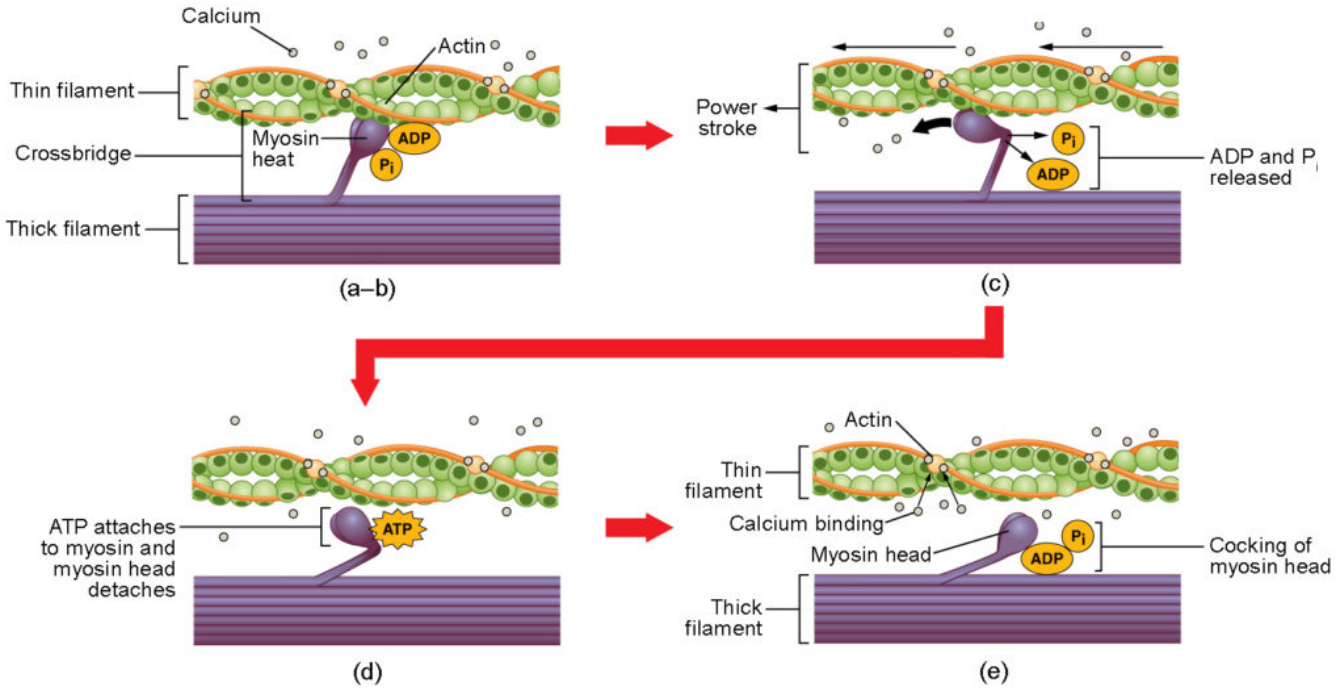


Figure 4. Skeletal Muscle Contraction. *(a) The active site on actin is exposed as calcium binds to troponin. (b) The myosin head is attracted to actin, and myosin binds actin at its actin-binding site, forming the cross-bridge. (c) During the power stroke, the phosphate generated in the previous contraction cycle is released. This results in the myosin head pivoting toward the center of the sarcomere, after which the attached ADP and phosphate group are released. (d) A new molecule of ATP attaches to the myosin head, causing the cross-bridge to detach. (e) The myosin head hydrolyzes ATP to ADP and phosphate, which returns the myosin to the cocked position.*

Cross-bridge formation occurs when the myosin head attaches to the actin while adenosine diphosphate (ADP) and inorganic phosphate (P_i) are still bound to myosin (Figure 4a,b). P_i is then released, causing myosin to form a stronger attachment to the actin, after which the myosin head moves toward the M-line, pulling the actin along with it. As actin is pulled, the filaments move approximately 10 nm toward the M-line. This movement is called the **power stroke**, as movement of the thin filament occurs at this step (Figure 4c). In the absence of ATP, the myosin head will not detach from actin.

One part of the myosin head attaches to the binding site on the actin, but the head has another binding site for ATP. ATP binding causes the myosin head to detach from the actin (Figure 4d). After this occurs, ATP is

converted to ADP and P_i by the intrinsic **ATPase** activity of myosin. The energy released during ATP hydrolysis changes the angle of the myosin head into a cocked position (Figure 4e). The myosin head is now in position for further movement.

When the myosin head is cocked, myosin is in a high-energy configuration. This energy is expended as the myosin head moves through the power stroke, and at the end of the power stroke, the myosin head is in a low-energy position. After the power stroke, ADP is released; however, the formed cross-bridge is still in place, and actin and myosin are bound together. As long as ATP is available, it readily attaches to myosin, the cross-bridge cycle can recur, and muscle contraction can continue.

Note that each thick filament of roughly 300 myosin molecules has multiple myosin heads, and many cross-bridges form and break continuously during muscle contraction. Multiply this by all of the sarcomeres in one myofibril, all the myofibrils in one muscle fiber, and all of the muscle fibers in one skeletal muscle, and you can understand why so much energy (ATP) is needed to keep skeletal muscles working. In fact, it is the loss of ATP that results in the rigor mortis observed soon after someone dies. With no further ATP production possible, there is no ATP available for myosin heads to detach from the actin-binding sites, so the cross-bridges stay in place, causing the rigidity in the skeletal muscles.

Sources of ATP

ATP supplies the energy for muscle contraction to take place. In addition to its direct role in the cross-bridge cycle, ATP also provides the energy for the active-transport Ca^{++} pumps in the SR. Muscle contraction does not occur without sufficient amounts of ATP. The amount of ATP stored in muscle is very low, only sufficient to power a few seconds worth of contractions. As it is broken down, ATP must therefore be regenerated and replaced quickly to allow for sustained contraction. There are three mechanisms by which ATP can be regenerated: creatine phosphate metabolism, anaerobic glycolysis, fermentation and aerobic respiration.

Creatine phosphate is a molecule that can store energy in its phosphate bonds. In a resting muscle, excess ATP transfers its energy to creatine, producing ADP and creatine phosphate. This acts as an energy reserve that can be used to quickly create more ATP. When the muscle starts to contract and needs energy, creatine phosphate transfers its phosphate back to ADP to form ATP and creatine. This reaction is catalyzed by the enzyme creatine kinase and occurs very quickly; thus, creatine phosphate-derived ATP powers the first few seconds of muscle contraction. However, creatine phosphate can only provide approximately 15 seconds worth of energy, at which point another energy source has to be used (Figure 5).

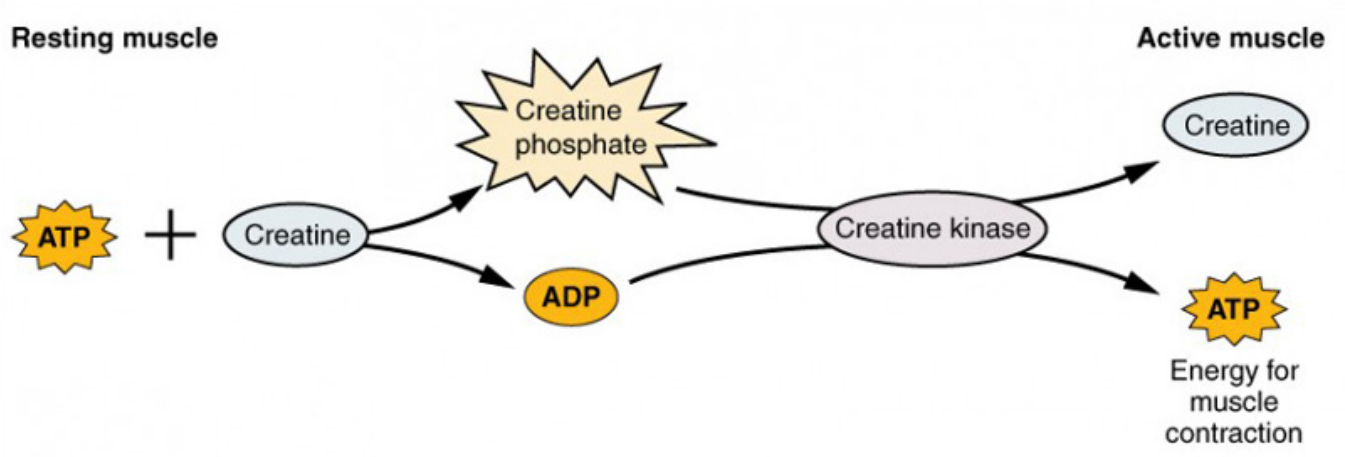


Figure 5. Muscle Metabolism. *Some ATP is stored in a resting muscle. As contraction starts, it is used up in seconds. More ATP is generated from creatine phosphate for about 15 seconds.*

As the ATP produced by creatine phosphate is depleted, muscles turn to glycolysis as an ATP source. **Glycolysis** is an anaerobic (non-oxygen-dependent) process that breaks down glucose (sugar) to produce ATP; however, glycolysis cannot generate ATP as quickly as creatine phosphate. Thus, the switch to glycolysis results in a slower rate of ATP availability to the muscle. The sugar used in glycolysis can be provided by blood glucose or by metabolizing glycogen that is stored in the muscle. The breakdown of one glucose molecule

produces two ATP and two molecules of **pyruvic acid**, which can be used in aerobic respiration or when oxygen levels are low, converted to lactic acid (Figure 6).

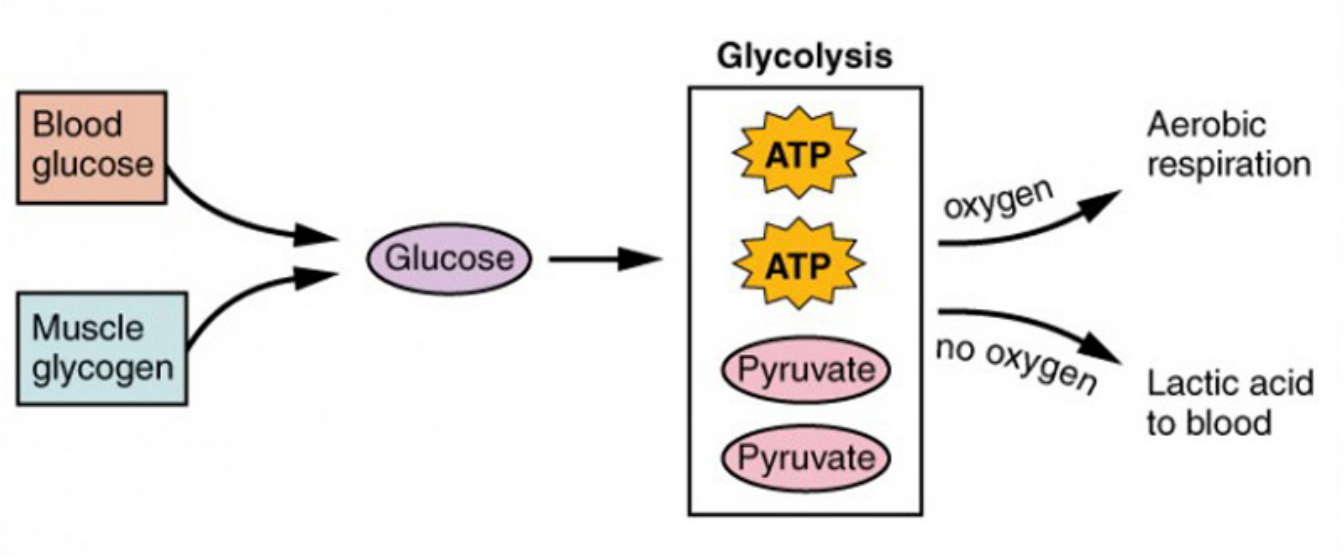


Figure 6. Glycolysis and Aerobic Respiration. *Each glucose molecule produces two ATP and two molecules of pyruvic acid, which can be used in aerobic respiration or converted to lactic acid. If oxygen is not available, pyruvic acid is converted to lactic acid, which may contribute to muscle fatigue. This occurs during strenuous exercise when high amounts of energy are needed but oxygen cannot be sufficiently delivered to muscle.*

If oxygen is available, pyruvic acid is used in aerobic respiration. However, if oxygen is not available, pyruvic acid is converted to **lactic acid**, which may contribute to muscle fatigue. This conversion allows the recycling of the enzyme NAD^+ from NADH, which is needed for glycolysis to continue. This occurs during strenuous exercise when high amounts of energy are needed but oxygen cannot be sufficiently delivered to muscle. Glycolysis itself cannot be sustained for very long (approximately 1 minute of muscle activity), but it is useful in facilitating short bursts of high-intensity output. This is because glycolysis does not utilize glucose very efficiently, producing a net gain of two ATPs per molecule of glucose, and the end product of lactic acid, which may contribute to muscle fatigue as it accumulates.

Aerobic respiration is the breakdown of glucose or other nutrients in the presence of oxygen (O_2) to produce carbon dioxide, water, and ATP. Approximately 95 percent of the ATP required for resting or moderately active muscles is provided by aerobic respiration, which takes place in mitochondria. The inputs for aerobic respiration include glucose circulating in the bloodstream, pyruvic acid, and fatty acids. Aerobic respiration is much more efficient than anaerobic glycolysis, producing approximately 36 ATPs per molecule of glucose versus four from glycolysis. However, aerobic respiration cannot be sustained without a steady supply of O_2 to the skeletal muscle and is much slower (Figure 7). To compensate, muscles store small amount of excess oxygen in proteins call myoglobin, allowing for more efficient muscle contractions and less fatigue. Aerobic training also increases the efficiency of the circulatory system so that O_2 can be supplied to the muscles for longer periods of time.

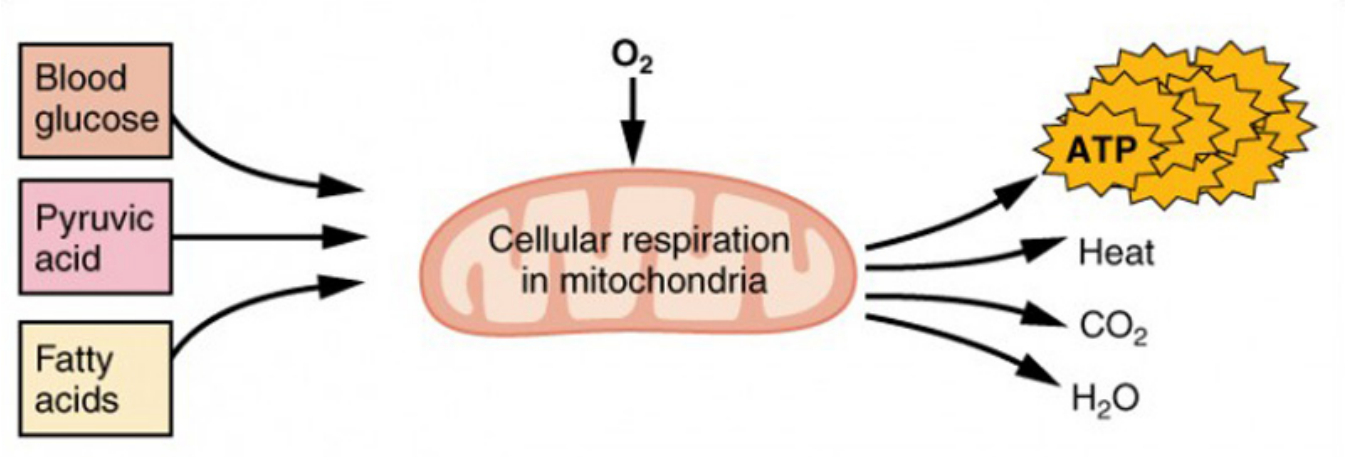


Figure 7. Cellular Respiration. *Aerobic respiration is the breakdown of glucose in the presence of oxygen (O_2) to produce carbon dioxide, water, and ATP. Approximately 95 percent of the ATP required for resting or moderately active muscles is provided by aerobic respiration, which takes place in mitochondria.*

Muscle fatigue occurs when a muscle can no longer contract in response to signals from the nervous system. The exact causes of muscle fatigue are not fully known, although certain factors have been correlated with the decreased muscle contraction that occurs during fatigue. ATP is needed for normal muscle contraction, and as ATP reserves are reduced, muscle function may decline. This may be more of a factor in brief, intense muscle output rather than sustained, lower intensity efforts. Lactic acid buildup may lower intracellular pH, affecting enzyme and protein activity. Imbalances in Na^+ and K^+ levels as a result of membrane depolarization may disrupt Ca^{++} flow out of the SR. Long periods of sustained exercise may damage the SR and the sarcolemma, resulting in impaired Ca^{++} regulation.

Intense muscle activity results in an **oxygen debt**, which is the amount of oxygen needed to compensate for ATP produced without oxygen during muscle contraction. Oxygen is required to restore ATP and creatine phosphate levels, convert lactic acid to pyruvic acid, and, in the liver, to convert lactic acid into glucose or glycogen. Other systems used during exercise also require oxygen, and all of these combined processes result in the increased breathing rate that occurs after exercise. Until the oxygen debt has been met, oxygen intake is elevated, even after exercise has stopped.

Relaxation of a Skeletal Muscle

Relaxing skeletal muscle fibers, and ultimately, the skeletal muscle, begins with the motor neuron, which stops releasing its chemical signal, ACh, into the synapse at the NMJ. The muscle fiber will repolarize, which closes the gates in the SR where Ca^{++} was being released. ATP-driven pumps will move Ca^{++} out of the sarcoplasm back into the SR. This results in the “reshielding” of the actin-binding sites on the thin filaments. Without the ability to form cross-bridges between the thin and thick filaments, the muscle fiber loses its tension and relaxes.

Muscle Strength

The number of skeletal muscle fibers in a given muscle is genetically determined and does not change. Muscle strength is directly related to the amount of myofibrils and sarcomeres within each fiber. Factors, such as hormones and stress (and artificial anabolic steroids), acting on the muscle can increase the production of sarcomeres and myofibrils within the muscle fibers, a change called hypertrophy, which results in the increased mass and bulk in a skeletal muscle. Likewise, decreased use of a skeletal muscle results in atrophy, where the number of sarcomeres and myofibrils disappear (but not the number of muscle fibers). It is common for a limb in a cast to show atrophied muscles when the cast is removed, and certain diseases, such as polio, show atrophied muscles.

Disorders of the Muscular System

Duchenne muscular dystrophy (DMD) is a progressive weakening of the skeletal muscles. It is one of several diseases collectively referred to as “muscular dystrophy.” DMD is caused by a lack of the protein dystrophin, which helps the thin filaments of myofibrils bind to the sarcolemma. Without sufficient dystrophin, muscle contractions cause the sarcolemma to tear, causing an influx of Ca^{++}, leading to cellular damage and muscle fiber degradation. Over time, as muscle damage accumulates, muscle mass is lost, and greater functional impairments develop.

DMD is an inherited disorder caused by an abnormal X chromosome. It primarily affects males, and it is usually diagnosed in early childhood. DMD usually first appears as difficulty with balance and motion, and then progresses to an inability to walk. It continues progressing upward in the body from the lower extremities to the upper body, where it affects the muscles responsible for breathing and circulation. It ultimately causes death due to respiratory failure, and those afflicted do not usually live past their 20s.

Because DMD is caused by a mutation in the gene that codes for dystrophin, it was thought that introducing healthy myoblasts into patients might be an effective treatment. Myoblasts are the embryonic cells responsible for muscle development, and ideally, they would carry healthy genes that could produce the dystrophin needed for normal muscle contraction. This approach has been largely unsuccessful in humans. A recent approach has involved attempting to boost the muscle’s production of utrophin, a protein similar to dystrophin that may be able to assume the role of dystrophin and prevent cellular damage from occurring.

Self-Check Questions

Visit your course online to take a quiz to check your understanding of Muscle Fiber Contraction and Relaxation:

NERVOUS SYSTEM CONTROL OF MUSCLE TENSION

Learning Objectives

- Explain concentric, isotonic, and eccentric contractions
- Describe the length-tension relationship
- Describe the three phases of a muscle twitch
- Define wave summation, tetanus, and treppe

To move an object, referred to as load, the sarcomeres in the muscle fibers of the skeletal muscle must shorten. The force generated by the contraction of the muscle (or shortening of the sarcomeres) is called **muscle tension**. However, muscle tension also is generated when the muscle is contracting against a load that does not move, resulting in two main types of skeletal muscle contractions: isotonic contractions and isometric contractions.

In **isotonic contractions**, where the tension in the muscle stays constant, a load is moved as the length of the muscle changes (shortens). There are two types of isotonic contractions: concentric and eccentric. A **concentric contraction** involves the muscle shortening to move a load. An example of this is the biceps brachii muscle

contracting when a hand weight is brought upward with increasing muscle tension. As the biceps brachii contract, the angle of the elbow joint decreases as the forearm is brought toward the body. Here, the biceps brachii contracts as sarcomeres in its muscle fibers are shortening and cross-bridges form; the myosin heads pull the actin. An **eccentric contraction** occurs as the muscle tension diminishes and the muscle lengthens. In this case, the hand weight is lowered in a slow and controlled manner as the amount of cross-bridges being activated by nervous system stimulation decreases. In this case, as tension is released from the biceps brachii, the angle of the elbow joint increases. Eccentric contractions are also used for movement and balance of the body.

An **isometric contraction** occurs as the muscle produces tension without changing the angle of a skeletal joint. Isometric contractions involve sarcomere shortening and increasing muscle tension, but do not move a load, as the force produced cannot overcome the resistance provided by the load. For example, if one attempts to lift a hand weight that is too heavy, there will be sarcomere activation and shortening to a point, and ever-increasing muscle tension, but no change in the angle of the elbow joint. In everyday living, isometric contractions are active in maintaining posture and maintaining bone and joint stability. However, holding your head in an upright position occurs not because the muscles cannot move the head, but because the goal is to remain stationary and not produce movement. Most actions of the body are the result of a combination of isotonic and isometric contractions working together to produce a wide range of outcomes (Figure 1).

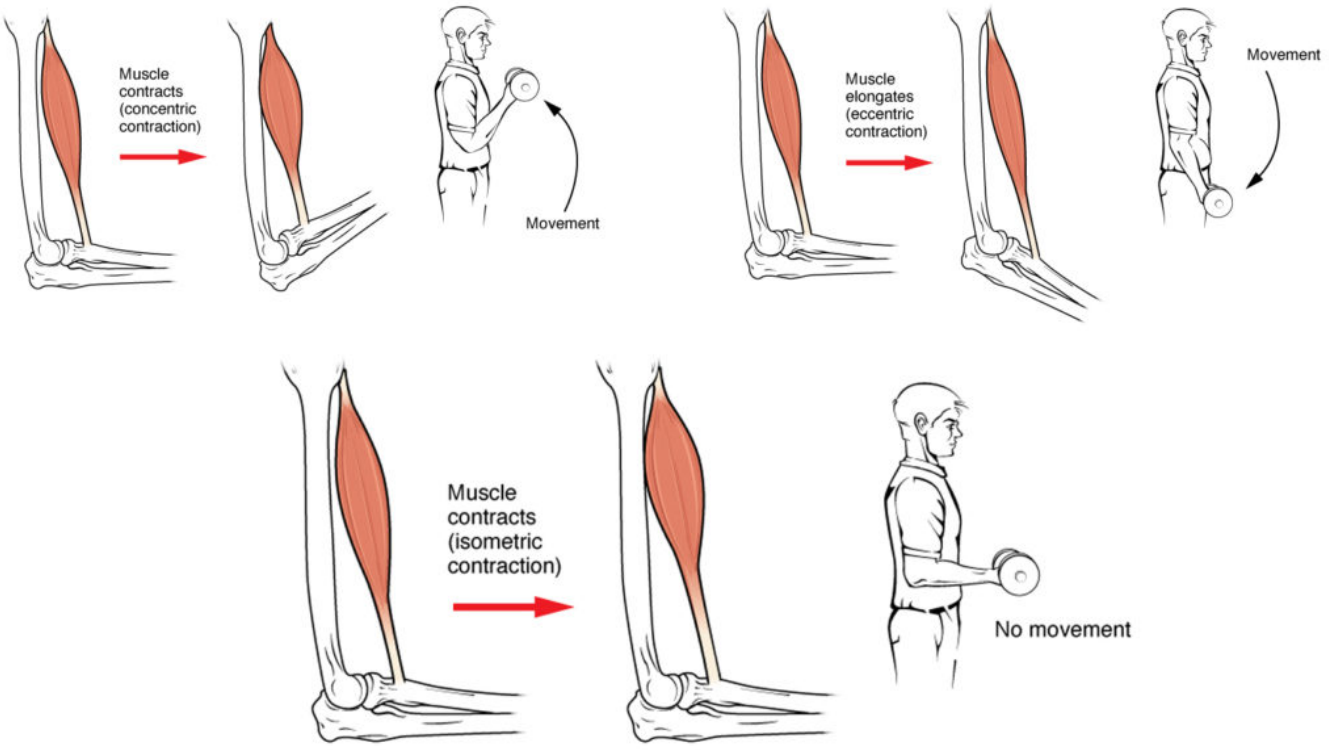


Figure 1. Types of Muscle Contractions. *During isotonic contractions, muscle length changes to move a load. During isometric contractions, muscle length does not change because the load exceeds the tension the muscle can generate.*

All of these muscle activities are under the exquisite control of the nervous system. Neural control regulates concentric, eccentric and isometric contractions, muscle fiber recruitment, and muscle tone. A crucial aspect of nervous system control of skeletal muscles is the role of motor units.

Motor Units

As you have learned, every skeletal muscle fiber must be innervated by the axon terminal of a motor neuron in order to contract. Each muscle fiber is innervated by only one motor neuron. The actual group of muscle fibers in a muscle innervated by a single motor neuron is called a **motor unit**. The size of a motor unit is variable depending on the nature of the muscle.

A small motor unit is an arrangement where a single motor neuron supplies a small number of muscle fibers in a muscle. Small motor units permit very fine motor control of the muscle. The best example in humans is the small motor units of the extraocular eye muscles that move the eyeballs. There are thousands of muscle fibers in each muscle, but every six or so fibers are supplied by a single motor neuron, as the axons branch to form synaptic connections at their individual NMJs. This allows for exquisite control of eye movements so that both eyes can quickly focus on the same object. Small motor units are also involved in the many fine movements of the fingers and thumb of the hand for grasping, texting, etc.

A large motor unit is an arrangement where a single motor neuron supplies a large number of muscle fibers in a muscle. Large motor units are concerned with simple, or “gross,” movements, such as powerfully extending the knee joint. The best example is the large motor units of the thigh muscles or back muscles, where a single motor neuron will supply thousands of muscle fibers in a muscle, as its axon splits into thousands of branches.

There is a wide range of motor units within many skeletal muscles, which gives the nervous system a wide range of control over the muscle. The small motor units in the muscle will have smaller, lower-threshold motor neurons that are more excitable, firing first to their skeletal muscle fibers, which also tend to be the smallest. Activation of these smaller motor units, results in a relatively small degree of contractile strength (tension) generated in the muscle. As more strength is needed, larger motor units, with bigger, higher-threshold motor neurons are enlisted to activate larger muscle fibers. This increasing activation of motor units produces an increase in muscle contraction known as **recruitment**. As more motor units are recruited, the muscle contraction grows progressively stronger. In some muscles, the largest motor units may generate a contractile force of 50 times more than the smallest motor units in the muscle. This allows a feather to be picked up using the biceps brachii arm muscle with minimal force, and a heavy weight to be lifted by the same muscle by recruiting the largest motor units.

When necessary, the maximal number of motor units in a muscle can be recruited simultaneously, producing the maximum force of contraction for that muscle, but this cannot last for very long because of the energy requirements to sustain the contraction. To prevent complete muscle fatigue, motor units are generally not all simultaneously active, but instead some motor units rest while others are active, which allows for longer muscle contractions. The nervous system uses recruitment as a mechanism to efficiently utilize a skeletal muscle.

The Length-Tension Range of a Sarcomere

When a skeletal muscle fiber contracts, myosin heads attach to actin to form cross-bridges followed by the thin filaments sliding over the thick filaments as the heads pull the actin, and this results in sarcomere shortening, creating the tension of the muscle contraction. The cross-bridges can only form where thin and thick filaments already overlap, so that the length of the sarcomere has a direct influence on the force generated when the sarcomere shortens. This is called the length-tension relationship.

The ideal length of a sarcomere to produce maximal tension occurs at 80 percent to 120 percent of its resting length, with 100 percent being the state where the medial edges of the thin filaments are just at the most-medial myosin heads of the thick filaments (Figure 2).

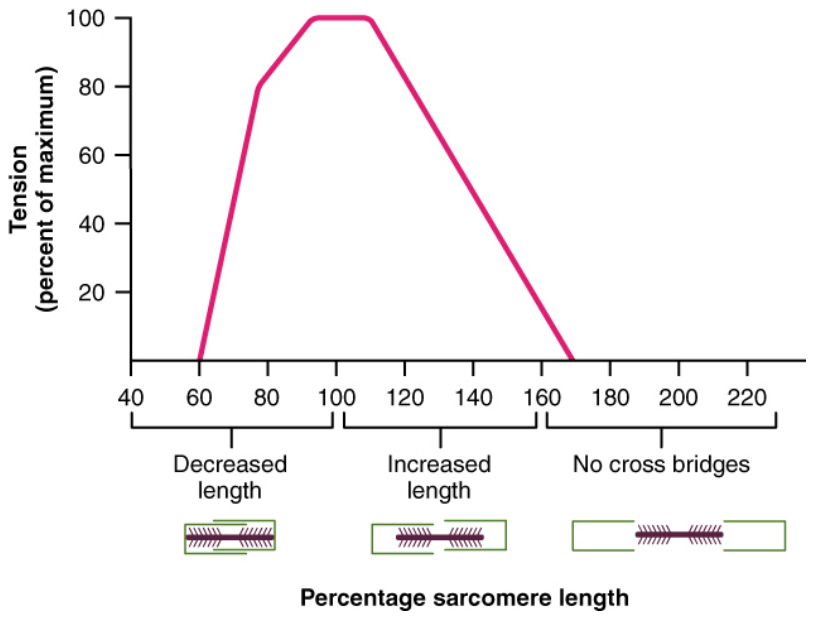


Figure 2. The Ideal Length of a Sarcomere. *Sarcomeres produce maximal tension when thick and thin filaments overlap between about 80 percent to 120 percent.*

This length maximizes the overlap of actin-binding sites and myosin heads. If a sarcomere is stretched past this ideal length (beyond 120 percent), thick and thin filaments do not overlap sufficiently, which results in less tension produced. If a sarcomere is shortened beyond 80 percent, the zone of

overlap is reduced with the thin filaments jutting beyond the last of the myosin heads and shrinks the H zone, which is normally composed of myosin tails.

Eventually, there is nowhere else for the thin filaments to go and the amount of tension is diminished. If the muscle is stretched to the point where thick and thin filaments do not overlap at all, no cross-bridges can be formed, and no tension is produced in that sarcomere. This amount of stretching does not usually occur, as accessory proteins and connective tissue oppose extreme stretching.

The Frequency of Motor Neuron Stimulation

A single action potential from a motor neuron will produce a single contraction in the muscle fibers of its motor unit. This isolated contraction is called a **twitch**. A twitch can last for a few milliseconds or 100 milliseconds, depending on the muscle type. The tension produced by a single twitch can be measured by a **myogram**, an instrument that measures the amount of tension produced over time (Figure 3). Each twitch undergoes three phases.

- The first phase is the **latent period**, during which the action potential is being propagated along the sarcolemma and Ca^{++} ions are released from the SR. This is the phase during which excitation and contraction are being coupled but contraction has yet to occur.
- The **contraction phase** occurs next. The Ca^{++} ions in the sarcoplasm have bound to troponin, tropomyosin has shifted away from actin-binding sites, cross-bridges formed, and sarcomeres are actively shortening to the point of peak tension.
- The last phase is the **relaxation phase**, when tension decreases as contraction stops. Ca^{++} ions are pumped out of the sarcoplasm into the SR, and cross-bridge cycling stops, returning the muscle fibers to their resting state.

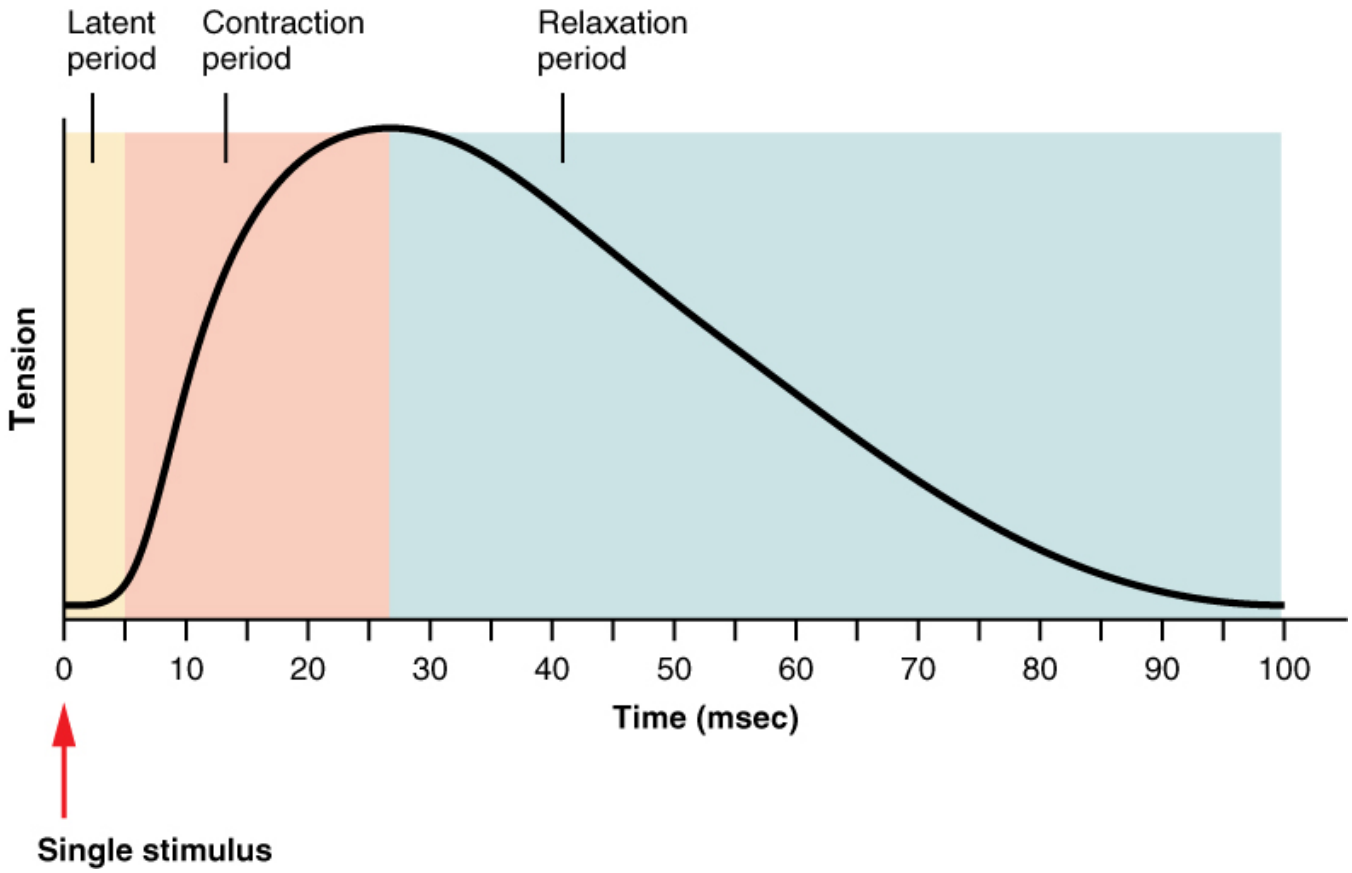


***Figure 3. A Myogram of a Muscle Twitch**. A single muscle twitch has a latent period, a contraction phase when tension increases, and a relaxation phase when tension decreases. During the latent period, the action potential is being propagated along the sarcolemma. During the contraction phase, Ca^{++} ions in the sarcoplasm bind to troponin, tropomyosin moves from*

actin-binding sites, cross-bridges form, and sarcomeres shorten. During the relaxation phase, tension decreases as Ca^{++} ions are pumped out of the sarcoplasm and cross-bridge cycling stops.

Although a person can experience a muscle "twitch," a single twitch does not produce any significant muscle activity in a living body. A series of action potentials to the muscle fibers is necessary to produce a muscle contraction that can produce work. Normal muscle contraction is more sustained, and it can be modified by input from the nervous system to produce varying amounts of force; this is called a **graded muscle response**. The frequency of action potentials (nerve impulses) from a motor neuron and the number of motor neurons transmitting action potentials both affect the tension produced in skeletal muscle.

The rate at which a motor neuron fires action potentials affects the tension produced in the skeletal muscle. If the fibers are stimulated while a previous twitch is still occurring, the second twitch will be stronger. This response is called **wave summation**, because the excitation-contraction coupling effects of successive motor neuron signaling is summed, or added together (Figure 4a). At the molecular level, summation occurs because the second stimulus triggers the release of more Ca^{++} ions, which become available to activate additional sarcomeres while the muscle is still contracting from the first stimulus. Summation results in greater contraction of the motor unit.

If the frequency of motor neuron signaling increases, summation and subsequent muscle tension in the motor unit continues to rise until it reaches a peak point. The tension at this point is about three to four times greater than the tension of a single twitch, a state referred to as incomplete tetanus. During incomplete tetanus, the muscle goes through quick cycles of contraction with a short relaxation phase for each. If the stimulus frequency is so high that the relaxation phase disappears completely, contractions become continuous in a process called complete **tetanus** (Figure 4b).

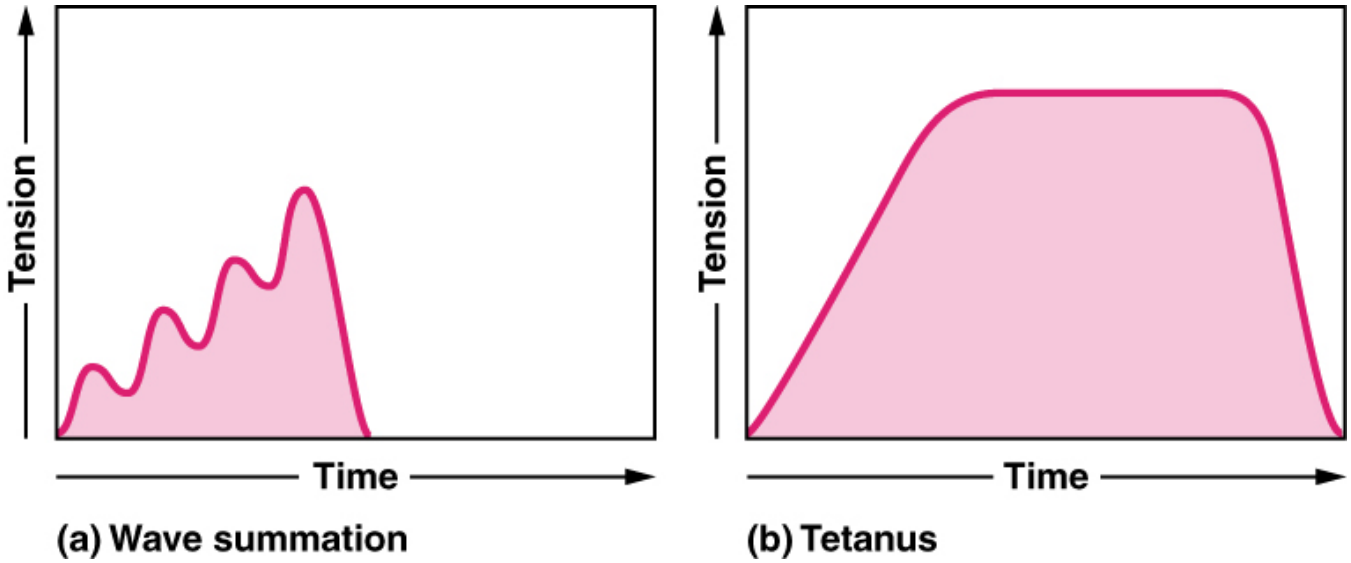


Figure 4. Wave Summation and Tetanus. *(a) The excitation-contraction coupling effects of successive motor neuron signaling is added together which is referred to as wave summation. The bottom of each wave, the end of the relaxation phase, represents the point of stimulus. (b) When the stimulus frequency is so high that the relaxation phase disappears completely, the contractions become continuous; this is called tetanus.*

During tetanus, the concentration of Ca^{++} ions in the sarcoplasm allows virtually all of the sarcomeres to form cross-bridges and shorten, so that a contraction can continue uninterrupted (until the muscle fatigues and can no longer produce tension).

Treppe

When a skeletal muscle has been dormant for an extended period and then activated to contract, with all other things being equal, the initial contractions generate about one-half the force of later contractions. The muscle tension increases in a graded manner that to some looks like a set of stairs. This tension increase is called **treppe**, a condition where muscle contractions become more efficient. It's also known as the "staircase effect" (Figure 5).

It is believed that treppe results from a higher concentration of Ca^{++} in the sarcoplasm resulting from the steady stream of signals from the motor neuron. It can only be maintained with adequate ATP.

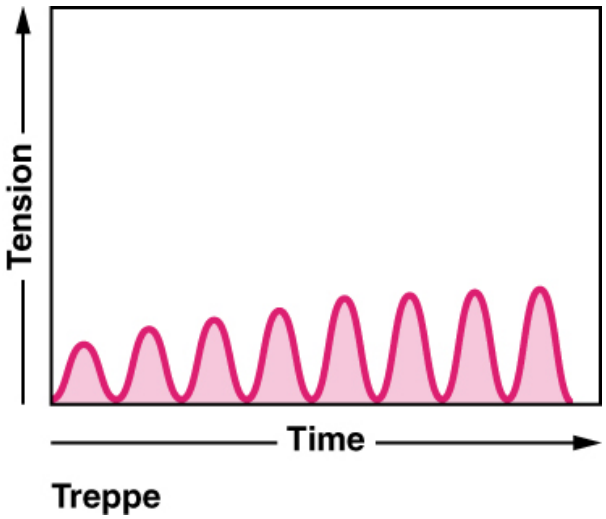


Figure 5. Treppe. *When muscle tension increases in a graded manner that looks like a set of stairs, it is called treppe. The bottom of each wave represents the point of stimulus.*

Muscle Tone

Skeletal muscles are rarely completely relaxed, or flaccid. Even if a muscle is not producing movement, it is contracted a small amount to maintain its contractile proteins and produce **muscle tone**. The tension produced by muscle tone allows muscles to continually stabilize joints and maintain posture.

Muscle tone is accomplished by a complex interaction between the nervous system and skeletal muscles that results in the activation of a few motor units at a time, most likely in a cyclical manner. In this manner, muscles never fatigue completely, as some motor units can recover while others are active.

The absence of the low-level contractions that lead to muscle tone is referred to as **hypotonia** or atrophy, and can result from damage to parts of the central nervous system (CNS), such as the cerebellum, or from loss of innervations to a skeletal muscle, as in poliomyelitis. Hypotonic muscles have a flaccid appearance and display functional impairments, such as weak reflexes. Conversely, excessive muscle tone is referred to as **hypertonia**, accompanied by hyperreflexia (excessive reflex responses), often the result of damage to upper motor neurons in the CNS. Hypertonia can present with muscle rigidity (as seen in Parkinson's disease) or spasticity, a phasic change in muscle tone, where a limb will "snap" back from passive stretching (as seen in some strokes).

TYPES OF MUSCLE FIBERS

Learning Objectives

- Describe the types of skeletal muscle fibers
- Explain fast and slow muscle fibers

Two criteria to consider when classifying the types of muscle fibers are how fast some fibers contract relative to others, and how fibers produce ATP. Using these criteria, there are three main types of skeletal muscle fibers. **Slow oxidative** (SO) fibers contract relatively slowly and use aerobic respiration (oxygen and glucose) to produce ATP. **Fast oxidative** (FO) fibers have fast contractions and primarily use aerobic respiration, but because they may switch to anaerobic respiration (glycolysis), can fatigue more quickly than SO fibers. Lastly, **fast glycolytic (FG)** fibers have fast contractions and primarily use anaerobic glycolysis. The FG fibers fatigue more quickly than the others. Most skeletal muscles in a human contain(s) all three types, although in varying proportions.

The speed of contraction is dependent on how quickly myosin's ATPase hydrolyzes ATP to produce cross-bridge action. Fast fibers hydrolyze ATP approximately twice as quickly as slow fibers, resulting in much quicker cross-bridge cycling (which pulls the thin filaments toward the center of the sarcomeres at a faster rate). The primary metabolic pathway used by a muscle fiber determines whether the fiber is classified as oxidative or glycolytic. If a fiber primarily produces ATP through aerobic pathways it is oxidative. More ATP can be produced during each metabolic cycle, making the fiber more resistant to fatigue. Glycolytic fibers primarily create ATP through anaerobic glycolysis, which produces less ATP per cycle. As a result, glycolytic fibers fatigue at a quicker rate.

The oxidative fibers contain many more mitochondria than the glycolytic fibers, because aerobic metabolism, which uses oxygen (O_2) in the metabolic pathway, occurs in the mitochondria. The SO fibers possess a large number of mitochondria and are capable of contracting for longer periods because of the large amount of ATP they can produce, but they have a relatively small diameter and do not produce a large amount of tension. SO fibers are extensively supplied with blood capillaries to supply O_2 from the red blood cells in the bloodstream. The SO fibers also possess myoglobin, an O_2-carrying molecule similar to O_2-carrying hemoglobin in the red blood cells. The myoglobin stores some of the needed O_2 within the fibers themselves (and gives SO fibers their red color). All of these features allow SO fibers to produce large quantities of ATP, which can sustain muscle activity without fatiguing for long periods of time.

The fact that SO fibers can function for long periods without fatiguing makes them useful in maintaining posture, producing isometric contractions, stabilizing bones and joints, and making small movements that happen often but do not require large amounts of energy. They do not produce high tension, and thus they are not used for powerful, fast movements that require high amounts of energy and rapid cross-bridge cycling.

FO fibers are sometimes called intermediate fibers because they possess characteristics that are intermediate between fast fibers and slow fibers. They produce ATP relatively quickly, more quickly than SO fibers, and thus can produce relatively high amounts of tension. They are oxidative because they produce ATP aerobically, possess high amounts of mitochondria, and do not fatigue quickly. However, FO fibers do not possess significant myoglobin, giving them a lighter color than the red SO fibers. FO fibers are used primarily for movements, such as walking, that require more energy than postural control but less energy than an explosive movement, such as sprinting. FO fibers are useful for this type of movement because they produce more tension than SO fibers but they are more fatigue-resistant than FG fibers.

FG fibers primarily use anaerobic glycolysis as their ATP source. They have a large diameter and possess high amounts of glycogen, which is used in glycolysis to generate ATP quickly to produce high levels of tension. Because they do not primarily use aerobic metabolism, they do not possess substantial numbers of mitochondria or significant amounts of myoglobin and therefore have a white color. FG fibers are used to produce rapid, forceful contractions to make quick, powerful movements. These fibers fatigue quickly, permitting them to only be used for short periods. Most muscles possess a mixture of each fiber type. The predominant fiber type in a muscle is determined by the primary function of the muscle.

EXERCISE AND MUSCLE PERFORMANCE

Learning Objectives

- Describe hypertrophy and atrophy
- Explain how resistance exercise builds muscle
- Explain how performance-enhancing substances affect muscle

Physical training alters the appearance of skeletal muscles and can produce changes in muscle performance. Conversely, a lack of use can result in decreased performance and muscle appearance. Although muscle cells can change in size, new cells are not formed when muscles grow. Instead, structural proteins are added to muscle fibers in a process called **hypertrophy**, so cell diameter increases. The reverse, when structural proteins are lost and muscle mass decreases, is called **atrophy**. Age-related muscle atrophy is called **sarcopenia**. Cellular components of muscles can also undergo changes in response to changes in muscle use.

Endurance Exercise

Slow fibers are predominantly used in endurance exercises that require little force but involve numerous repetitions. The aerobic metabolism used by slow-twitch fibers allows them to maintain contractions over long periods. Endurance training modifies these slow fibers to make them even more efficient by producing more mitochondria to enable more aerobic metabolism and more ATP production. Endurance exercise can also increase the amount of myoglobin in a cell, as increased aerobic respiration increases the need for oxygen. Myoglobin is found in the sarcoplasm and acts as an oxygen storage supply for the mitochondria.

The training can trigger the formation of more extensive capillary networks around the fiber, a process called **angiogenesis**, to supply oxygen and remove metabolic waste. To allow these capillary networks to supply the deep portions of the muscle, muscle mass does not greatly increase in order to maintain a smaller area for the diffusion of nutrients and gases. All of these cellular changes result in the ability to sustain low levels of muscle contractions for greater periods without fatiguing.

Figure 1. Marathoners. *Long-distance runners have a large number of SO fibers and relatively few FO and FG fibers. (credit: "Tseo2"/Wikimedia Commons)*

The proportion of SO muscle fibers in muscle determines the suitability of that muscle for endurance, and may benefit those participating in endurance activities. Postural muscles have a large number of SO fibers and relatively few FO and FG fibers, to keep the back straight (Figure 1). Endurance athletes, like marathon-runners also would benefit from a larger proportion of SO fibers, but it is unclear if the most-successful marathoners are those with naturally high numbers of SO fibers, or whether the most successful marathon runners develop high numbers of SO fibers with repetitive training. Endurance training can result in overuse injuries such as stress fractures and joint and tendon inflammation.

Resistance Exercise

Resistance exercises, as opposed to endurance exercise, require large amounts of FG fibers to produce short, powerful movements that are not repeated over long periods. The high rates of ATP hydrolysis and cross-bridge formation in FG fibers result in powerful muscle contractions. Muscles used for power have a higher ratio of FG to SO/FO fibers, and trained athletes possess even higher levels of FG fibers in their muscles.

Resistance exercise affects muscles by increasing the formation of myofibrils, thereby increasing the thickness of muscle fibers. This added structure causes hypertrophy, or the enlargement of muscles, exemplified by the large skeletal muscles seen in body builders and other athletes (Figure 2). Because this muscular enlargement is achieved by the addition of structural proteins, athletes trying to build muscle mass often ingest large amounts of protein.

Figure 2. Hypertrophy. *Body builders have a large number of FG fibers and relatively few FO and SO fibers. (credit: Lin Mei/flickr)*

Except for the hypertrophy that follows an increase in the number of sarcomeres and myofibrils in a skeletal muscle, the cellular changes observed during endurance training do not usually occur with resistance training. There is usually no significant increase in mitochondria or capillary density. However, resistance training does increase the development of connective tissue, which adds to the overall mass of the muscle and helps to contain muscles as they produce increasingly powerful contractions. Tendons also become stronger to prevent tendon damage, as the force produced by muscles is transferred to tendons that attach the muscle to bone.

For effective strength training, the intensity of the exercise must continually be increased. For instance, continued weight lifting without increasing the weight of the load does not increase muscle size. To produce ever-greater results, the weights lifted must become increasingly heavier, making it more difficult for muscles to move the load. The muscle then adapts to this heavier load, and an even heavier load must be used if even greater muscle mass is desired.

If done improperly, resistance training can lead to overuse injuries of the muscle, tendon, or bone. These injuries can occur if the load is too heavy or if the muscles are not given sufficient time between workouts to recover or if joints are not aligned properly during the exercises. Cellular damage to muscle fibers that occurs after intense exercise includes damage to the sarcolemma and myofibrils. This muscle damage contributes to the feeling of soreness after strenuous exercise, but muscles gain mass as this damage is repaired, and additional structural proteins are added to replace the damaged ones. Overworking skeletal muscles can also lead to tendon damage and even skeletal damage if the load is too great for the muscles to bear.

Performance-Enhancing Substances

Some athletes attempt to boost their performance by using various agents that may enhance muscle performance. Anabolic steroids are one of the more widely known agents used to boost muscle mass and increase power output. Anabolic steroids are a form of testosterone, a male sex hormone that stimulates muscle formation, leading to increased muscle mass.

Endurance athletes may also try to boost the availability of oxygen to muscles to increase aerobic respiration by using substances such as erythropoietin (EPO), a hormone normally produced in the kidneys, which triggers the production of red blood cells. The extra oxygen carried by these blood cells can then be used by muscles for aerobic respiration. Human growth hormone (hGH) is another supplement, and although it can facilitate building muscle mass, its main role is to promote the healing of muscle and other tissues after strenuous exercise. Increased hGH may allow for faster recovery after muscle damage, reducing the rest required after exercise, and allowing for more sustained high-level performance.

Although performance-enhancing substances often do improve performance, most are banned by governing bodies in sports and are illegal for nonmedical purposes. Their use to enhance performance raises ethical issues of cheating because they give users an unfair advantage over nonusers. A greater concern, however, is that their use carries serious health risks. The side effects of these substances are often significant, nonreversible, and in some cases fatal. The physiological strain caused by these substances is often greater than what the body can handle, leading to effects that are unpredictable and dangerous. Anabolic steroid use has been linked to infertility, aggressive behavior, cardiovascular disease, and brain cancer.

Similarly, some athletes have used creatine to increase power output. Creatine phosphate provides quick bursts of ATP to muscles in the initial stages of contraction. Increasing the amount of creatine available to cells is thought to produce more ATP and therefore increase explosive power output, although its effectiveness as a supplement has been questioned.

Everyday Connection: Aging and Muscle Tissue

Although atrophy due to disuse can often be reversed with exercise, muscle atrophy with age, referred to as sarcopenia, is irreversible. This is a primary reason why even highly trained athletes succumb to declining performance with age. This decline is noticeable in athletes whose sports require strength and powerful movements, such as sprinting, whereas the effects of age are less noticeable in endurance athletes such as marathon runners or long-distance cyclists. As muscles age, muscle fibers die, and they are replaced by connective tissue and adipose tissue (Figure 3).

Because those tissues cannot contract and generate force as muscle can, muscles lose the ability to produce powerful contractions. The decline in muscle mass causes a loss of strength, including the strength required for posture and mobility. This may be caused by a reduction in FG fibers that hydrolyze ATP quickly to produce short, powerful contractions. Muscles in older people sometimes possess greater numbers of SO fibers, which are responsible for longer contractions and do not produce powerful movements. There may also be a reduction in the size of motor units, resulting in fewer fibers being stimulated and less muscle tension being produced.

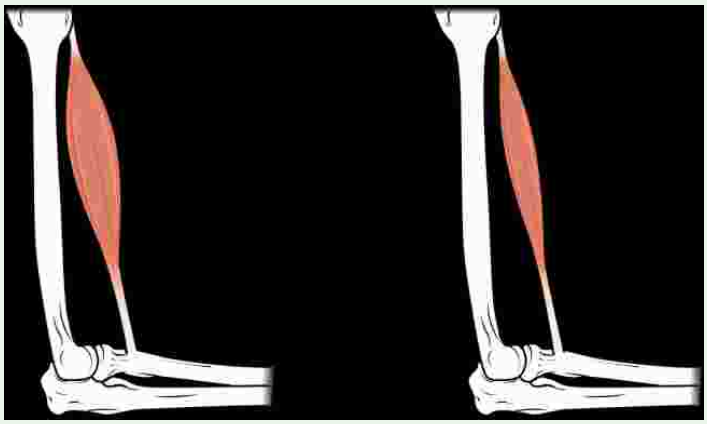


Figure 3. Atrophy. *Muscle mass is reduced as muscles atrophy with disuse.*

Sarcopenia can be delayed to some extent by exercise, as training adds structural proteins and causes cellular changes that can offset the effects of atrophy. Increased exercise can produce greater numbers of cellular mitochondria, increase capillary density, and increase the mass and strength of connective tissue. The effects of age-related atrophy are especially pronounced in people who are sedentary, as the loss of muscle cells is displayed as functional impairments such as trouble with locomotion, balance, and posture. This can lead to a decrease in quality of life and medical problems, such as joint problems because the muscles that stabilize bones and joints are weakened. Problems with locomotion and balance can also cause various injuries due to falls.

CARDIAC MUSCLE TISSUE

Learning Objectives

- Describe intercalated discs and gap junctions
- Describe a desmosome

Cardiac muscle tissue is only found in the heart. Highly coordinated contractions of cardiac muscle pump blood into the vessels of the circulatory system. Similar to skeletal muscle, cardiac muscle is striated and organized into sarcomeres, possessing the same banding organization as skeletal muscle (Figure 1).

However, cardiac muscle fibers are shorter than skeletal muscle fibers and usually contain only one nucleus, which is located in the central region of the cell. Cardiac muscle fibers also possess many mitochondria and myoglobin, as ATP is produced primarily through aerobic metabolism. Cardiac muscle fibers cells also are extensively branched and are connected to one another at their ends by intercalated discs. An **intercalated disc** allows the cardiac muscle cells to contract in a wave-like pattern so that the heart can work as a pump.

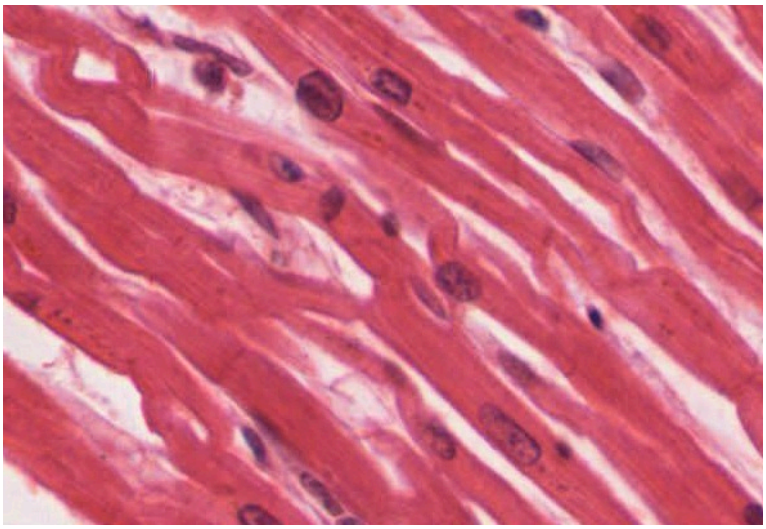


Figure 1. Cardiac Muscle Tissue. *Cardiac muscle tissue is only found in the heart. LM × 1600. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

View the University of Michigan WebScope to explore the tissue sample in greater detail.

Intercalated discs are part of the sarcolemma and contain two structures important in cardiac muscle contraction: gap junctions and desmosomes. A gap junction forms channels between adjacent cardiac muscle fibers that allow the depolarizing current produced by cations to flow from one cardiac muscle cell to the next. This joining is called electric coupling, and in cardiac muscle it allows the quick transmission of action potentials and the coordinated contraction of the entire heart. This network of electrically connected cardiac muscle cells creates a functional unit of contraction called a syncytium. The remainder of the intercalated disc is composed of desmosomes.
A **desmosome** is a cell structure that anchors the ends of cardiac muscle fibers together so the cells do not pull apart during the stress of individual fibers contracting (Figure 2).

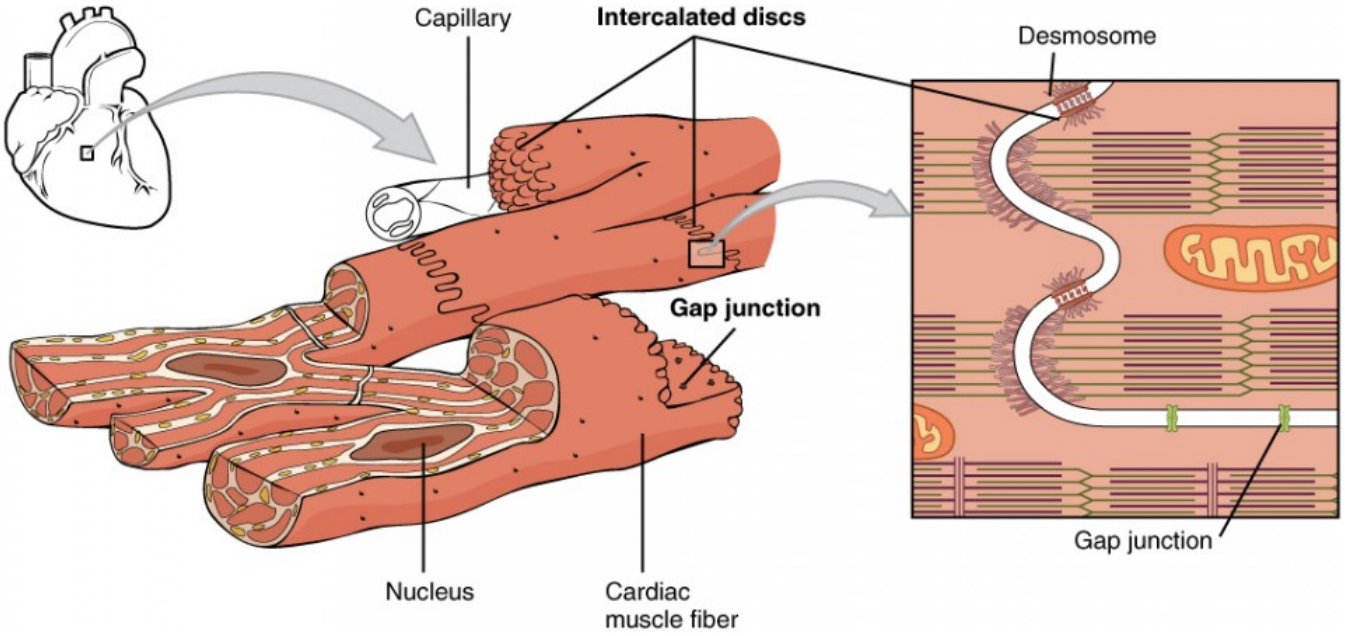


Figure 2. Cardiac Muscle. *Intercalated discs are part of the cardiac muscle sarcolemma and they contain gap junctions and desmosomes.*

Contractions of the heart (heartbeats) are controlled by specialized cardiac muscle cells called pacemaker cells that directly control heart rate. Although cardiac muscle cannot be consciously controlled, the pacemaker cells respond to signals from the autonomic nervous system (ANS) to speed up or slow down the heart rate. The pacemaker cells can also respond to various hormones that modulate heart rate to control blood pressure.

The wave of contraction that allows the heart to work as a unit, called a functional syncytium, begins with the pacemaker cells. This group of cells is self-excitable and able to depolarize to threshold and fire action potentials on their own, a feature called **autorhythmicity**; they do this at set intervals which determine heart rate. Because they are connected with gap junctions to surrounding muscle fibers and the specialized fibers of the heart's conduction system, the pacemaker cells are able to transfer the depolarization to the other cardiac muscle fibers in a manner that allows the heart to contract in a coordinated manner.

Another feature of cardiac muscle is its relatively long action potentials in its fibers, having a sustained depolarization "plateau." The plateau is produced by Ca^{++} entry though voltage-gated calcium channels in the sarcolemma of cardiac muscle fibers. This sustained depolarization (and Ca^{++} entry) provides for a longer contraction than is produced by an action potential in skeletal muscle. Unlike skeletal muscle, a large percentage of the Ca^{++} that initiates contraction in cardiac muscles comes from outside the cell rather than from the SR.

Self-Check Questions

Visit your course online to take a quiz to check your understanding of Cardiac Muscle Tissue:

SMOOTH MUSCLE

Learning Objectives

- Describe a dense body
- Explain how smooth muscle works with internal organs and passageways through the body
- Explain how smooth muscles differ from skeletal and cardiac muscles
- Explain the difference between single-unit and multi-unit smooth muscle

Smooth muscle (so-named because the cells do not have striations) is present in the walls of hollow organs like the urinary bladder, uterus, stomach, intestines, and in the walls of passageways, such as the arteries and veins of the circulatory system, and the tracts of the respiratory, urinary, and reproductive systems (Figure 1). Smooth muscle is also present in the eyes, where it functions to change the size of the iris and alter the shape of the lens; and in the skin where it causes hair to stand erect in response to cold temperature or fear.

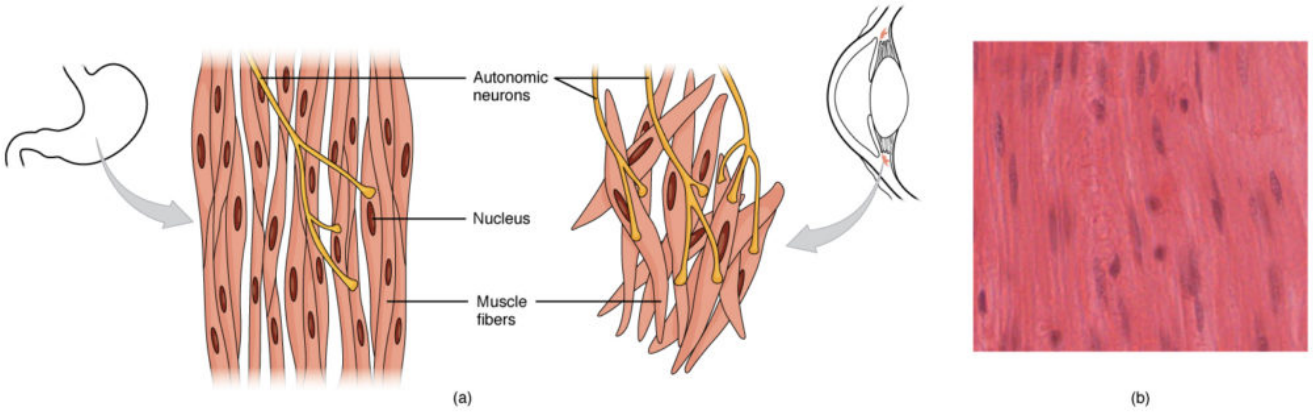


Figure 1. Smooth Muscle Tissue. *Smooth muscle tissue is found around organs in the digestive, respiratory, reproductive tracts and the iris of the eye. LM × 1600. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

View the University of Michigan WebScope to explore the tissue sample in greater detail.

Smooth muscle fibers are spindle-shaped (wide in the middle and tapered at both ends, somewhat like a football) and have a single nucleus; they range from about 30 to 200 μm (thousands of times shorter than skeletal muscle fibers), and they produce their own connective tissue, endomysium. Although they do not have striations and sarcomeres, smooth muscle fibers do have actin and myosin contractile proteins, and thick and thin filaments. These thin filaments are anchored by dense bodies. A **dense body** is analogous to the Z-discs of skeletal and cardiac muscle fibers and is fastened to the sarcolemma. Calcium ions are supplied by the SR in the fibers and by sequestration from the extracellular fluid through membrane indentations called calveoli.

Because smooth muscle cells do not contain troponin, cross-bridge formation is not regulated by the troponin-tropomyosin complex but instead by the regulatory protein **calmodulin**. In a smooth muscle fiber, external Ca^{++} ions passing through opened calcium channels in the sarcolemma, and additional Ca^{++} released from SR, bind to calmodulin. The Ca^{++}-calmodulin complex then activates an enzyme called myosin (light chain) kinase, which, in turn, activates the myosin heads by phosphorylating them (converting ATP to ADP and P_i, with the P_i attaching to the head). The heads can then attach to actin-binding sites and pull on the thin filaments. The thin filaments also are anchored to the dense bodies; the structures invested in the inner membrane of the sarcolemma (at adherens junctions) that also have cord-like intermediate filaments attached to them.

When the thin filaments slide past the thick filaments, they pull on the dense bodies, structures tethered to the sarcolemma, which then pull on the intermediate filaments networks throughout the sarcoplasm. This arrangement causes the entire muscle fiber to contract in a manner whereby the ends are pulled toward the center, causing the midsection to bulge in a corkscrew motion (Figure 2).

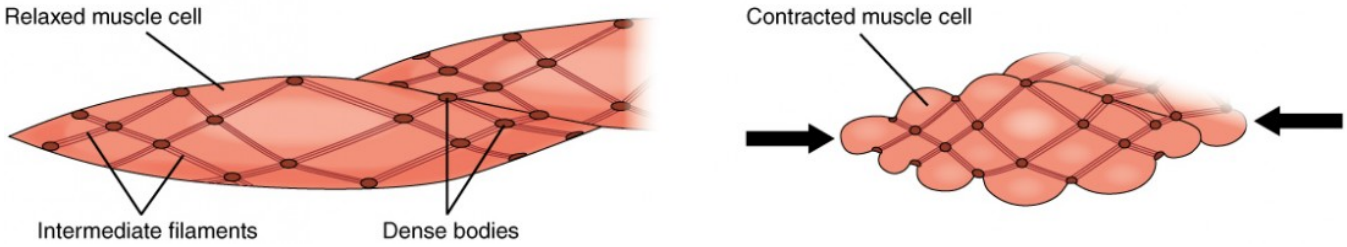


Figure 2. Muscle Contraction. *The dense bodies and intermediate filaments are networked through the sarcoplasm, which cause the muscle fiber to contract.*

Although smooth muscle contraction relies on the presence of Ca^{++} ions, smooth muscle fibers have a much smaller diameter than skeletal muscle cells. T-tubules are not required to reach the interior of the cell and therefore not necessary to transmit an action potential deep into the fiber. Smooth muscle fibers have a limited calcium-storing SR but have calcium channels in the sarcolemma (similar to cardiac muscle fibers) that open during the action potential along the sarcolemma. The influx of extracellular Ca^{++} ions, which diffuse into the sarcoplasm to reach the calmodulin, accounts for most of the Ca^{++} that triggers contraction of a smooth muscle cell.

Muscle contraction continues until ATP-dependent calcium pumps actively transport Ca^{++} ions back into the SR and out of the cell. However, a low concentration of calcium remains in the sarcoplasm to maintain muscle tone. This remaining calcium keeps the muscle slightly contracted, which is important in certain tracts and around blood vessels.

Because most smooth muscles must function for long periods without rest, their power output is relatively low, but contractions can continue without using large amounts of energy. Some smooth muscle can also maintain contractions even as Ca^{++} is removed and myosin kinase is inactivated/dephosphorylated. This can happen as a subset of cross-bridges between myosin heads and actin, called **latch-bridges**, keep the thick and thin filaments linked together for a prolonged period, and without the need for ATP. This allows for the maintaining of muscle “tone” in smooth muscle that lines arterioles and other visceral organs with very little energy expenditure.

Smooth muscle is not under voluntary control; thus, it is called involuntary muscle. The triggers for smooth muscle contraction include hormones, neural stimulation by the ANS, and local factors. In certain locations, such as the walls of visceral organs, stretching the muscle can trigger its contraction (the stretch-relaxation response).

Axons of neurons in the ANS do not form the highly organized NMJs with smooth muscle, as seen between motor neurons and skeletal muscle fibers. Instead, there is a series of neurotransmitter-filled bulges called varicosities as an axon courses through smooth muscle, loosely forming motor units (Figure 3). A **varicosity** releases neurotransmitters into the synaptic cleft. Also, visceral muscle in the walls of the hollow organs (except the heart) contains pacesetter cells. A **pacesetter cell** can spontaneously trigger action potentials and contractions in the muscle.

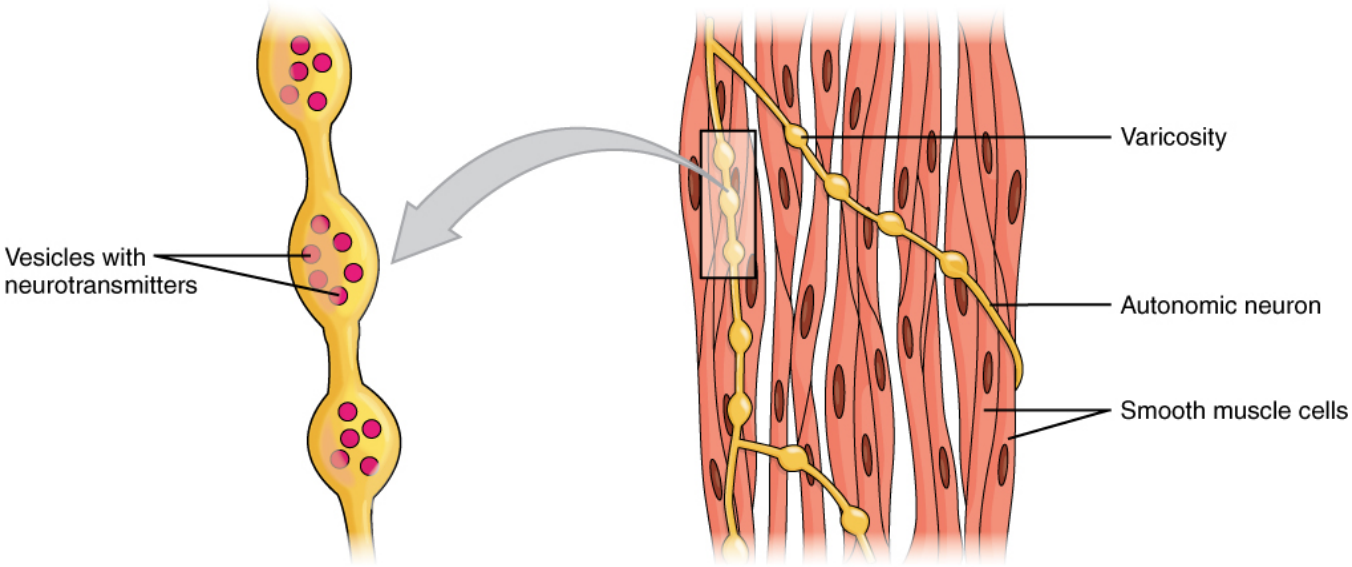


Figure 3. Motor Units. *A series of axon-like swelling, called varicosities or "boutons," from autonomic neurons form motor units through the smooth muscle.*

Smooth muscle is organized in two ways: as single-unit smooth muscle, which is much more common; and as multiunit smooth muscle. The two types have different locations in the body and have different characteristics.

Single-unit muscle has its muscle fibers joined by gap junctions so that the muscle contracts as a single unit. This type of smooth muscle is found in the walls of all visceral organs except the heart (which has cardiac muscle in its walls), and so it is commonly called **visceral muscle**. Because the muscle fibers are not constrained by the organization and stretchability limits of sarcomeres, visceral smooth muscle has a **stress-relaxation response**. This means that as the muscle of a hollow organ is stretched when it fills, the mechanical stress of the stretching will trigger contraction, but this is immediately followed by relaxation so that the organ does not empty its contents prematurely. This is important for hollow organs, such as the stomach or urinary bladder, which continuously expand as they fill. The smooth muscle around these organs also can maintain a muscle tone when the organ empties and shrinks, a feature that prevents "flabbiness" in the empty organ. In general, visceral smooth muscle produces slow, steady contractions that allow substances, such as food in the digestive tract, to move through the body.

Multiunit smooth muscle cells rarely possess gap junctions, and thus are not electrically coupled. As a result, contraction does not spread from one cell to the next, but is instead confined to the cell that was originally stimulated. Stimuli for multiunit smooth muscles come from autonomic nerves or hormones but not from stretching. This type of tissue is found around large blood vessels, in the respiratory airways, and in the eyes.

Hyperplasia in Smooth Muscle

Similar to skeletal and cardiac muscle cells, smooth muscle can undergo hypertrophy to increase in size. Unlike other muscle, smooth muscle can also divide to produce more cells, a process called **hyperplasia**. This can most evidently be observed in the uterus at puberty, which responds to increased estrogen levels by producing more uterine smooth muscle fibers, and greatly increases the size of the myometrium.

DEVELOPMENT AND REGENERATION OF MUSCLE TISSUE

Learning Objectives

- Describe the function of satellite cells
- Define fibrosis
- Explain which muscle has the greatest regeneration ability

Most muscle tissue of the body arises from embryonic mesoderm. Paraxial mesodermal cells adjacent to the neural tube form blocks of cells called **somites**. Skeletal muscles, excluding those of the head and limbs, develop from mesodermal somites, whereas skeletal muscle in the head and limbs develop from general mesoderm. Somites give rise to myoblasts. A **myoblast** is a muscle-forming stem cell that migrates to different regions in the body and then fuse(s) to form a syncytium, or **myotube**. As a myotube is formed from many different myoblast cells, it contains many nuclei, but has a continuous cytoplasm. This is why skeletal muscle cells are multinucleate, as the nucleus of each contributing myoblast remains intact in the mature skeletal muscle cell. However, cardiac and smooth muscle cells are not multinucleate because the myoblasts that form their cells do not fuse.

Gap junctions develop in the cardiac and single-unit smooth muscle in the early stages of development. In skeletal muscles, ACh receptors are initially present along most of the surface of the myoblasts, but spinal nerve innervation causes the release of growth factors that stimulate the formation of motor end-plates and NMJs. As neurons become active, electrical signals that are sent through the muscle influence the distribution of slow and fast fibers in the muscle.

Although the number of muscle cells is set during development, satellite cells help to repair skeletal muscle cells. A **satellite cell** is similar to a myoblast because it is a type of stem cell; however, satellite cells are incorporated into muscle cells and facilitate the protein synthesis required for repair and growth. These cells are located outside the sarcolemma and are stimulated to grow and fuse with muscle cells by growth factors that are released by muscle fibers under certain forms of stress. Satellite cells can regenerate muscle fibers to a very limited extent, but they primarily help to repair damage in living cells. If a cell is damaged to a greater extent than can be repaired by satellite cells, the muscle fibers are replaced by scar tissue in a process called **fibrosis**. Because scar tissue cannot contract, muscle that has sustained significant damage loses strength and cannot produce the same amount of power or endurance as it could before being damaged.

Smooth muscle tissue can regenerate from a type of stem cell called a **pericyte**, which is found in some small blood vessels. Pericytes allow smooth muscle cells to regenerate and repair much more readily than skeletal and cardiac muscle tissue. Similar to skeletal muscle tissue, cardiac muscle does not regenerate to a great extent. Dead cardiac muscle tissue is replaced by scar tissue, which cannot contract. As scar tissue accumulates, the heart loses its ability to pump because of the loss of contractile power. However, some minor regeneration may occur due to stem cells found in the blood that occasionally enter cardiac tissue.

Career Connections: Physical Therapist

As muscle cells die, they are not regenerated but instead are replaced by connective tissue and adipose tissue, which do not possess the contractile abilities of muscle tissue. Muscles atrophy when they are not used, and over time if atrophy is prolonged, muscle cells die. It is therefore important that those who are susceptible to muscle atrophy exercise to maintain muscle function and prevent the complete loss of muscle tissue. In extreme cases, when movement is not possible, electrical stimulation can be introduced to a muscle

from an external source. This acts as a substitute for endogenous neural stimulation, stimulating the muscle to contract and preventing the loss of proteins that occurs with a lack of use.

Physiotherapists work with patients to maintain muscles. They are trained to target muscles susceptible to atrophy, and to prescribe and monitor exercises designed to stimulate those muscles. There are various causes of atrophy, including mechanical injury, disease, and age. After breaking a limb or undergoing surgery, muscle use is impaired and can lead to disuse atrophy. If the muscles are not exercised, this atrophy can lead to long-term muscle weakness. A stroke can also cause muscle impairment by interrupting neural stimulation to certain muscles. Without neural inputs, these muscles do not contract and thus begin to lose structural proteins. Exercising these muscles can help to restore muscle function and minimize functional impairments. Age-related muscle loss is also a target of physical therapy, as exercise can reduce the effects of age-related atrophy and improve muscle function.

The goal of a physiotherapist is to improve physical functioning and reduce functional impairments; this is achieved by understanding the cause of muscle impairment and assessing the capabilities of a patient, after which a program to enhance these capabilities is designed. Some factors that are assessed include strength, balance, and endurance, which are continually monitored as exercises are introduced to track improvements in muscle function. Physiotherapists can also instruct patients on the proper use of equipment, such as crutches, and assess whether someone has sufficient strength to use the equipment and when they can function without it.

VIDEO: ANATOMY OF A MUSCLE FIBER

Watch this video online: https://youtu.be/uY2ZOsCnXIA

GLOSSARY: MUSCLE TISSUE

ATPase: enzyme that hydrolyzes ATP to ADP

acetylcholine (ACh): neurotransmitter that binds at a motor end-plate to trigger depolarization

actin: protein that makes up most of the thin myofilaments in a sarcomere muscle fiber

action potential: change in voltage of a cell membrane in response to a stimulus that results in transmission of an electrical signal; unique to neurons and muscle fibers

aerobic respiration: production of ATP in the presence of oxygen

angiogenesis: formation of blood capillary networks

aponeurosis: broad, tendon-like sheet of connective tissue that attaches a skeletal muscle to another skeletal muscle or to a bone

atrophy: loss of structural proteins from muscle fibers

autorhythmicity: heart's ability to control its own contractions

calmodulin: regulatory protein that facilitates contraction in smooth muscles

cardiac muscle: striated muscle found in the heart; joined to one another at intercalated discs and under the regulation of pacemaker cells, which contract as one unit to pump blood through the circulatory system. Cardiac muscle is under involuntary control.

concentric contraction: muscle contraction that shortens the muscle to move a load

contractility: ability to shorten (contract) forcibly

contraction phase: twitch contraction phase when tension increases

creatine phosphate: phosphagen used to store energy from ATP and transfer it to muscle

dense body: sarcoplasmic structure that attaches to the sarcolemma and shortens the muscle as thin filaments slide past thick filaments

depolarize: to reduce the voltage difference between the inside and outside of a cell's plasma membrane (the sarcolemma for a muscle fiber), making the inside less negative than at rest

desmosome: cell structure that anchors the ends of cardiac muscle fibers to allow contraction to occur

eccentric contraction: muscle contraction that lengthens the muscle as the tension is diminished

elasticity: ability to stretch and rebound

endomysium: loose, and well-hydrated connective tissue covering each muscle fiber in a skeletal muscle

epimysium: outer layer of connective tissue around a skeletal muscle

excitability: ability to undergo neural stimulation

excitation-contraction coupling: sequence of events from motor neuron signaling to a skeletal muscle fiber to contraction of the fiber's sarcomeres

extensibility: ability to lengthen (extend)

fascicle: bundle of muscle fibers within a skeletal muscle

fast glycolytic (FG): muscle fiber that primarily uses anaerobic glycolysis

fast oxidative (FO): intermediate muscle fiber that is between slow oxidative and fast glycolytic fibers

fibrosis: replacement of muscle fibers by scar tissue

glycolysis: anaerobic breakdown of glucose to ATP

graded muscle response: modification of contraction strength

hyperplasia: process in which one cell splits to produce new cells

hypertonia: abnormally high muscle tone

hypertrophy: addition of structural proteins to muscle fibers

hypotonia: abnormally low muscle tone caused by the absence of low-level contractions

intercalated disc: part of the sarcolemma that connects cardiac tissue, and contains gap junctions and desmosomes

isometric contraction: muscle contraction that occurs with no change in muscle length

isotonic contraction: muscle contraction that involves changes in muscle length

lactic acid: product of anaerobic glycolysis

latch-bridges: subset of a cross-bridge in which actin and myosin remain locked together

latent period: the time when a twitch does not produce contraction

motor end-plate: sarcolemma of muscle fiber at the neuromuscular junction, with receptors for the neurotransmitter acetylcholine

motor unit: motor neuron and the group of muscle fibers it innervates

muscle tension: force generated by the contraction of the muscle; tension generated during isotonic contractions and isometric contractions

muscle tone: low levels of muscle contraction that occur when a muscle is not producing movement

myoblast: muscle-forming stem cell

myofibril: long, cylindrical organelle that runs parallel within the muscle fiber and contains the sarcomeres

myogram: instrument used to measure twitch tension

myosin: protein that makes up most of the thick cylindrical myofilament within a sarcomere muscle fiber

myotube: fusion of many myoblast cells

neuromuscular junction (NMJ): synapse between the axon terminal of a motor neuron and the section of the membrane of a muscle fiber with receptors for the acetylcholine released by the terminal

neurotransmitter: signaling chemical released by nerve terminals that bind to and activate receptors on target cells

oxygen debt: amount of oxygen needed to compensate for ATP produced without oxygen during muscle contraction

pacesetter cell: cell that triggers action potentials in smooth muscle

pericyte: stem cell that regenerates smooth muscle cells

perimysium: connective tissue that bundles skeletal muscle fibers into fascicles within a skeletal muscle

power stroke: action of myosin pulling actin inward (toward the M line)

pyruvic acid: product of glycolysis that can be used in aerobic respiration or converted to lactic acid

recruitment: increase in the number of motor units involved in contraction

relaxation phase: period after twitch contraction when tension decreases

sarcolemma: plasma membrane of a skeletal muscle fiber

sarcomere: longitudinally, repeating functional unit of skeletal muscle, with all of the contractile and associated proteins involved in contraction

sarcopenia: age-related muscle atrophy

sarcoplasmic reticulum (SR): specialized smooth endoplasmic reticulum, which stores, releases, and retrieves Ca^{++}

sarcoplasm: cytoplasm of a muscle cell

satellite cell: stem cell that helps to repair muscle cells

skeletal muscle: striated, multinucleated muscle that requires signaling from the nervous system to trigger contraction; most skeletal muscles are referred to as voluntary muscles that move bones and produce movement

slow oxidative (SO): muscle fiber that primarily uses aerobic respiration

smooth muscle: nonstriated, mononucleated muscle in the skin that is associated with hair follicles; assists in moving materials in the walls of internal organs, blood vessels, and internal passageways

somites: blocks of paraxial mesoderm cells

stress-relaxation response: relaxation of smooth muscle tissue after being stretched

synaptic cleft: space between a nerve (axon) terminal and a motor end-plate

T-tubule: projection of the sarcolemma into the interior of the cell

tetanus: a continuous fused contraction

thick filament: the thick myosin strands and their multiple heads projecting from the center of the sarcomere toward, but not all to way to, the Z-discs

thin filament: thin strands of actin and its troponin-tropomyosin complex projecting from the Z-discs toward the center of the sarcomere

treppe: stepwise increase in contraction tension

triad: the grouping of one T-tubule and two terminal cisternae

tropomyosin: regulatory protein that covers myosin-binding sites to prevent actin from binding to myosin

troponin: regulatory protein that binds to actin, tropomyosin, and calcium

twitch: single contraction produced by one action potential

varicosity: enlargement of neurons that release neurotransmitters into synaptic clefts

visceral muscle: smooth muscle found in the walls of visceral organs

voltage-gated sodium channels: membrane proteins that open sodium channels in response to a sufficient voltage change, and initiate and transmit the action potential as Na^+ enters through the channel

wave summation: addition of successive neural stimuli to produce greater contraction

PRACTICE TEST: MUSCLE TISSUE

Review the material from this module by completing the practice in course online.

LAB AND STUDY PACKET: MUSCLE TISSUE

Instructors, make a copy of this packet to modify this worksheet and lab to fit your classroom needs:

https://docs.google.com/document/d/1DCbbH47uQBwZ0s1sgK0wZ2YYypL8-IRsraCvTHJX4T8/edit?usp=sharing

MODULE 12: THE MUSCULAR SYSTEM

INTRODUCTION TO THE MUSCULAR SYSTEM

Learning Objectives

- Describe the actions and roles of agonists and antagonists
- Explain the structure and organization of muscle fascicles and their role in generating force
- Explain the criteria used to name skeletal muscles
- Identify the skeletal muscles and their actions on the skeleton and soft tissues of the body
- Identify the origins and insertions of skeletal muscles and the prime movements

Think about the things that you do each day—talking, walking, sitting, standing, and running—all of these activities require movement of particular skeletal muscles. Skeletal muscles are even used during sleep. The diaphragm is a sheet of skeletal muscle that has to contract and relax for you to breathe day and night. If you recall from your study of the skeletal system and joints, body movement occurs around the joints in the body. The focus of this chapter is on skeletal muscle organization. The system to name skeletal muscles will be explained; in some cases, the muscle is named by its shape, and in other cases it is named by its location or attachments to the skeleton. If you understand the meaning of the name of the muscle, often it will help you remember its location and/or what it does.

Figure 1. A Body in Motion. *The muscular system allows us to move, flex and contort our bodies. Practicing yoga, as pictured here, is a good example of the voluntary use of the muscular system. (credit: Dmitry Yanchylenko)*

This chapter also will describe how skeletal muscles are arranged to accomplish movement, and how other muscles may assist, or be arranged on the skeleton to resist or carry out the opposite movement. The actions of the skeletal muscles will be covered in a regional manner, working from the head down to the toes.

INTERACTIONS OF SKELETAL MUSCLES

Learning Objectives

- Compare and contrast agonist and antagonist muscles
- Describe how fascicles are arranged within a skeletal muscle
- Explain the major events of a skeletal muscle contraction within a muscle in generating force

To move the skeleton, the tension created by the contraction of the fibers in most skeletal muscles is transferred to the tendons. The tendons are strong bands of dense, regular connective tissue that connect muscles to bones. The bone connection is why this muscle tissue is called skeletal muscle.

Interactions of Skeletal Muscles in the Body

To pull on a bone, that is, to change the angle at its synovial joint, which essentially moves the skeleton, a skeletal muscle must also be attached to a fixed part of the skeleton. The moveable end of the muscle that attaches to the bone being pulled is called the muscle's **insertion**, and the end of the muscle attached to a fixed (stabilized) bone is called the **origin**. During forearm **flexion**—bending the elbow—the brachioradialis assists the brachialis.

Although a number of muscles may be involved in an action, the principal muscle involved is called the **prime mover**, or **agonist**. To lift a cup, a muscle called the biceps brachii is actually the prime mover; however, because it can be assisted by the brachialis, the brachialis is called a **synergist** in this action (Figure 1). A synergist can also be a **fixator** that stabilizes the bone that is the attachment for the prime mover's origin.

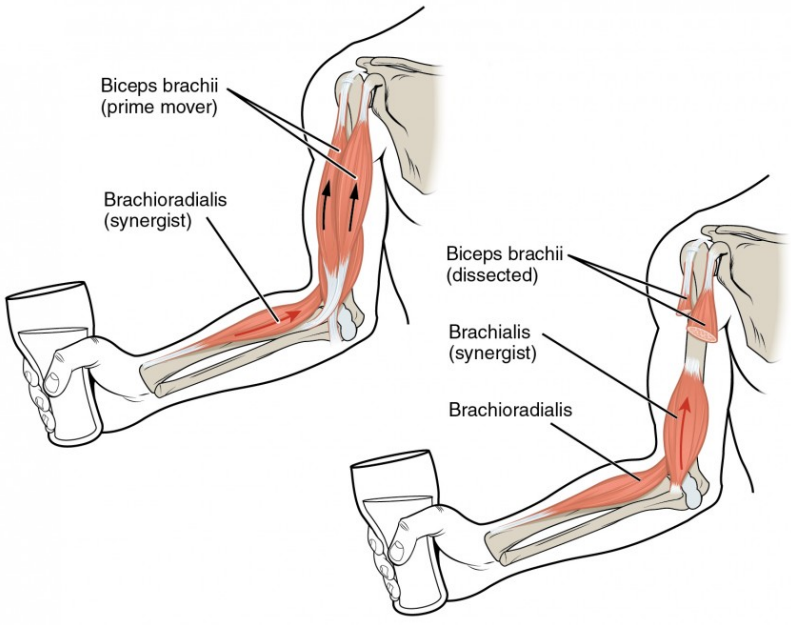


Figure 1. Prime Movers and Synergists. *The biceps brachii flex the lower arm. The brachoradialis, in the forearm, and brachialis, located deep to the biceps in the upper arm, are both synergists that aid in this motion.*

A muscle with the opposite action of the prime mover is called an **antagonist**. Antagonists play two important roles in muscle function:

1. They maintain body or limb position, such as holding the arm out or standing erect
2. They control rapid movement, as in shadow boxing without landing a punch or the ability to check the motion of a limb

For example, to extend the knee, a group of four muscles called the quadriceps femoris in the anterior compartment of the thigh are activated (and would be called the agonists of knee extension). However, to flex the knee joint, an opposite or antagonistic set of muscles called the hamstrings is activated.

As you can see, these terms would also be reversed for the opposing action. If you consider the first action as the knee bending, the hamstrings would be called the agonists and the quadriceps femoris would then be called the antagonists. See Table 1 for a list of some agonists and antagonists.

Table 1. Agonist and Antagonist Skeletal Muscle Pairs

Agonist	Antagonist	Movement
Biceps brachii: in the anterior compartment of the arm	Triceps brachii: in the posterior compartment of the arm	The biceps brachii flexes the forearm, whereas the triceps brachii extends it.
Hamstrings: group of three muscles in the posterior compartment of the thigh	Quadriceps femoris: group of four muscles in the anterior compartment of the thigh	The hamstrings flex the leg, whereas the quadriceps femoris extend it.
Flexor digitorum superficialis and flexor digitorum profundus: in the anterior compartment of the forearm	Extensor digitorum: in the posterior compartment of the forearm	The flexor digitorum superficialis and flexor digitorum profundus flex the fingers and the hand at the wrist, whereas the extensor digitorum extends the fingers and the hand at the wrist.

There are also skeletal muscles that do not pull against the skeleton for movements. For example, there are the muscles that produce facial expressions. The insertions and origins of facial muscles are in the skin, so that certain individual muscles contract to form a smile or frown, form sounds or words, and raise the eyebrows. There also are skeletal muscles in the tongue, and the external urinary and anal sphincters that allow for voluntary regulation of urination and defecation, respectively. In addition, the diaphragm contracts and relaxes to change the volume of the pleural cavities but it does not move the skeleton to do this.

Everyday Connections: Exercise and Stretching

When exercising, it is important to first warm up the muscles. Stretching pulls on the muscle fibers and it also results in an increased blood flow to the muscles being worked. Without a proper warm-up, it is possible that you may either damage some of the muscle fibers or pull a tendon. A pulled tendon, regardless of location, results in pain, swelling, and diminished function; if it is moderate to severe, the injury could immobilize you for an extended period.

Recall the discussion about muscles crossing joints to create movement. Most of the joints you use during exercise are synovial joints, which have synovial fluid in the joint space between two bones. Exercise and stretching may also have a beneficial effect on synovial joints. Synovial fluid is a thin, but viscous film with the consistency of egg whites. When you first get up and start moving, your joints feel stiff for a number of reasons. After proper stretching and warm-up, the synovial fluid may become less viscous, allowing for better joint function.

Patterns of Fascicle Organization

Skeletal muscle is enclosed in connective tissue scaffolding at three levels. Each muscle fiber (cell) is covered by endomysium and the entire muscle is covered by epimysium. When a group of muscle fibers is “bundled” as a unit within the whole muscle by an additional covering of a connective tissue called perimysium, that bundled group of muscle fibers is called a **fascicle**. Fascicle arrangement by perimysia is correlated to the force generated by a muscle; it also affects the range of motion of the muscle. Based on the patterns of fascicle arrangement, skeletal muscles can be classified in several ways. What follows are the most common fascicle arrangements.

Parallel muscles have fascicles that are arranged in the same direction as the long axis of the muscle (Figure 2). The majority of skeletal muscles in the body have this type of organization. Some parallel muscles are flat sheets

that expand at the ends to make broad attachments. Other parallel muscles are rotund with tendons at one or both ends. Muscles that seem to be plump have a large mass of tissue located in the middle of the muscle, between the insertion and the origin, which is known as the central body. A more common name for this muscle is **belly**. When a muscle contracts, the contractile fibers shorten it to an even larger bulge. For example, extend and then flex your biceps brachii muscle; the large, middle section is the belly (Figure 3). When a parallel muscle has a central, large belly that is spindle-shaped, meaning it tapers as it extends to its origin and insertion, it sometimes is called **fusiform**.

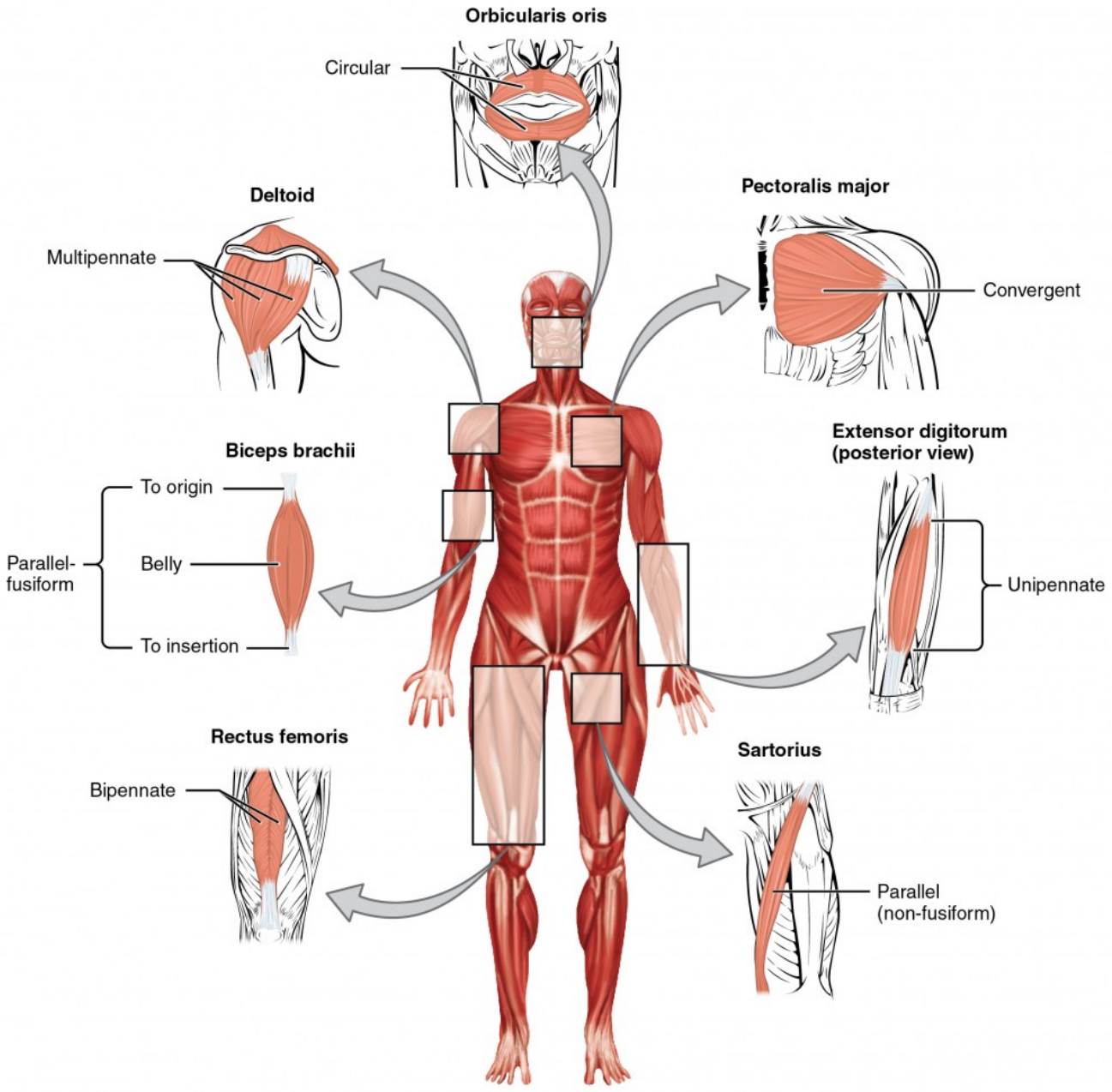


Figure 2. Muscle Shapes and Fiber Alignment. *The skeletal muscles of the body typically come in seven different general shapes.*

Circular muscles are also called sphincters (see Figure 2). When they relax, the sphincters' concentrically arranged bundles of muscle fibers increase the size of the opening, and when they contract, the size of the opening shrinks to the point of closure. The orbicularis oris muscle is a circular muscle that goes around the mouth. When it contracts, the oral opening becomes smaller, as when puckering the lips for whistling. Another example is the orbicularis oculi, one of which surrounds each eye. Consider, for example, the names of the two orbicularis muscles (orbicularis oris and oribicularis oculi), where part of the first name of both muscles is the same. The first part of orbicularis, orb (orb = "circular"), is a reference to a round or circular structure; it may also make one think of orbit, such as the moon's path around the earth. The word oris (oris = "oral") refers to the oral cavity, or the mouth. The word oculi (ocular = "eye") refers to the eye.

Figure 3. Biceps Brachii Muscle Contraction. *The large mass at the center of a muscle is called the belly. Tendons emerge from both ends of the belly and connect the muscle to the bones, allowing the skeleton to move. The tendons of the bicep connect to the upper arm and the forearm. (credit: Victoria Garcia)*

There are other muscles throughout the body named by their shape or location. The deltoid is a large, triangular-shaped muscle that covers the shoulder. It is so-named because the Greek letter delta looks like a triangle. The rectus abdomis (rector = "straight") is the straight muscle in the anterior wall of the abdomen, while the rectus femoris is the straight muscle in the anterior compartment of the thigh.

When a muscle has a widespread expansion over a sizable area, but then the fascicles come to a single, common attachment point, the muscle is called convergent. The attachment point for a convergent muscle could be a tendon, an aponeurosis (a flat, broad tendon), or a raphe (a very slender tendon). The large muscle on the chest, the pectoralis major, is an example of a convergent muscle because it converges on the greater tubercle of the humerus via a tendon. The temporalis muscle of the cranium is another.

Pennate muscles (penna = "feathers") blend into a tendon that runs through the central region of the muscle for its whole length, somewhat like the quill of a feather with the muscle arranged similar to the feathers. Due to this design, the muscle fibers in a pennate muscle can only pull at an angle, and as a result, contracting pennate muscles do not move their tendons very far. However, because a pennate muscle generally can hold more muscle fibers within it, it can produce relatively more tension for its size. There are three subtypes of pennate muscles.

In a unipennate muscle, the fascicles are located on one side of the tendon. The extensor digitorum of the forearm is an example of a unipennate muscle. A bipennate muscle has fascicles on both sides of the tendon. In some pennate muscles, the muscle fibers wrap around the tendon, sometimes forming individual fascicles in the process. This arrangement is referred to as multipennate. A common example is the deltoid muscle of the shoulder, which covers the shoulder but has a single tendon that inserts on the deltoid tuberosity of the humerus.

Because of fascicles, a portion of a multipennate muscle like the deltoid can be stimulated by the nervous system to change the direction of the pull. For example, when the deltoid muscle contracts, the arm abducts (moves away from midline in the sagittal plane), but when only the anterior fascicle is stimulated, the arm will abduct and flex (move anteriorly at the shoulder joint).

The Lever System of Muscle and Bone Interactions

Skeletal muscles do not work by themselves. Muscles are arranged in pairs based on their functions. For muscles attached to the bones of the skeleton, the connection determines the force, speed, and range of movement. These characteristics depend on each other and can explain the general organization of the muscular and skeletal systems.

The skeleton and muscles act together to move the body. Have you ever used the back of a hammer to remove a nail from wood? The handle acts as a lever and the head of the hammer acts as a fulcrum, the fixed point that the force is applied to when you pull back or push down on the handle. The effort applied to this system is the pulling or pushing on the handle to remove the nail, which is the load, or “resistance” to the movement of the handle in the system. Our musculoskeletal system works in a similar manner, with bones being stiff levers and the articular endings of the bones—encased in synovial joints—acting as fulcrums. The load would be an object being lifted or any resistance to a movement (your head is a load when you are lifting it), and the effort, or applied force, comes from contracting skeletal muscle.

Self-Check Questions

Visit your course online to take a quiz to check your understanding of the Interactions of Skeletal Muscles:

NAMING SKELETAL MUSCLES

Learning Objectives

- Describe the criteria used to name skeletal muscles
- Explain how understanding the muscle names helps describe shapes, location, and actions of various muscles

The Greeks and Romans conducted the first studies done on the human body in Western culture. The educated class of subsequent societies studied Latin and Greek, and therefore the early pioneers of anatomy continued to apply Latin and Greek terminology or roots when they named the skeletal muscles. The large number of muscles in the body and unfamiliar words can make learning the names of the muscles in the body seem daunting, but understanding the etymology can help. Etymology is the study of how the root of a particular word entered a language and how the use of the word evolved over time. Taking the time to learn the root of the words is crucial to understanding the vocabulary of anatomy and physiology. When you understand the names of muscles it will help you remember where the muscles are located and what they do (Figure 1, Table 1, and Table 2). Pronunciation of words and terms will take a bit of time to master, but after you have some basic information; the correct names and pronunciations will become easier.

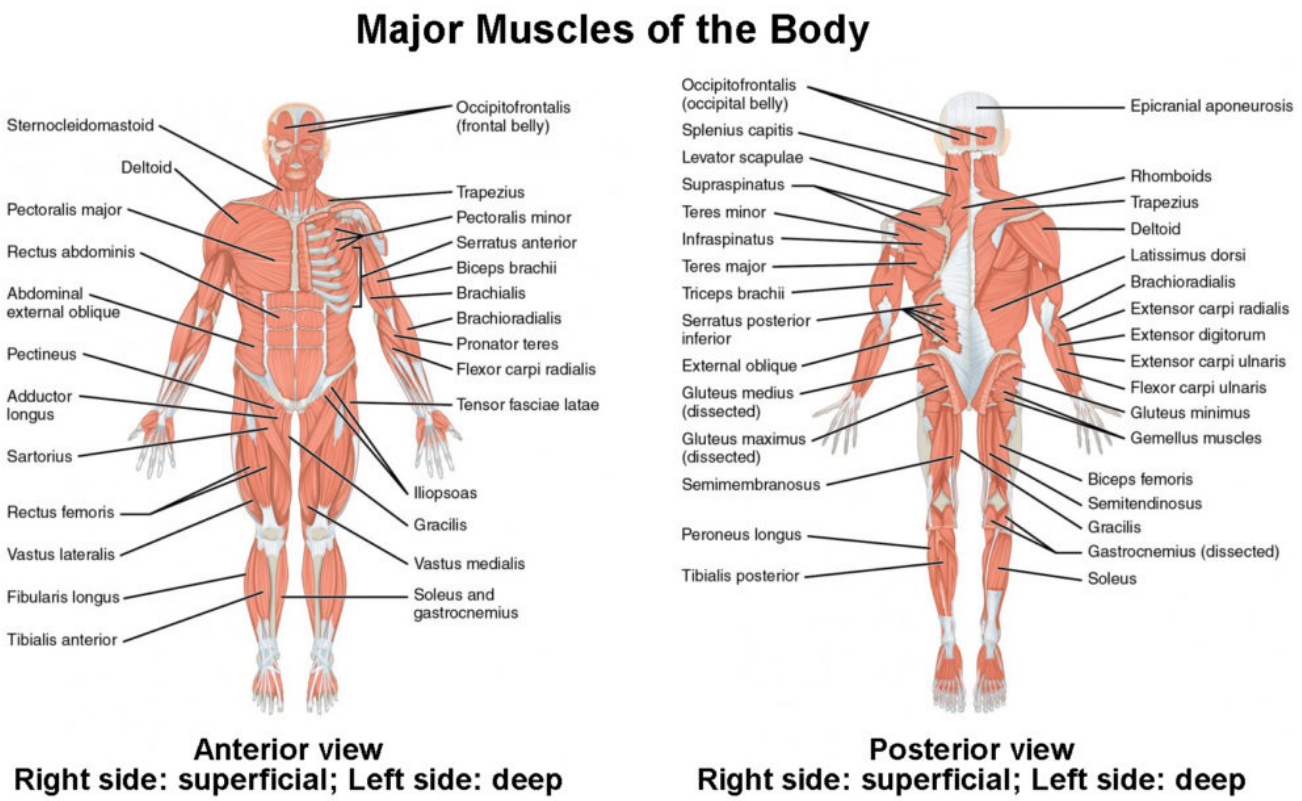


Figure 1. Overview of the Muscular System. *On the anterior and posterior views of the muscular system above, superficial muscles (those at the surface) are shown on the right side of the body while deep muscles (those underneath the superficial muscles) are shown on the left half of the body. For the legs, superficial muscles are shown in the anterior view while the posterior view shows both superficial and deep muscles.*

Table 1. Understanding a Muscle Name from the Latin

Example	Word	Latin Root 1	Latin Root 2	Meaning	Translation
abductor digiti minimi	abductor	*ab* = away from	*duct* = to move	a muscle that moves away from	A muscle that moves the little finger or toe away
	digiti	*digitus* = digit		refers to a finger or toe	
	minimi	*minimus* = mini, tiny		little	
adductor digiti minimi	adductor	*ad* = to, toward	*duct* = to move	a muscle that moves towards	A muscle that moves the little finger or toe toward
	digiti	*digitus* = digit		refers to a finger or toe	
	minimi	*minimus* = mini, tiny		little	

Table 2. Mnemonic Device for Latin Roots		
Example	Latin or Greek Translation	Mnemonic Device
ad	to; toward	ADvance toward your goal
ab	away from	n/a
sub	under	SUBmarines move under water.
ductor	something that moves	A conDUCTOR makes a train move.
anti	against	If you are antisocial, you are against engaging in social activities.
epi	on top of	n/a
apo	to the side of	n/a
longissimus	longest	“Longissimus” is longer than the word “long.”
longus	long	long
brevis	short	brief
maximus	large	max
medius	medium	“Medius” and “medium” both begin with “med.”
minimus	tiny; little	mini
rectus	straight	To RECTify a situation is to straighten it out.
multi	many	If something is MULTIcolored, it has many colors.
uni	one	A UNIcorn has one horn.
bi/di	two	If a ring is DIcast, it is made of two metals.
tri	three	TRIple the amount of money is three times as much.
quad	four	QUADruplets are four children born at one birth.
externus	outside	EXternal
internus	inside	INternal

Anatomists name the skeletal muscles according to a number of criteria, each of which describes the muscle in some way. These include naming the muscle after its shape, its size compared to other muscles in the area, its location in the body or the location of its attachments to the skeleton, how many origins it has, or its action.

The skeletal muscle’s anatomical location or its relationship to a particular bone often determines its name. For example, the frontalis muscle is located on top of the frontal bone of the skull. Similarly, the shapes of some muscles are very distinctive and the names, such as orbicularis, reflect the shape. For the buttocks, the size of the muscles influences the names: gluteus **maximus** (largest), gluteus **medius** (medium), and the gluteus **minimus** (smallest). Names were given to indicate length— **brevis** (short), **longus** (long)—and to identify position relative to the midline: **lateralis** (to the outside away from the midline), and **medialis** (toward the midline).

The direction of the muscle fibers and fascicles are used to describe muscles relative to the midline, such as the **rectus** (straight) abdominis, or the **oblique** (at an angle) muscles of the abdomen.

Some muscle names indicate the number of muscles in a group. One example of this is the quadriceps, a group of four muscles located on the anterior (front) thigh. Other muscle names can provide information as to how many origins a particular muscle has, such as the biceps brachii. The prefix **bi** indicates that the muscle has two origins and **tri** indicates three origins.

The location of a muscle's attachment can also appear in its name. When the name of a muscle is based on the attachments, the origin is always named first. For instance, the sternocleidomastoid muscle of the neck has a dual origin on the sternum (sterno) and clavicle (cleido), and it inserts on the mastoid process of the temporal bone. The last feature by which to name a muscle is its action. When muscles are named for the movement they produce, one can find action words in their name. Some examples are **flexor** (decreases the angle at the joint), **extensor** (increases the angle at the joint), **abductor** (moves the bone away from the midline), or **adductor** (moves the bone toward the midline).

AXIAL MUSCLES OF THE HEAD, NECK, AND BACK

Learning Objectives

- Identify the axial muscles of the face, head, and neck
- Identify the movement and function of the face, head, and neck muscles

The skeletal muscles are divided into **axial** (muscles of the trunk and head) and **appendicular** (muscles of the arms and legs) categories. This system reflects the bones of the skeleton system, which are also arranged in this manner. The axial muscles are grouped based on location, function, or both. Some of the axial muscles may seem to blur the boundaries because they cross over to the appendicular skeleton. The first grouping of the axial muscles you will review includes the muscles of the head and neck, then you will review the muscles of the vertebral column, and finally you will review the oblique and rectus muscles.

Muscles That Create Facial Expression

The origins of the muscles of facial expression are on the surface of the skull (remember, the origin of a muscle does not move). The insertions of these muscles have fibers intertwined with connective tissue and the dermis of the skin. Because the muscles insert in the skin rather than on bone, when they contract, the skin moves to create facial expression (Figure 1).

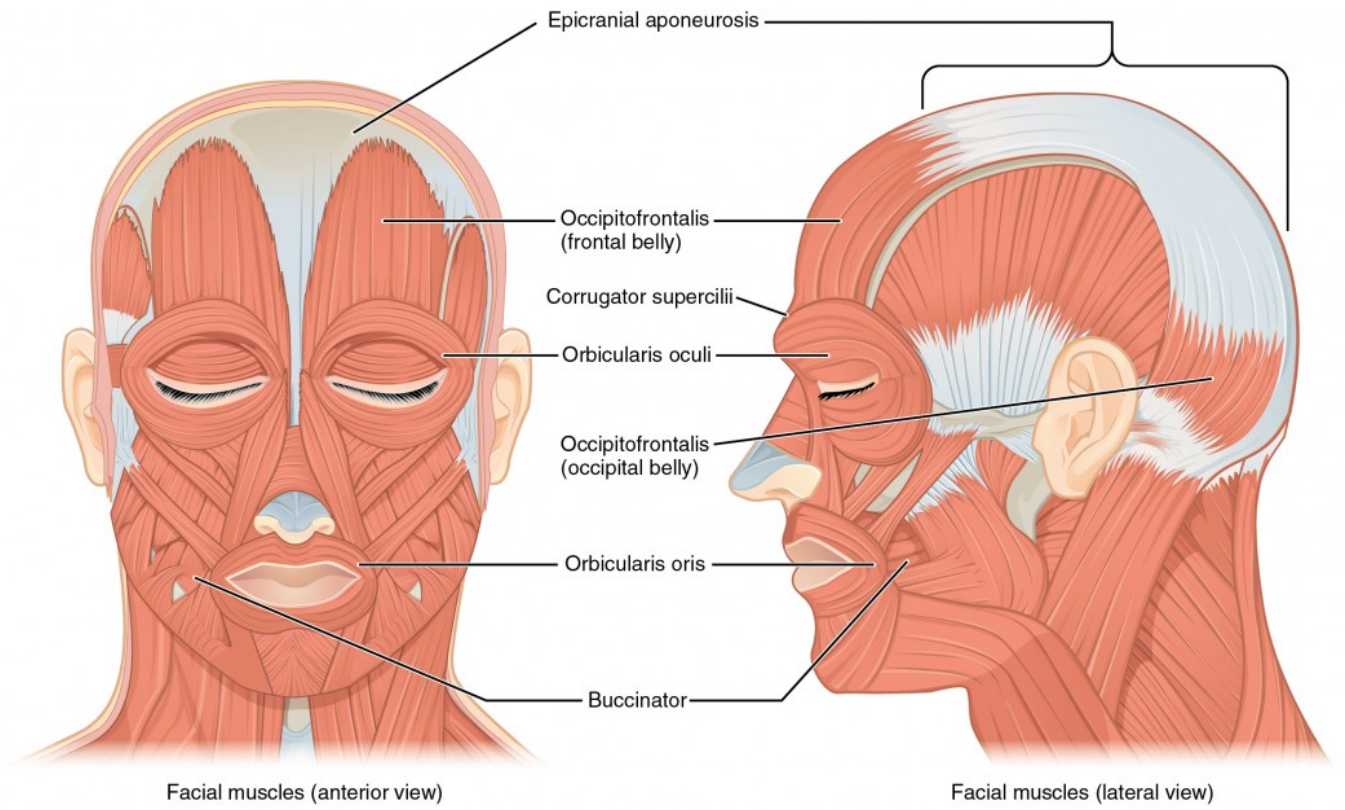


Figure 1. Muscles of Facial Expression. *Many of the muscles of facial expression insert into the skin surrounding the eyelids, nose and mouth, producing facial expressions by moving the skin rather than bones.*

The **orbicularis oris** is a circular muscle that moves the lips, and the **orbicularis oculi** is a circular muscle that closes the eye. The **occipitofrontalis** muscle moves up the scalp and eyebrows. The muscle has a frontal belly and an occipital (near the occipital bone on the posterior part of the skull) belly. In other words, there is a muscle on the forehead (**frontalis**) and one on the back of the head (**occipitalis**), but there is no muscle across the top of the head. Instead, the two bellies are connected by a broad tendon called the **epicranial aponeurosis**, or galea aponeurosis (galea = “apple”). The physicians originally studying human anatomy thought the skull looked like an apple.

The majority of the face is composed of the **buccinator** muscle, which compresses the cheek. This muscle allows you to whistle, blow, and suck; and it contributes to the action of chewing. There are several small facial muscles, one of which is the **corrugator supercilii**, which is the prime mover of the eyebrows. Place your finger on your eyebrows at the point of the bridge of the nose. Raise your eyebrows as if you were surprised and lower your eyebrows as if you were frowning. With these movements, you can feel the action of the corrugator supercilli. Additional muscles of facial expression are presented in Table 1.

Table 1. Muscles in Facial Expression

Movement	Target	Target motion direction	Prime mover	Origin	Insertion
Brow					
Furrowing brow	Skin of the scalp	Anterior	Occipitofrontalis, frontal belly	Epicraneal aponeurosis	Underneath the skin of the forehead

Table 1. Muscles in Facial Expression					
Movement	Target	Target motion direction	Prime mover	Origin	Insertion
Unfurrowing brow	Skin of the scalp	Posterior	Occipitofrontalis, occipital belly	Occipital bone; mastoid process (temporal bone)	Epicraneal aponeurosis
Lowering eyebrows (e.g., scowling, frowning	Skin underneath the eyebrows	Inferior	Corrugator supercilii	Frontal bone	Skin underneath the eyebrow
Nose					
Flaring nostrils	Nasal cartilage (pushes nostrils open when cartilage is compressed)	Inferior compression; posterior compression	Nasalis	Maxilla	Nasal bone
Mouth					
Raising upper lip	Upper lip tissue	Elevation	Levator labii superioris	Maxilla	Underneath skin at the corners of the mouth; orbicularis oris
Lowering lower lip	Lower lip	Depression	Depressor labii inferioris	Mandible	Underneath skin of the lower lip
Opening mouth and sliding lower jaw left and right	Lower jaw	Depression, lateral	Depressor angulus oris	Mandible	Underneath skin at the corners of the mouth
Smiling	Corners of the mouth	Lateral elevation	Zygomaticus major	Zygomatic bone	Underneath skin at the corners of the mouth (dimple area); orbicularis oris
Shaping of lips (as during speech)	Lips	Multiple	Orbicularis oris	Tissue surrounding the lips	Underneath skin at the corners of the mouth
Lateral movement of cheeks (e.g., sucking on a straw; also used to	Cheeks	Lateral	Buccinator	Maxilla, mandible; sphenoid bone (via pterygomandibular raphae)	Orbicularis oris

Table 1. Muscles in Facial Expression					
Movement	Target	Target motion direction	Prime mover	Origin	Insertion
compress air in mouth while blowing)					
Pursing of lips by straightening them laterally	Corners of the mouth	Lateral	Risorius	Fascia of the parotid salivary gland	Underneath skin at the corners of the mouth
Protrusion of lower lip (e.g, pouting expression)	Lower lip and the skin of the chin	Protraction	Mentalis	Mandible	Underneath skin of the chin
Raising upper lip	Upper lip	Elevation	Levator labii superioris	Maxilla	Underneath skin at the corners of the mouth; orbicularis oris

Muscles That Move the Eyes

The movement of the eyeball is under the control of the **extrinsic eye muscles**, which originate outside the eye and insert onto the outer surface of the white of the eye. These muscles are located inside the eye socket and cannot be seen on any part of the visible eyeball (Figure 2 and Table 2). If you have ever been to a doctor who held up a finger and asked you to follow it up, down, and to both sides, he or she is checking to make sure your eye muscles are acting in a coordinated pattern.

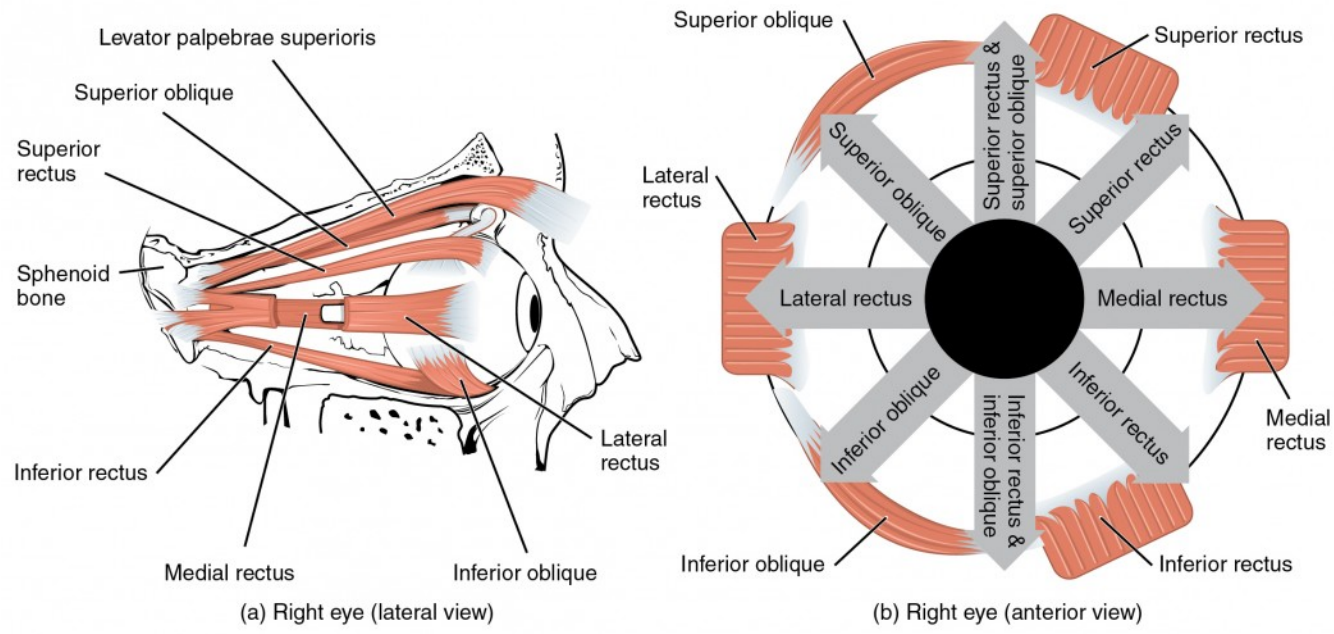


Figure 2. Muscles of the Eyes. *(a) The extrinsic eye muscles originate outside of the eye on the skull. (b) Each muscle inserts onto the eyeball.*

Table 2. Muscles of the Eyes					
Movement	Target	Target motion direction	Prime mover	Origin	Insertion
Moves eyes up and toward nose; rotates eyes from 1 o'clock to 3 o'clock	Eyeballs	Superior (elevates); medial (adducts)	Superior rectus	Common tendinous ring (ring attaches to optic foramen)	Superior surface of eyeball
Moves eyes down and toward nose; rotates eyes from 6 o'clock to 3 o'clock	Eyeballs	Inferior (depresses) medial (adducts)	Inferior rectus	Common tendinous rind (ring attaches to optic foramen)	Inferior surface of eyeball
Moves eyes away from nose	Eyeballs	Lateral (abducts)	Lateral rectus	Common tendinous ring (ring attaches to optic foramen)	Lateral surface of eyeball
Moves eyes toward nose	Eyeballs	Medial (adducts)	Medial rectus	Common tendinous ring (ring attaches to optic foramen)	Medial surface of eyeball
Moves eyes up and away from nose; rotates eyeball from 12 o'clock to 9 o'clock	Eyeballs	Superior (elevates; lateral (abducts)	Inferior oblique	Floor of orbit (maxilla)	Surface of eyeball between inferior rectus and lateral rectus
Moves eyes down and away from nose; rotates eyeball from 6 o'clock to 9 o'clock	Eyeballs	Superior (elevates); lateral (abducts)	Superior oblique	Sphenoid bone	Surface of eyeball between superior rectus and lateral rectus
Opens eyes	Upper eyelid	Superior (elevates)	Levator palpabrae superioris	Roof of orbit (sphenoid bone)	Skin of upper eyelids
Closes eyelids	Eyelid skin	Compression along superior–inferior axis	Orbicularis oculi	Medial bones composing the orbit	Circumference of orbit

Muscles That Move the Lower Jaw

In anatomical terminology, chewing is called **mastication**. Muscles involved in chewing must be able to exert enough pressure to bite through and then chew food before it is swallowed (Figure 3 and Table 3). The **masseter** muscle is the main muscle used for chewing because it elevates the mandible (lower jaw) to close the mouth, and it is assisted by the **temporalis** muscle, which retracts the mandible. You can feel the temporalis move by putting your fingers to your temple as you chew.

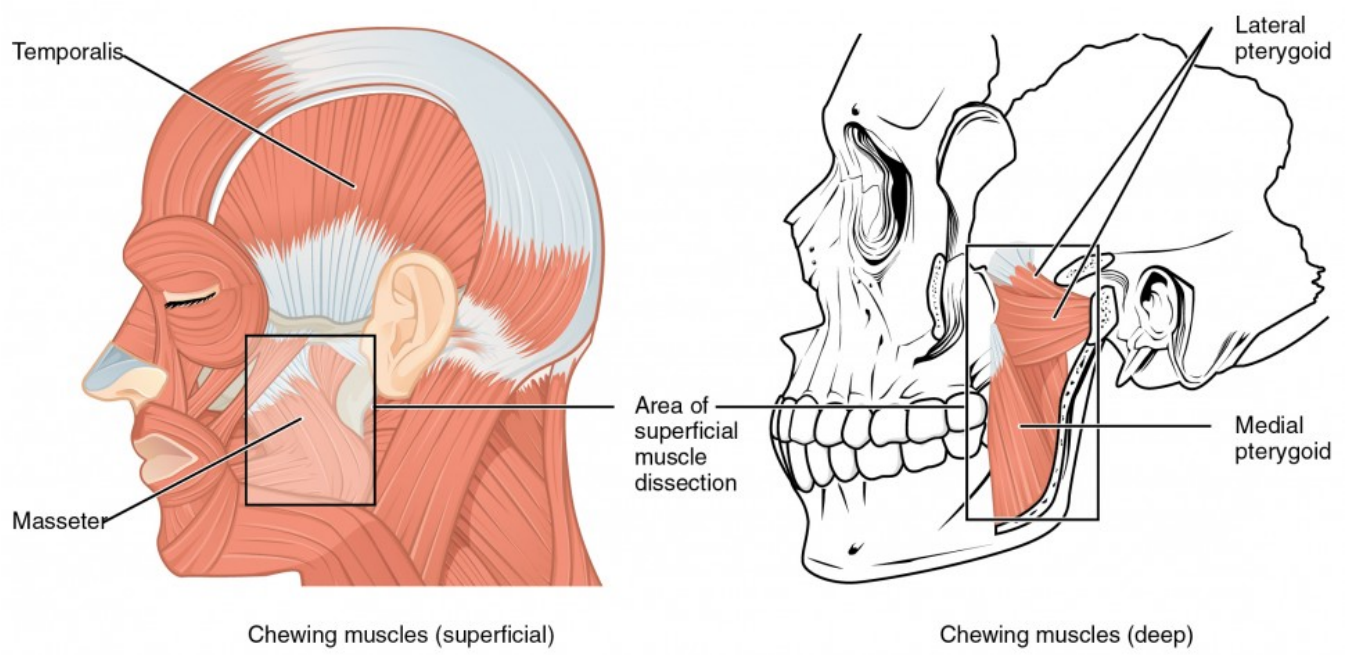


Figure 3. Muscles That Move the Lower Jaw. *The muscles that move the lower jaw are typically located within the cheek and originate from processes in the skull. This provides the jaw muscles with the large amount of leverage needed for chewing.*

Table 3. Muscles of the Lower Jaw

Movement	Target	Target motion direction	Prime mover	Origin	Insertion
Closes mouth; aids chewing	Mandible	Superior (elevates)	Masseter	Maxilla arch; zygomatic arch (for master)	Mandible
Closes mouth; pulls lower jaw in under upper jaw	Mandible	Superior (elevates); posterior (retracts)	Temporalis	Temporal bone	Mandible
Opens mouth; pushes lower jaw out under upper jaw; moves lower jaw side-to-side	Mandible	Inferior (depresses); posterior (protracts); lateral (abducts); medial (adducts)	Lateral pterygoid	Pterygoid process of sphenoid bone	Mandible
Closes mouth; pushes lower jaw out under upper jaw; moves lower jaw side-to-side	Mandible	Superior (elevates); posterior (protracts); lateral (abducts); medial (adducts)	Medial pterygoid	Sphenoid bone; maxilla	Mandible; temporo-mandibular joint

Although the masseter and temporalis are responsible for elevating and closing the jaw to break food into digestible pieces, the **medial pterygoi** and **lateral pterygoid** muscles provide assistance in chewing and moving food within the mouth.

Muscles That Move the Tongue

Although the tongue is obviously important for tasting food, it is also necessary for mastication, **deglutition** (swallowing), and speech (Figure 4 and Table 4). Because it is so moveable, the tongue facilitates complex speech patterns and sounds.

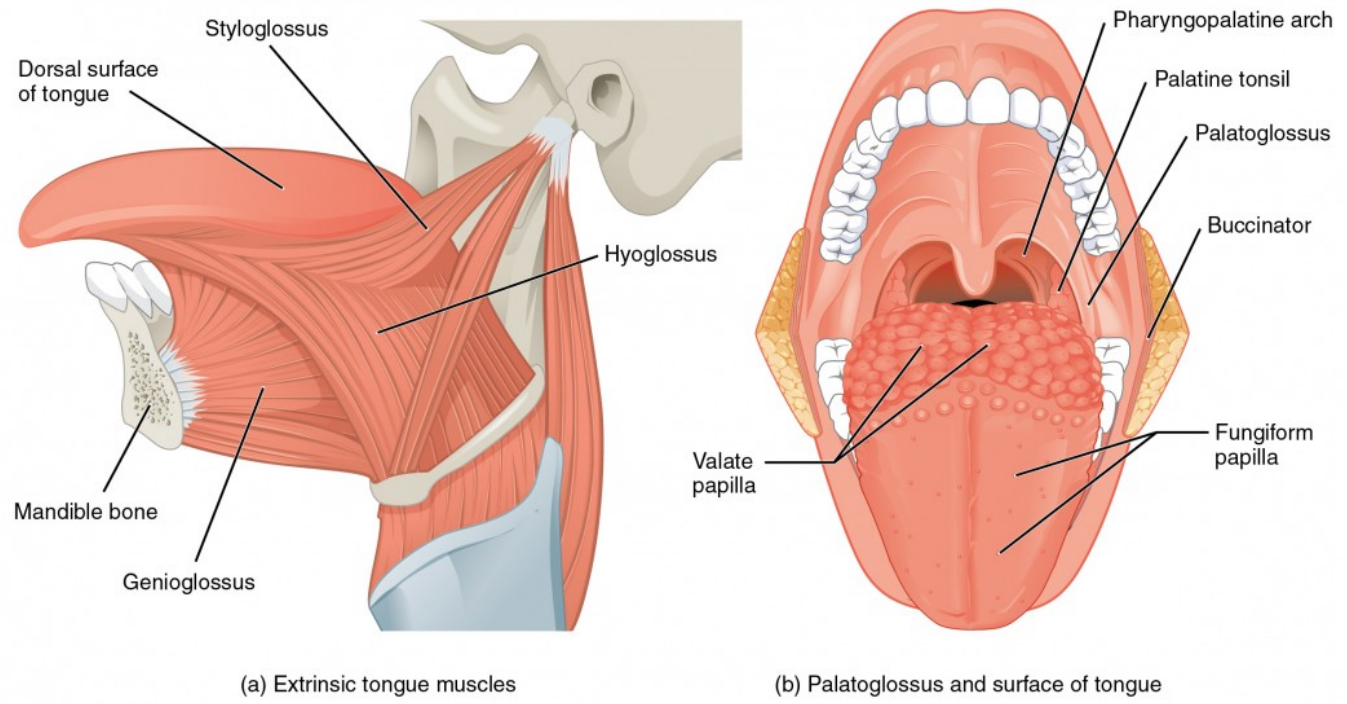


Figure 4. Muscles that Move the Tongue

Table 4. Muscles for Tongue Movement, Swallowing, and Speech					
Movement	**Target**	**Target motion direction**	**Prime mover**	**Origin**	**Insertion**
Tongue					
Moves the tongue down; sticks tongue out of the mouth	Tongue	Inferior (depresses); anterior (protracts)	Genioglossus	Mandible	Tongue undersurface; hyoid bone
Moves tongue up; retracts the tongue back into the mouth	Tongue	Superior (elevates); posterior (retracts)	Styloglossus	Temporal bone (styloid process)	Tongue undersurface and sides
Flattens tongue	Tongue	Inferior (depresses)	Hyoglossus	Hyoid bone	Sides of tongue
Bulges tongue	Tongue	Superior (elevation)	Palatoglossus	Soft palate	Side of tongue
Swallowing and speaking					

Table 4. Muscles for Tongue Movement, Swallowing, and Speech					
Movement	Target	Target motion direction	Prime mover	Origin	Insertion
Raises the hyoid bone in a way that also raises the larynx, allowing the epiglottis to cover the glottis during deglutition; also assists in opening the mouth by depressing the mandible	Hyoid bone; larynx	Superior (elevates)	Digastric	Mandible; temporal bone	Hyoid bone
Raises and retracts the hyoid bone in a way that elongates the oral cavity during deglutition	Hyoid bone	Superior (elevates); posterior (retracts)	Stylohyoid	Temporal bone (styloid process)	Hyoid bone
Raises the hyoid bone in a way that presses the tongue against the roof of the mouth, pushing food back into the pharynx during deglutition	Hyoid bone	Superior (elevates)	Mylohyoid	Mandible	Hyoid bone; median raphe
Raises and moves the hyoid bone forward, widening the pharynx during deglutition	Hyoid bone	Superior (elevates); anterior (protracts)	Geniohyoid	Mandible	Hyoid bone
Retracts the hyoid bone and moves it down during later phases of deglutition	Hyoid bone	Inferior (depresses); posterior (retracts)	Omohyoid	Scapula	Hyoid bone
Depresses the hyoid bone during swallowing and speaking	Hyoid bone	Inferior (depresses)	Sternohyoid	Clavicle	Hyoid bone
Shrinks distance between thyroid cartilage and the hyoid bone, allowing production of high-pitch vocalizations	Hyoid bone; thyroid cartilage	Hyoid bone: inferior (depresses); thyroid cartilage: superior (elevates)	Thyrohyoid	Thyroid cartilage	Hyoid bone
Depresses larynx, thyroid cartilage, and hyoid bone to create different vocal tones	Larynx; thyroid cartilage; hyoid bone	Inferior (depresses)	Sternothyroid	Sternum	Thyroid cartilage

Table 4. Muscles for Tongue Movement, Swallowing, and Speech					
Movement	Target	Target motion direction	Prime mover	Origin	Insertion
Rotates and tilts head to the side and forward	Skull; cervical vertebrae	Individually: medial rotation; lateral flexion; bilaterally; anterior (flexes)	Sternocleidomastoid; semispinalis capitis	Sternum; clavicle	Temporal bone (mastoid process); occipital bone
Rotates and tilts the head to the side and backwards	Skull; cervical vertebrae	Individually: lateral rotation; lateral flexion; bilaterally: anterior (flexes)	Splenius capitis; longissimus capitis	Sternum; clavicle	Temporal bone (mastoid process); occipital bone

Tongue muscles can be extrinsic or intrinsic. Extrinsic tongue muscles insert into the tongue from outside origins, and the intrinsic tongue muscles insert into the tongue from origins within it. The extrinsic muscles move the whole tongue in different directions, whereas the intrinsic muscles allow the tongue to change its shape (such as, curling the tongue in a loop or flattening it).

The extrinsic muscles all include the word root glossus (glossus = “tongue”), and the muscle names are derived from where the muscle originates. The **genioglossus** (genio = “chin”) originates on the mandible and allows the tongue to move downward and forward. The **styloglossus** originates on the styloid bone, and allows upward and backward motion. The **palatoglossus** originates on the soft palate to elevate the back of the tongue, and the **hyoglossus** originates on the hyoid bone to move the tongue downward and flatten it.

Everyday Connections: Anesthesia and the Tongue Muscles

Before surgery, a patient must be made ready for general anesthesia. The normal homeostatic controls of the body are put “on hold” so that the patient can be prepped for surgery. Control of respiration must be switched from the patient’s homeostatic control to the control of the anesthesiologist. The drugs used for anesthesia relax a majority of the body’s muscles.

Among the muscles affected during general anesthesia are those that are necessary for breathing and moving the tongue. Under anesthesia, the tongue can relax and partially or fully block the airway, and the muscles of respiration may not move the diaphragm or chest wall. To avoid possible complications, the safest procedure to use on a patient is called endotracheal intubation. Placing a tube into the trachea allows the doctors to maintain a patient’s (open) airway to the lungs and seal the airway off from the oropharynx. Post-surgery, the anesthesiologist gradually changes the mixture of the gases that keep the patient unconscious, and when the muscles of respiration begin to function, the tube is removed. It still takes about 30 minutes for a patient to wake up, and for breathing muscles to regain control of respiration. After surgery, most people have a sore or scratchy throat for a few days.

Muscles of the Anterior Neck

The muscles of the anterior neck assist in deglutition (swallowing) and speech by controlling the positions of the larynx (voice box), and the hyoid bone, a horseshoe-shaped bone that functions as a solid foundation on which the tongue can move. The muscles of the neck are categorized according to their position relative to the hyoid bone (Figure 5). **Suprahyoid muscles** are superior to it, and the **infrahyoid muscles** are located inferiorly.

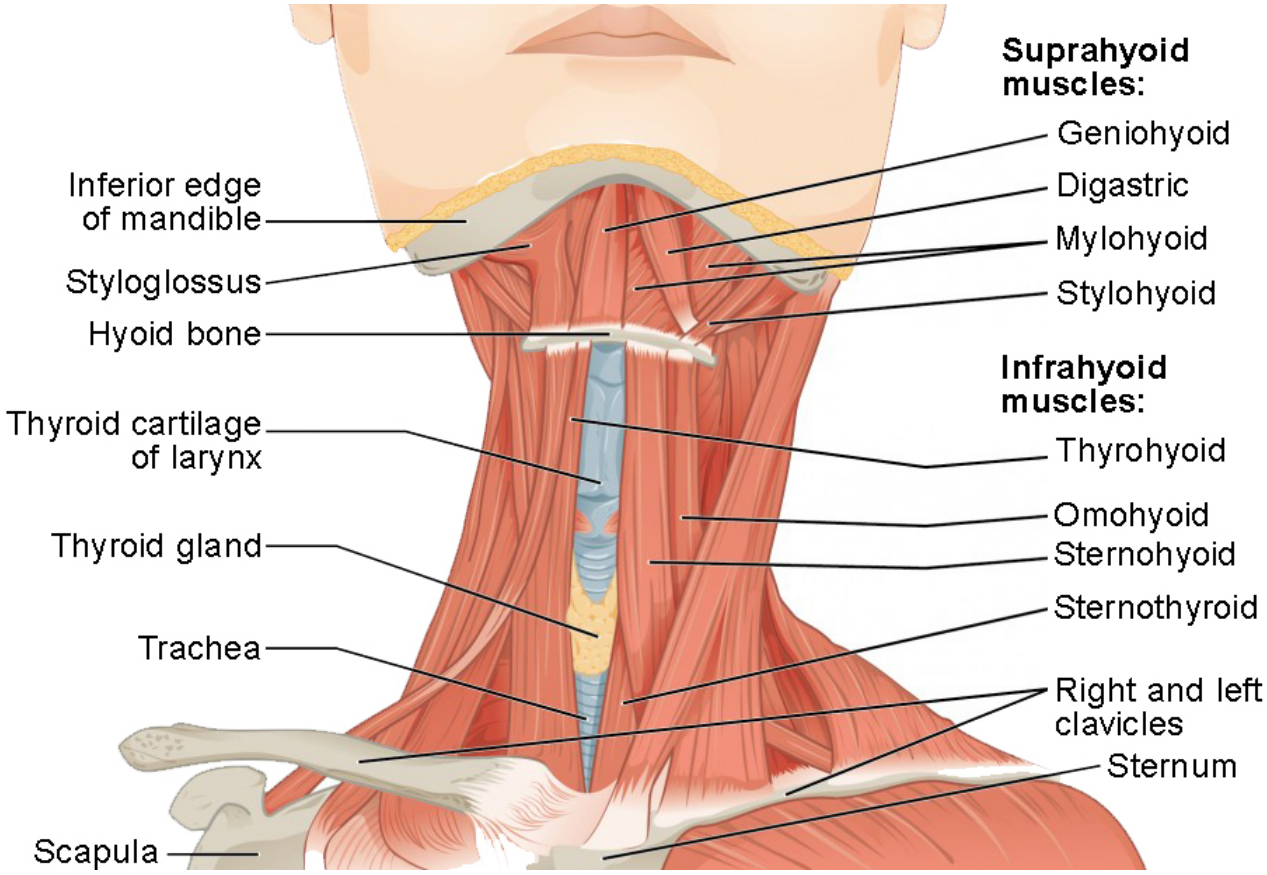


Figure 5. Muscles of the Anterior Neck. *The anterior muscles of the neck facilitate swallowing and speech. The suprahyoid muscles originate from above the hyoid bone in the chin region. The infrahyoid muscles originate below the hyoid bone in the lower neck.*

The suprahyoid muscles raise the hyoid bone, the floor of the mouth, and the larynx during deglutition. These include the **digastric** muscle, which has anterior and posterior bellies that work to elevate the hyoid bone and larynx when one swallows; it also depresses the mandible. The **stylohyoid** muscle moves the hyoid bone posteriorly, elevating the larynx, and the **mylohyoid** muscle lifts it and helps press the tongue to the top of the mouth. The **geniohyoid** depresses the mandible in addition to raising and pulling the hyoid bone anteriorly.

The strap-like infrahyoid muscles generally depress the hyoid bone and control the position of the larynx. The **omohyoid** muscle, which has superior and inferior bellies, depresses the hyoid bone in conjunction with the **sternohyoid** and **thyrohyoid** muscles. The thyrohyoid muscle also elevates the larynx's thyroid cartilage, whereas the **sternothyroid** depresses it to create different tones of voice.

Muscles That Move the Head

The head, attached to the top of the vertebral column, is balanced, moved, and rotated by the neck muscles (Table 5). When these muscles act unilaterally, the head rotates. When they contract bilaterally, the head flexes or extends. The major muscle that laterally flexes and rotates the head is the **sternocleidomastoid**. In addition, both muscles working together are the flexors of the head. Place your fingers on both sides of the neck and turn your head to the left and to the right. You will feel the movement originate there. This muscle divides the neck into anterior and posterior triangles when viewed from the side (Figure 6).

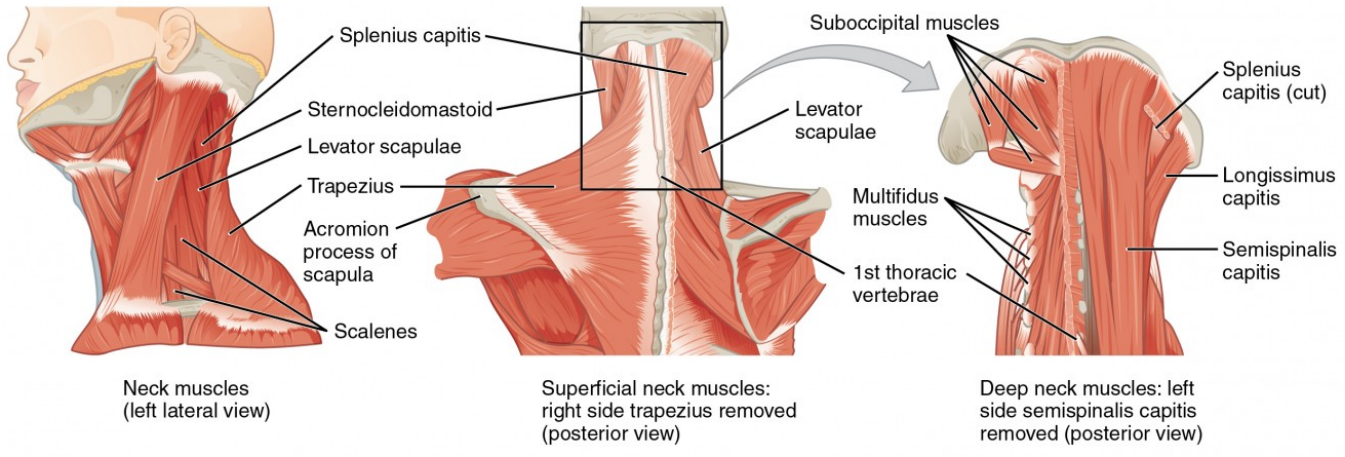


Figure 6. Posterior and Lateral Views of the Neck. *The superficial and deep muscles of the neck are responsible for moving the head, cervical vertebrae, and scapulas.*

Table 5. Muscles That Move the Head

Movement	Target	Target motion direction	Prime mover	Origin	Insertion
Rotates and tilts head to the side; tilts head forward	Skull; vertebrae	Individually: rotates head to opposite side; bilaterally: flexion	Sternocleidomastoid	Sternum; clavicle	Temporal bone (mastoid process); occipital bone
Rotates and tilts head backward	Skull; vertebrae	Individually: laterally flexes and rotates head to same side; bilaterally: extension	Semispinalis capitis	Transverse and articular processes of cervical and thoracic vertebra	Occipital bone
Rotates and tilts head to the side; tilts head backward	Skull; vertebrae	Individually: laterally flexes and rotates head to same side; bilaterally: extension	Splenius capitis	Spinous processes of cervical and thoracic vertebra	Temporal bone (mastoid process); occipital bone
Rotates and tilts head to the side; tilts head backward	Skull; vertebrae	Individually: laterally flexes and rotates head to same side; bilaterally: extension	Longissimus capitis	Transverse and articular processes of cervical and thoracic vertebra	Temporal bone (mastoid process)

Muscles of the Posterior Neck and the Back

The posterior muscles of the neck are primarily concerned with head movements, like extension. The back muscles stabilize and move the vertebral column, and are grouped according to the lengths and direction of the fascicles.

The **splenius** muscles originate at the midline and run laterally and superiorly to their insertions. From the sides and the back of the neck, the **splenius capitis** inserts onto the head region, and the **splenius cervicis** extends onto the cervical region. These muscles can extend the head, laterally flex it, and rotate it (Figure 7).

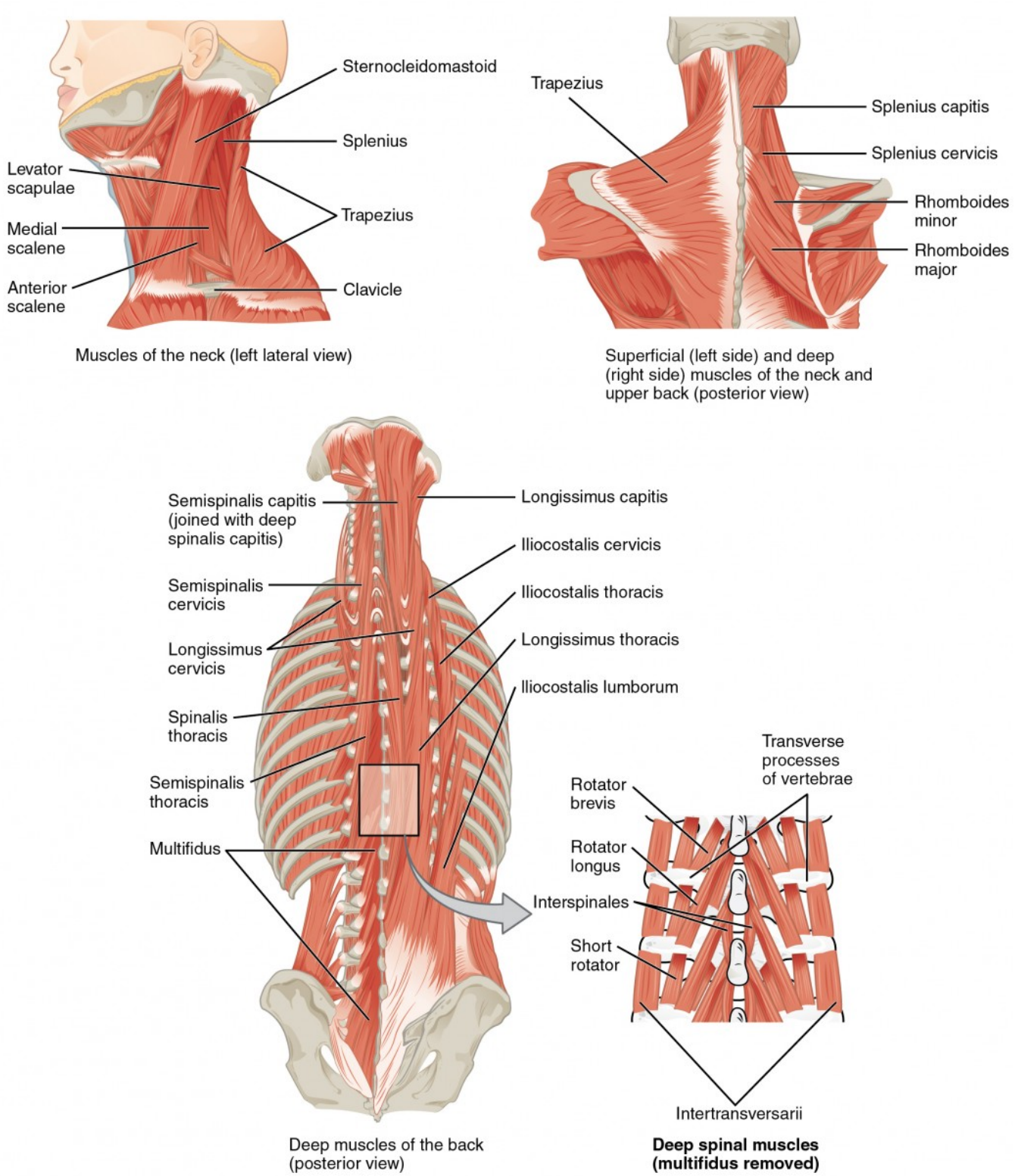


Figure 7. Muscles of the Neck and Back. *The large, complex muscles of the neck and back move the head, shoulders, and vertebral column.*

The **erector spinae group** forms the majority of the muscle mass of the back and it is the primary extensor of the vertebral column. It controls flexion, lateral flexion, and rotation of the vertebral column, and maintains the lumbar curve. The erector spinae comprises the iliocostalis (laterally placed) group, the longissimus (intermediately placed) group, and the spinalis (medially placed) group.

The **iliocostalis group** includes the **iliocostalis cervicis**, associated with the cervical region; the **iliocostalis thoracis**, associated with the thoracic region; and the **iliocostalis lumborum**, associated with the lumbar region. The three muscles of the **longissimus group** are the **longissimus capitis**, associated with the head region; the **longissimus cervicis**, associated with the cervical region; and the **longissimus thoracis**, associated with the thoracic region. The third group, the **spinalis group**, comprises the **spinalis capitis** (head region), the **spinalis cervicis** (cervical region), and the **spinalis thoracis** (thoracic region).

The **transversospinales** muscles run from the transverse processes to the spinous processes of the vertebrae. Similar to the erector spinae muscles, the semispinalis muscles in this group are named for the areas of the body with which they are associated. The semispinalis muscles include the **semispinalis capitis**, the **semispinalis cervicis**, and the **semispinalis thoracis**. The **multifidus** muscle of the lumbar region helps extend and laterally flex the vertebral column.

Important in the stabilization of the vertebral column is the **segmental muscle group**, which includes the interspinales and intertransversarii muscles. These muscles bring together the spinous and transverse processes of each consecutive vertebra. Finally, the **scalene muscles** work together to flex, laterally flex, and rotate the head. They also contribute to deep inhalation. The scalene muscles include the **anterior scalene** muscle (anterior to the middle scalene), the **middle scalene** muscle (the longest, intermediate between the anterior and posterior scalenes), and the **posterior scalene** muscle (the smallest, posterior to the middle scalene).

Self-Check Questions

Visit your course online to take a quiz to check your understanding of the Axial Muscles of the Head, Neck, and Back:

AXIAL MUSCLES OF THE ABDOMINAL WALL AND THORAX

Learning Objectives

- Identify the intrinsic skeletal muscles of the back and neck, and the skeletal muscles of the abdominal wall and thorax
- Identify the movement and function of the intrinsic skeletal muscles of the back and neck, and the skeletal muscles of the abdominal wall and thorax

It is a complex job to balance the body on two feet and walk upright. The muscles of the vertebral column, thorax, and abdominal wall extend, flex, and stabilize different parts of the body's trunk. The deep muscles of the core of the body help maintain posture as well as carry out other functions. The brain sends out electrical impulses to these various muscle groups to control posture by alternate contraction and relaxation. This is necessary so that

no single muscle group becomes fatigued too quickly. If any one group fails to function, body posture will be compromised.

Muscles of the Abdomen

There are four pairs of abdominal muscles that cover the anterior and lateral abdominal region and meet at the anterior midline. These muscles of the anterolateral abdominal wall can be divided into four groups: the external obliques, the internal obliques, the transversus abdominis, and the rectus abdominis (Figure 1, Figure 2, and Table 1).

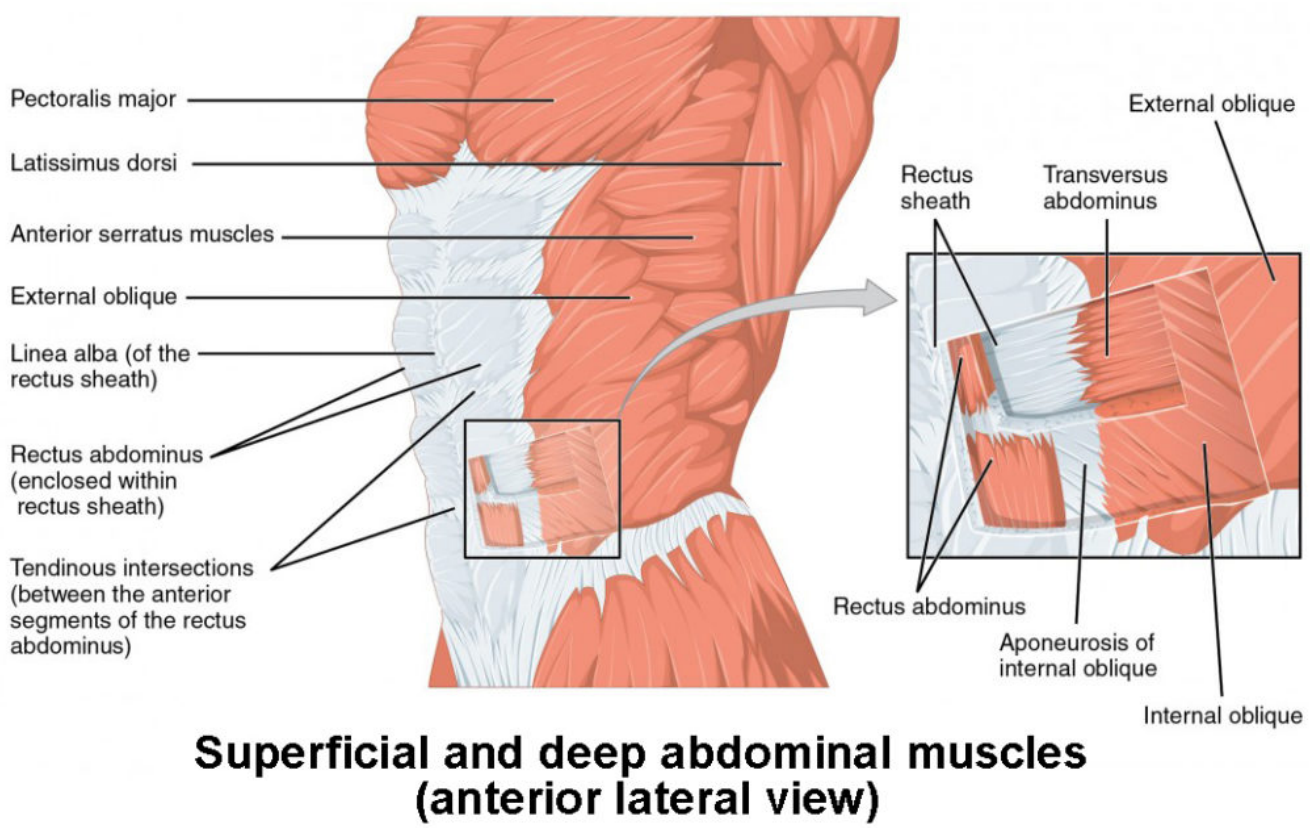


Figure 1. Muscles of the Abdomen. The anterior abdominal muscles include the medially located rectus femoris, which is covered by a sheet of connective tissue called the linea alba. On the flanks of the body, medial to the rectus femoris, the abdominal wall is composed of three layers. The external oblique muscles form the outermost layer, while the internal oblique muscles form the middle layer, and the transverses abdominus forms the innermost layer.

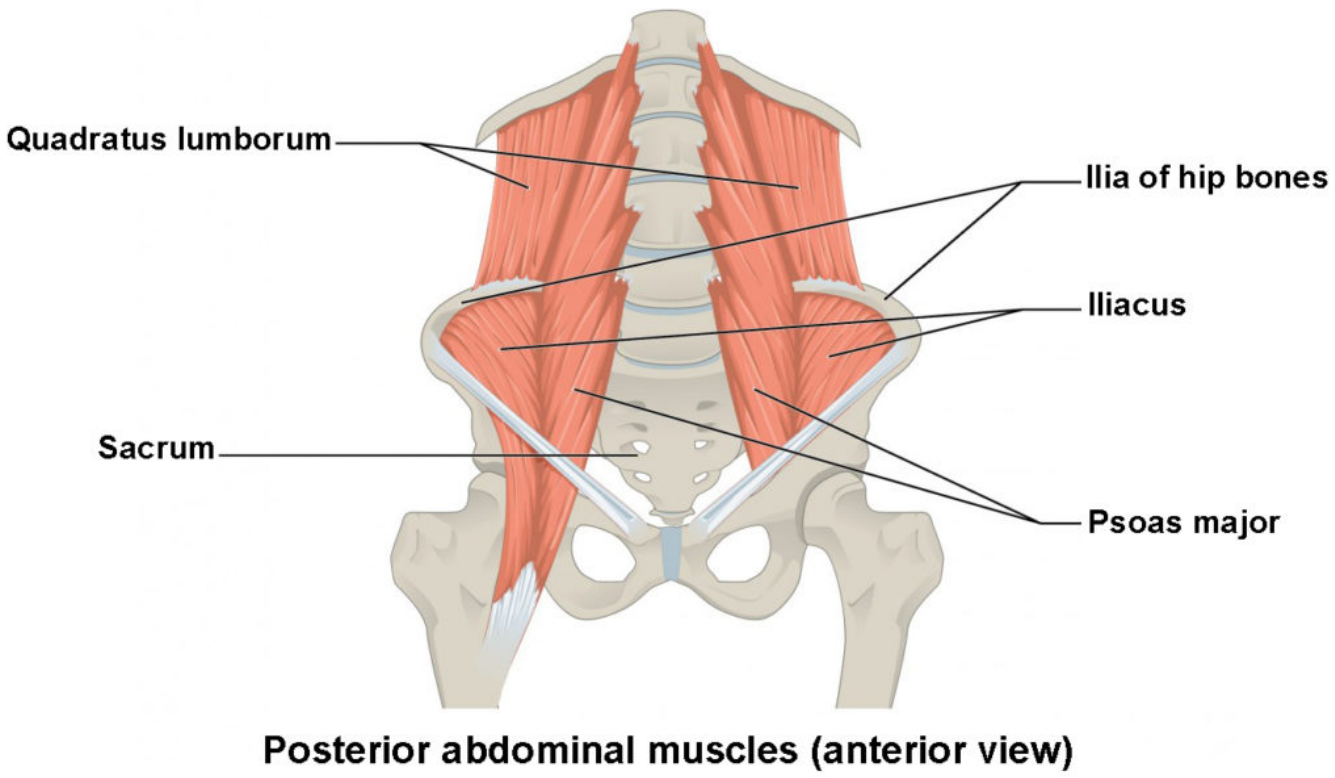


Figure 2. Muscles of the Abdomen. The muscles of the lower back move the lumbar spine but also assist in femur movements.

Table 1. Muscles of the Abdomen

Movement	Target	Target motion direction	Prime mover	Origin	Insertion
Twisting at waist; also bending to the side	Vertebral column	Supination; lateral flexion	External obliques; internal obliques	Ribs 5–12; ilium	Ribs 7–10; linea alba; ilium
Squeezing abdomen during forceful exhalations, defecation, urination, and childbirth	Abdominal cavity	Compression	Transversus abdominus	Ilium; ribs 5–10	Sternum; linea alba; pubis
Sitting up	Vertebral column	Flexion	Rectus abdominis	Pubis	Sternum; ribs 5 and 7
Bending to the side	Vertebral column	Lateral flexion	Quadratus lumborum	Ilium; ribs 5–10	Rib 12; vertebrae L1–L4

There are three flat skeletal muscles in the antero-lateral wall of the abdomen. The **external oblique**, closest to the surface, extend inferiorly and medially, in the direction of sliding one's four fingers into pants pockets. Perpendicular to it is the intermediate **internal oblique**, extending superiorly and medially, the direction the thumbs usually go when the other fingers are in the pants pocket. The deep muscle, the **transversus abdominis**, is arranged transversely around the abdomen, similar to the front of a belt on a pair of pants. This arrangement of three bands of muscles in different orientations allows various movements and rotations of the trunk. The three layers of muscle also help to protect the internal abdominal organs in an area where there is no bone.

The **linea alba** is a white, fibrous band that is made of the bilateral **rectus sheaths** that join at the anterior midline of the body. These enclose the **rectus abdominis** muscles (a pair of long, linear muscles, commonly called the "sit-up" muscles) that originate at the pubic crest and symphysis, and extend the length of the body's trunk. Each muscle is segmented by three transverse bands of collagen fibers called the **tendinous intersections**. This results in the look of "six-pack abs," as each segment hypertrophies on individuals at the gym who do many sit-ups.

The posterior abdominal wall is formed by the lumbar vertebrae, parts of the ilia of the hip bones, psoas major and iliacus muscles, and **quadratus lumborum** muscle. This part of the core plays a key role in stabilizing the rest of the body and maintaining posture.

Career Connections: Physical Therapists

Those who have a muscle or joint injury will most likely be sent to a physical therapist (PT) after seeing their regular doctor. PTs have a master's degree or doctorate, and are highly trained experts in the mechanics of body movements. Many PTs also specialize in sports injuries.

If you injured your shoulder while you were kayaking, the first thing a physical therapist would do during your first visit is to assess the functionality of the joint. The range of motion of a particular joint refers to the normal movements the joint performs. The PT will ask you to abduct and adduct, circumduct, and flex and extend the arm. The PT will note the shoulder's degree of function, and based on the assessment of the injury, will create an appropriate physical therapy plan.

The first step in physical therapy will probably be applying a heat pack to the injured site, which acts much like a warm-up to draw blood to the area, to enhance healing. You will be instructed to do a series of exercises to continue the therapy at home, followed by icing, to decrease inflammation and swelling, which will continue for several weeks. When physical therapy is complete, the PT will do an exit exam and send a detailed report on the improved range of motion and return of normal limb function to your doctor. Gradually, as the injury heals, the shoulder will begin to function correctly. A PT works closely with patients to help them get back to their normal level of physical activity.

Muscles of the Thorax

The muscles of the chest serve to facilitate breathing by changing the size of the thoracic cavity (Table 2). When you inhale, your chest rises because the cavity expands. Alternately, when you exhale, your chest falls because the thoracic cavity decreases in size.

Table 2. Muscles of the Thorax

Movement	Target	Target motion direction	Prime mover	Origin	Insertion
Inhalation; exhalation	Thoracic cavity	Compression; expansion	Diaphragm	Sternum; ribs 6–12; lumbar vertebrae	Central tendon
Inhalation; exhalation	Ribs	Elevation (expands thoracic cavity)	External intercostals	Rib superior to each intercostal muscle	Rib inferior to each muscle
Forced exhalation	Ribs	Movement along superior/ inferior axis to bring ribs closer together	Internal intercostals	Rib inferior to each intercostal muscle	Rib superior to each intercostal muscle

The Diaphragm

The change in volume of the thoracic cavity during breathing is due to the alternate contraction and relaxation of the **diaphragm** (Figure 3). It separates the thoracic and abdominal cavities, and is dome-shaped at rest. The superior surface of the diaphragm is convex, creating the elevated floor of the thoracic cavity. The inferior surface is concave, creating the curved roof of the abdominal cavity.

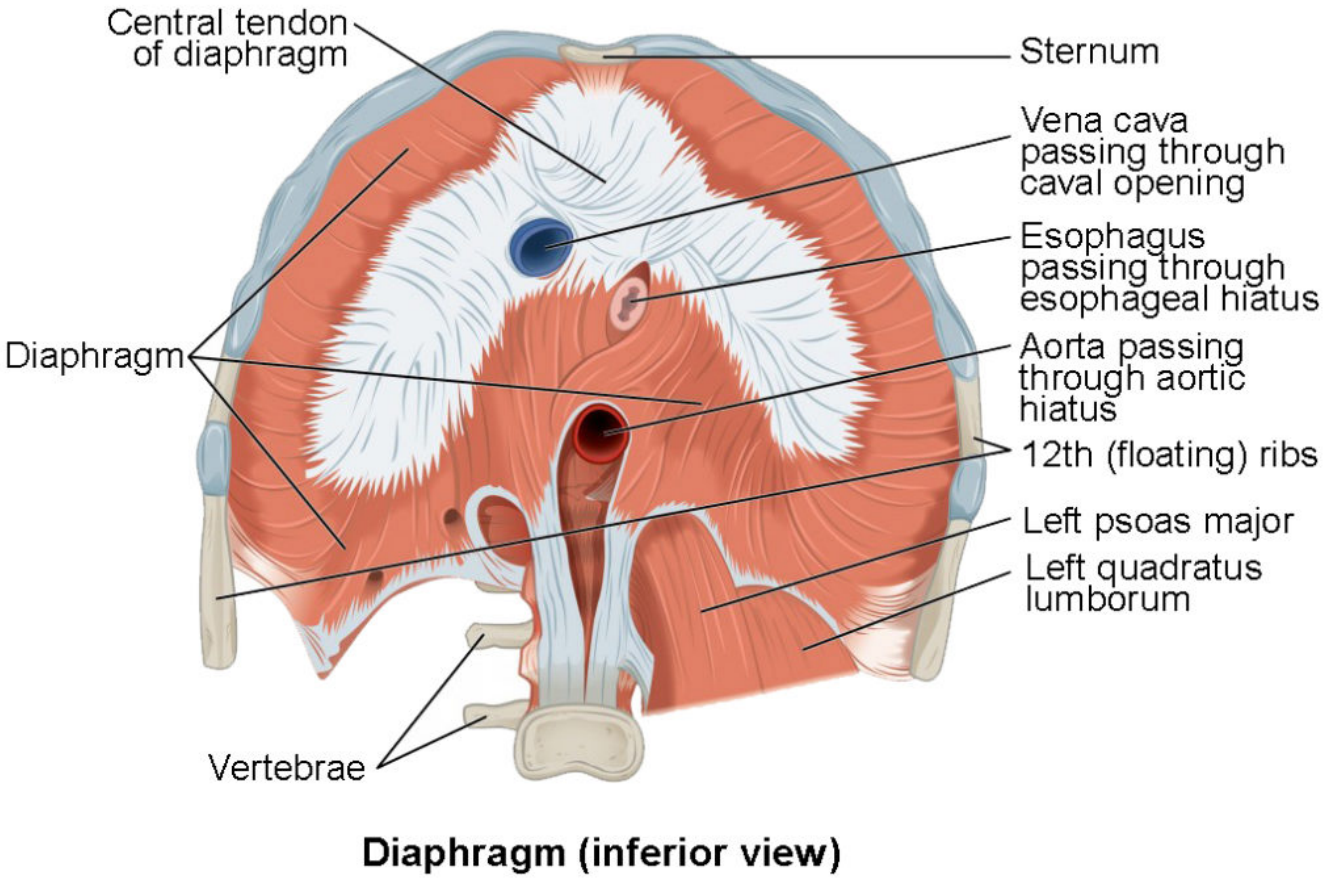


Figure 3. Muscles of the Diaphragm. *The diaphragm separates the thoracic and abdominal cavities.*

Defecating, urination, and even childbirth involve cooperation between the diaphragm and abdominal muscles (this cooperation is referred to as the “Valsalva maneuver”). You hold your breath by a steady contraction of the diaphragm; this stabilizes the volume and pressure of the peritoneal cavity. When the abdominal muscles contract, the pressure cannot push the diaphragm up, so it increases pressure on the intestinal tract (defecation), urinary tract (urination), or reproductive tract (childbirth).

The inferior surface of the pericardial sac and the inferior surfaces of the pleural membranes (parietal pleura) fuse onto the central tendon of the diaphragm. To the sides of the tendon are the skeletal muscle portions of the diaphragm, which insert into the tendon while having a number of origins including the xiphoid process of the sternum anteriorly, the inferior six ribs and their cartilages laterally, and the lumbar vertebrae and 12th ribs posteriorly.

The diaphragm also includes three openings for the passage of structures between the thorax and the abdomen. The inferior vena cava passes through the **caval opening**, and the esophagus and attached nerves pass through the esophageal hiatus. The aorta, thoracic duct, and azygous vein pass through the aortic hiatus of the posterior diaphragm.

The Intercostal Muscles

There are three sets of muscles, called **intercostal muscles**, which span each of the intercostal spaces. The principal role of the intercostal muscles is to assist in breathing by changing the dimensions of the rib cage (Figure 4).

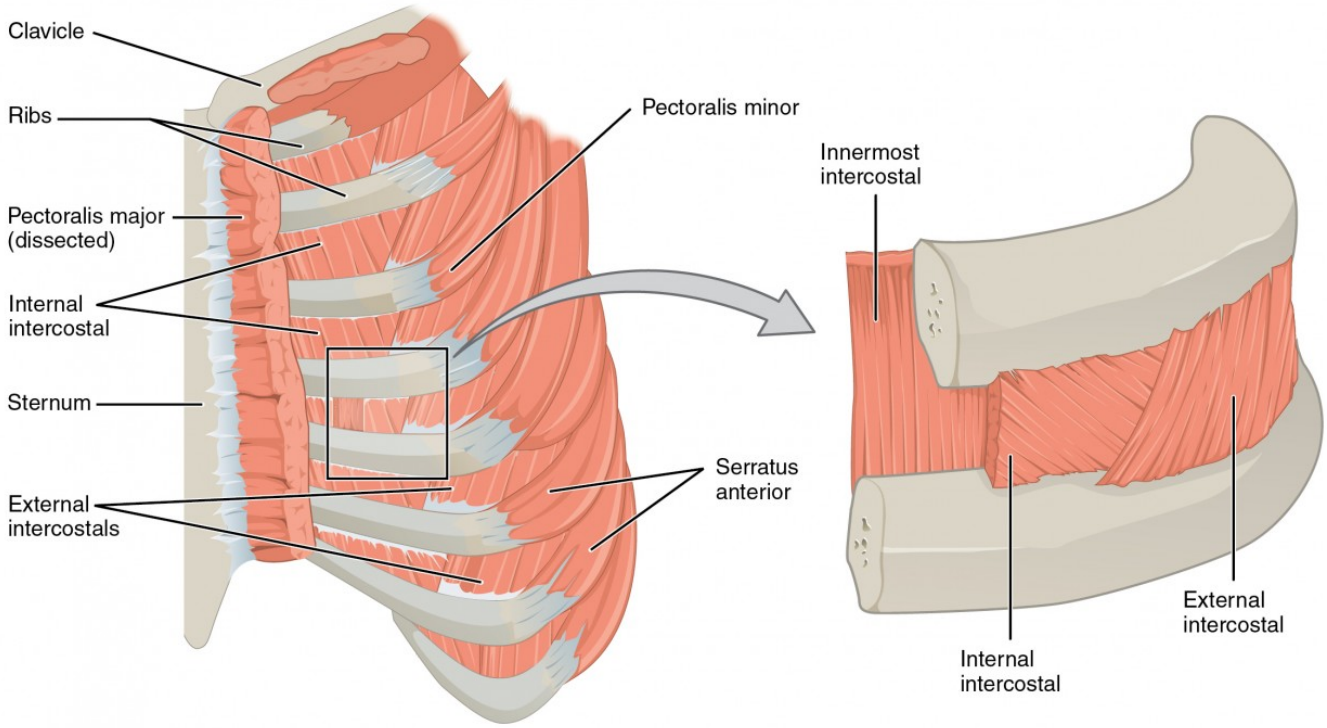


Figure 4. Intercostal Muscles. *The external intercostals are located laterally on the sides of the body. The internal intercostals are located medially near the sternum. The innermost intercostals are located deep to both the internal and external intercostals.*

The 11 pairs of superficial **external intercostal** muscles aid in inspiration of air during breathing because when they contract, they raise the rib cage, which expands it. The 11 pairs of **internal intercostal** muscles, just under the externals, are used for expiration because they draw the ribs together to constrict the rib cage. The **innermost intercostal** muscles are the deepest, and they act as synergists for the action of the internal intercostals.

Muscles of the Pelvic Floor and Perineum

The pelvic floor is a muscular sheet that defines the inferior portion of the pelvic cavity. The **pelvic diaphragm**, spanning anteriorly to posteriorly from the pubis to the coccyx, comprises the levator ani and the ischiococcygeus. Its openings include the anal canal and urethra, and the vagina in women.

The large **levator ani** consists of two skeletal muscles, the **pubococcygeus** and the **iliococcygeus** (Figure 5). The levator ani is considered the most important muscle of the pelvic floor because it supports the pelvic viscera. It resists the pressure produced by contraction of the abdominal muscles so that the pressure is applied to the colon to aid in defecation and to the uterus to aid in childbirth (assisted by the **ischiococcygeus**, which pulls the coccyx anteriorly). This muscle also creates skeletal muscle sphincters at the urethra and anus.

The **perineum** is the diamond-shaped space between the pubic symphysis (anteriorly), the coccyx (posteriorly), and the ischial tuberosities (laterally), lying just inferior to the pelvic diaphragm (levator ani and coccygeus). Divided transversely into triangles, the anterior is the **urogenital triangle**, which includes the external genitals. The posterior is the **anal triangle**, which contains the anus (Figure 6). The perineum is also divided into superficial and deep layers with some of the muscles common to men and women (Table 3). Women also have the **compressor urethrae** and the **sphincter urethrovaginalis**, which function to close the vagina. In men, there is the **deep transverse perineal** muscle that plays a role in ejaculation.

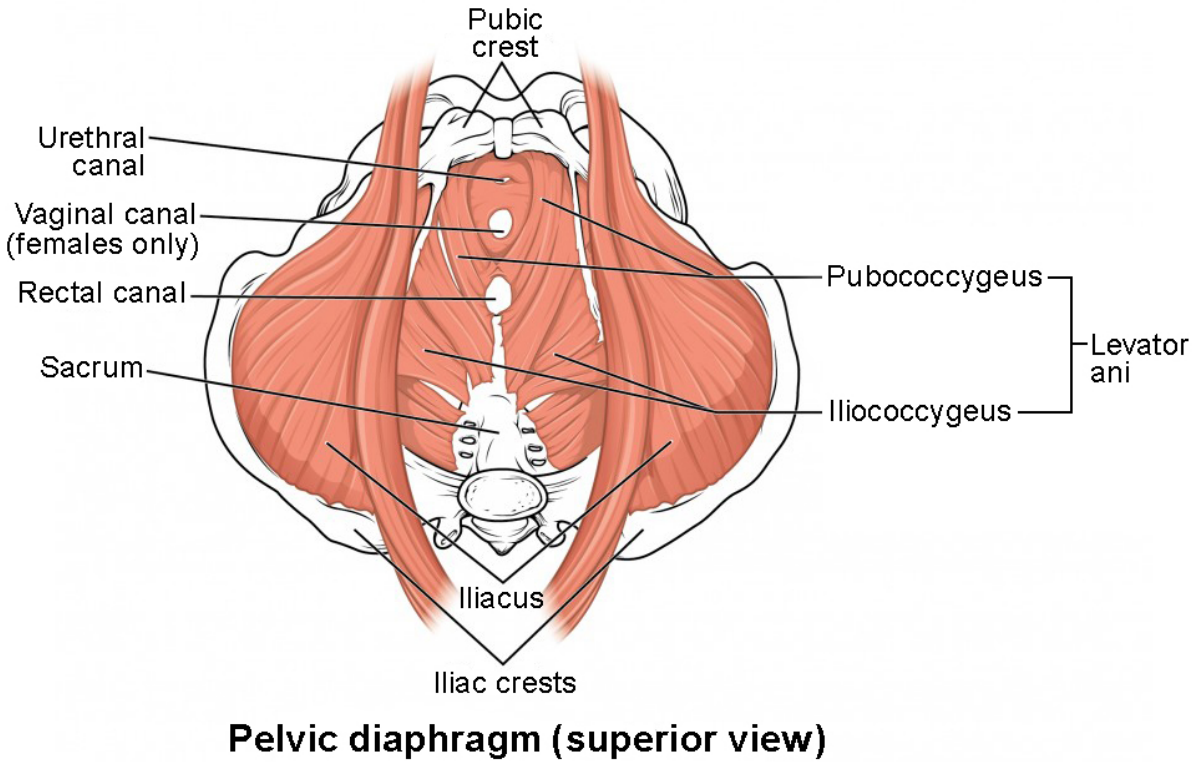


Figure 5. Muscles of the Pelvic Floor. *The pelvic floor muscles support the pelvic organs, resist intra-abdominal pressure, and work as sphincters for the urethra, rectum, and vagina.*

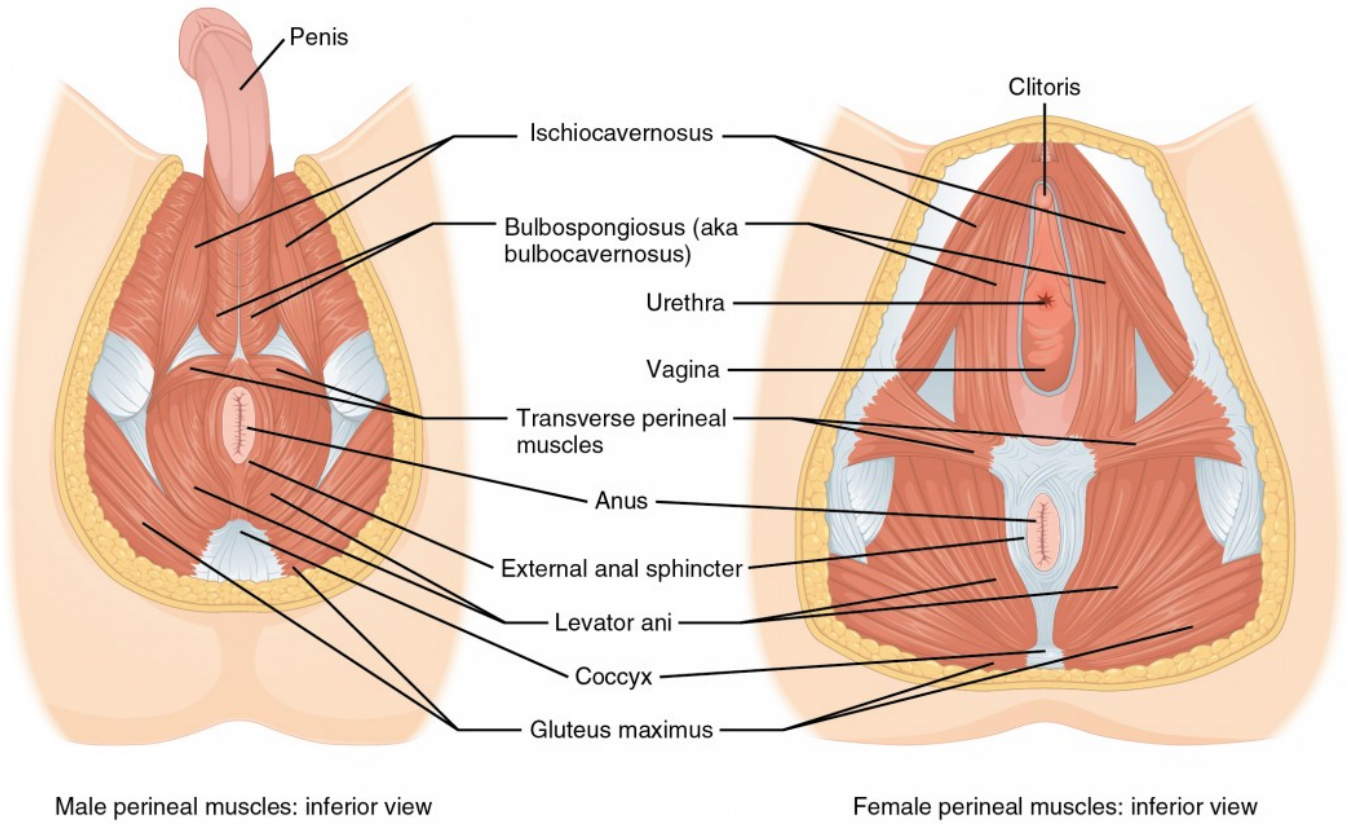


Figure 6. Muscles of the Perineum. The perineum muscles play roles in urination in both sexes, ejaculation in men, and vaginal contraction in women.

Table 3. Muscles of the Perineum Common to Men and Women					
Movement	Target	Target motion direction	Prime mover	Origin	Insertion
Defecation; urination; birth; coughing	Abdominal cavity	Superior (resists pressure during abdominal compression)	Levator and pubococcygeus; elevator ani iliococcygeus	Pubis; ischium	Urethra; anal canal; perineal body; coccyx
Superficial muscles					
None—supports perineal body maintaining anus at center of perineum	Perineal body	None	Superficial transverse perineal	Ischium	Perineal body
Involuntary response that compresses urethra when excreting urine in both sexes or while ejaculating in males; also aids in erection of penis in males	Urethra	Compression	Bulbospongiosus	Perineal body	Perineal membrane; corpus spongiosum of penis; deep fascia of penis; clitoris in female
Compresses veins to maintain erection of penis in males; erection of clitoris in females	Veins of penis and clitoris	Compression	Ischiocavernosus	Ischium; ischial rami; pubic rami	Pubic symphysis; corpus cavernosum of penis in male; clitoris of female
Deep muscles					
Voluntarily compresses urethra during urination	Urethra	Compression	External urethral sphincter	Ischial rami; pubic rami	Male: median raphe; female: vaginal wall
Closes anus	Anus	Sphincter	External anal sphincter	Anococcygeal ligament	Perineal body

Videos: Muscles and Bones of the Thoracic Wall

Watch this video online: https://youtu.be/mVLXqICrsdo
Watch this video online: https://youtu.be/PoA-Uq9w-7s

Self-Check Questions

Visit your course online to take a quiz to check your understanding of the Axial Muscles of the Abdominal Wall and Thorax:

MUSCLES OF THE PECTORAL GIRDLE AND UPPER LIMBS

Learning Objectives

- Identify the muscles of the pectoral girdle and upper limbs
- Identify the movement and function of the pectoral girdle and upper limbs

Muscles of the shoulder and upper limb can be divided into four groups: muscles that stabilize and position the pectoral girdle, muscles that move the arm, muscles that move the forearm, and muscles that move the wrists, hands, and fingers. The **pectoral girdle**, or shoulder girdle, consists of the lateral ends of the clavicle and scapula, along with the proximal end of the humerus, and the muscles covering these three bones to stabilize the shoulder joint. The girdle creates a base from which the head of the humerus, in its ball-and-socket joint with the glenoid fossa of the scapula, can move the arm in multiple directions.

Muscles That Position the Pectoral Girdle

Muscles that position the pectoral girdle are located either on the anterior thorax or on the posterior thorax (Figure 1 and Table 1).

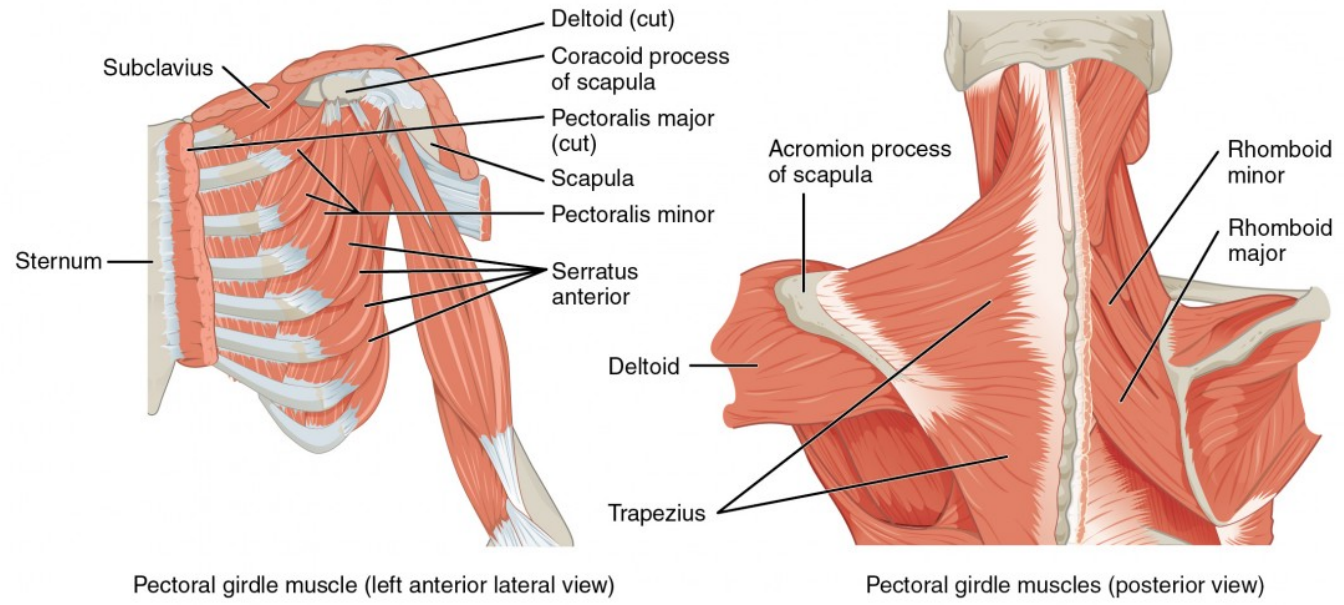


Figure 1. Muscles That Position the Pectoral Girdle. *The muscles that stabilize the pectoral girdle make it a steady base on which other muscles can move the arm. Note that the pectoralis major and deltoid, which move the humerus, are cut here to show the deeper positioning muscles.*

The anterior muscles include the **subclavius**, **pectoralis minor**, and **serratus anterior**. The posterior muscles include the **trapezius**, **rhomboid major**, and **rhomboid minor**. When the rhomboids are contracted, your scapula moves medially, which can pull the shoulder and upper limb posteriorly.

Table 1. Muscles that Position the Pectoral Girdle

Position in the Thorax	Movement	Target	Target motion direction	Prime mover	Origin	Insertion
Anterior thorax	Stabilizes clavicle during movement by depressing it	Clavicle	Depression	Subclavius	First rib	Inferior surface of clavicle
Anterior thorax	Rotates shoulder anteriorly (throwing motion); assists with inhalation	Scapula; ribs	Scapula: depresses; ribs: elevates	Pectoralis minor	Anterior surfaces of certain ribs (2–4 or 3–5)	Coracoid process of scapula
Anterior thorax	Moves arm from side of body to front of body; assists with inhalation	Scapula; ribs	Scapula: protracts; ribs: elevates	Serratus anterior	Muscle slips from certain ribs (1–8 or 1–9)	Anterior surface of vertebral border of scapula
Posterior thorax	Elevates shoulders (shrugging); pulls shoulder blades together; tilts head backwards	Scapula; cervical spine	Scapula: rotates inferiorly, retracts, elevates, and depresses; spine: extends	Trapezius	Skull; vertebral column	Acromion and spine of scapula; clavicle

Table 1. Muscles that Position the Pectoral Girdle						
Position in the Thorax	Movement	Target	Target motion direction	Prime mover	Origin	Insertion
Posterior thorax	Stabilizes scapula during pectoral girdle movement	Scapula	Retracts; rotates inferiorly	Rhomboid major	Thoracic vertebrae (T2–T5)	Medial border of scapula
Posterior thorax	Stabilizes scapula during pectoral girdle movement	Scapula	Retracts; rotates inferiorly	Rhomboid minor	Cervical and thoracic vertebrae (C7 and T1)	Medial border of scapula

Muscles That Move the Humerus

Similar to the muscles that position the pectoral girdle, muscles that cross the shoulder joint and move the humerus bone of the arm include both axial and scapular muscles (Figure 2, Figure 3, and Table 2).

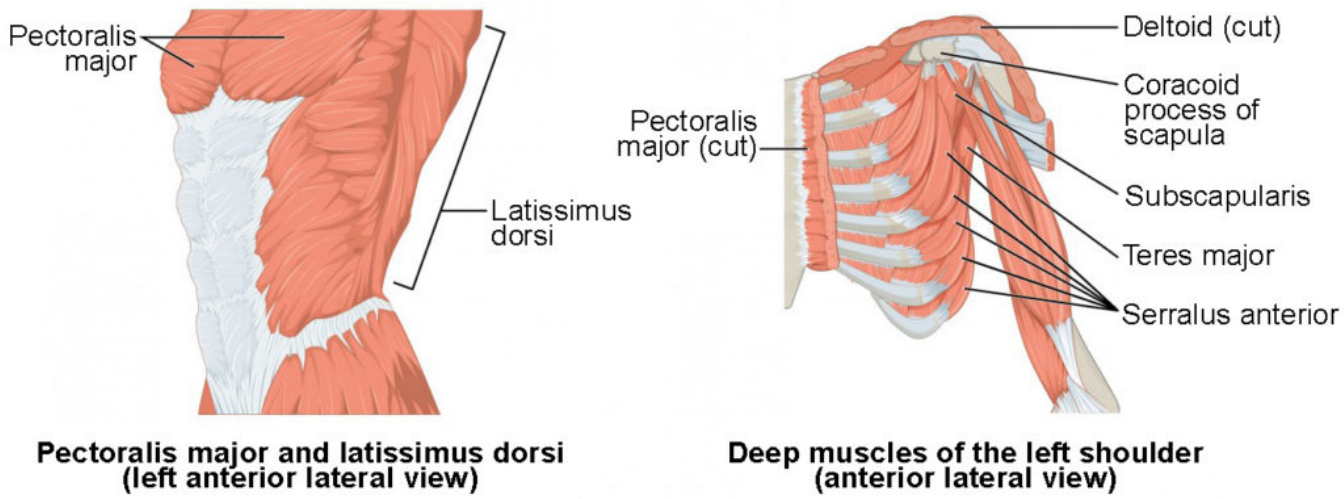


Figure 2. Muscles That Move the Humerus. *The muscles that move the humerus anteriorly are generally located on the anterior side of the body and originate from the sternum (e.g., pectoralis major) or the anterior side of the scapula (e.g., subscapularis).*

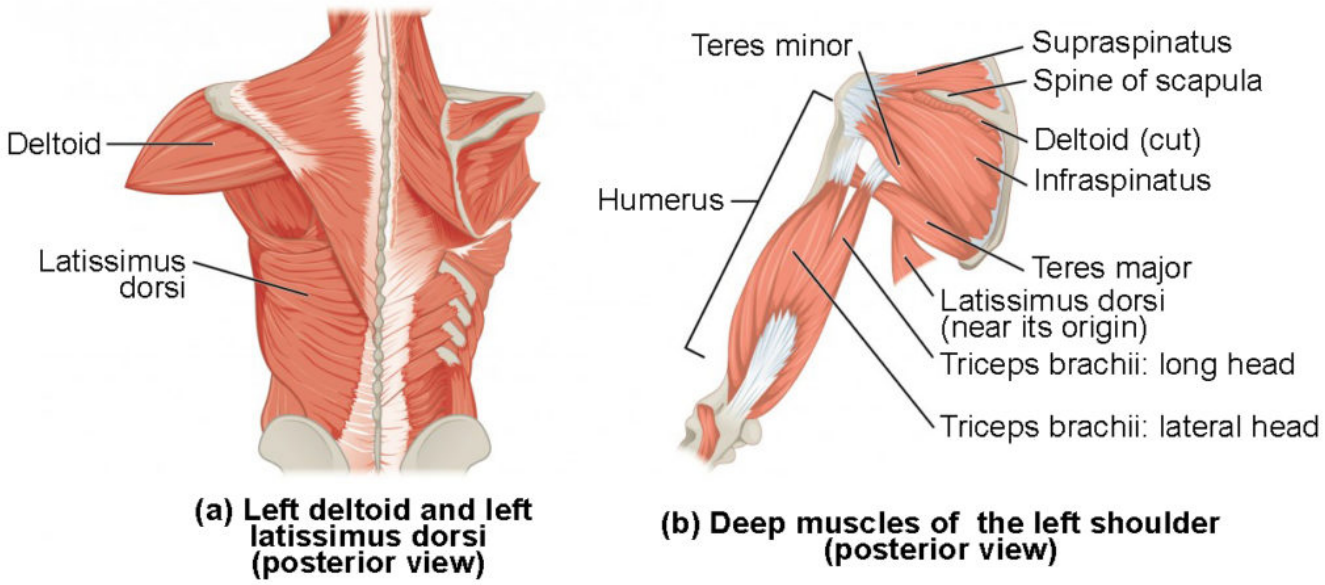


Figure 3. Muscles That Move the Humerus. *(b) The muscles that move the humerus superiorly generally originate from the superior surfaces of the scapula and/or the clavicle (e.g., deltoids). The muscles that move the humerus inferiorly generally originate from middle or lower back (e.g., latissiumus dorsi). (d) The muscles that move the humerus posteriorly are generally located on the posterior side of the body and insert into the scapula (e.g., infraspinatus).*

The two axial muscles are the pectoralis major and the latissimus dorsi. The **pectoralis major** is thick and fan-shaped, covering much of the superior portion of the anterior thorax. The broad, triangular **latissimus dorsi** is located on the inferior part of the back, where it inserts into a thick connective tissue shealth called an aponeurosis.

Table 2. Muscles That Move the Humerus

Movement	Target	Target motion direction	Prime mover	Origin	Insertion
Axial muscles					
Brings elbows together; moves elbow up (as during an uppercut punch)	Humerus	Flexion; adduction; medial rotation	Pectoralis major	Clavicle; sternum; cartilage of ribs (1–6 or 1–7); aponeurosis of external oblique muscle	Greater tubercle of humerus
Moves elbow back (as in elbowing someone standing behind you); spreads elbows apart	Humerus; scapula	Humerus: extension, adduction, and medial rotation; scapula: depression	Latissimus dorsi	Thoracic vertebrae (T7–T12); lumbar vertebrae; lower ribs (9–12); iliac crest	Intertubercular sulcus of humerus
Scapular muscles					
Lifts arms at the shoulder	Humerus	Abduction; flexion;	Deltoid	Trapezius; clavicle;	Nasal bone

Table 2. Muscles That Move the Humerus					
Movement	Target	Target motion direction	Prime mover	Origin	Insertion
		extension; medial and lateral rotation		acromion; spine of scapula	
Assists the pectoralis major in bringing the elbows together and stabilizes the shoulder joint during movement of the pectoral girdle	Humerus	Medial rotation	Subscapularis	Subscapular fossa of the scapula	Lesser tubercle of humerus
Rotates the elbow outwards, as during a tennis swing	Humerus	Abduction	Supraspinatus	Supraspinous fossa of the scapula	Greater tubercle of humerus
Rotates the elbow outwards, as during a tennis swing	Humerus	Extension; adduction	Infraspinatus	Infraspinous fossa of the scapula	Greater tubercle of humerus
Assists the infraspinatus in rotating the elbow outwards	Humerus	Extension; adduction	Teres major	Posterior surface of the scapula	Intertubercular sulcus of humerus
Assists the infraspinatus in rotating the elbow outwards	Humerus	Extension; adduction	Teres minor	Lateral border of the dorsal scapular surface	Greater tubercle of humerus
Moves the elbow up and across the body, as when putting a hand on the chest	Humerus	Flexion; adduction	Coracobra chialis	Coracoid process of the scapula	Medial surface of humerus shaft

The rest of the shoulder muscles originate on the scapula. The anatomical and ligamental structure of the shoulder joint and the arrangements of the muscles covering it, allows the arm to carry out different types of movements. The ***deltoid***, the thick muscle that creates the rounded lines of the shoulder is the major abductor of the arm, but it also facilitates flexing and medial rotation, as well as extension and lateral rotation.
The **subscapularis** originates on the anterior scapula and medially rotates the arm. Named for their locations, the **supraspinatus** (superior to the spine of the scapula) and the **infraspinatus** (inferior to the spine of the scapula) abduct the arm, and laterally rotate the arm, respectively. The thick and flat **teres major** is inferior to the teres minor and extends the arm, and assists in adduction and medial rotation of it. The long **teres minor** laterally rotates and extends the arm. Finally, the **coracobrachialis** flexes and adducts the arm.

The tendons of the deep subscapularis, supraspinatus, infraspinatus, and teres minor connect the scapula to the humerus, forming the **rotator cuff** (musculotendinous cuff), the circle of tendons around the shoulder joint. When baseball pitchers undergo shoulder surgery it is usually on the rotator cuff, which becomes pinched and inflamed, and may tear away from the bone due to the repetitive motion of bring the arm overhead to throw a fast pitch.

Muscles That Move the Forearm

The forearm, made of the radius and ulna bones, has four main types of action at the hinge of the elbow joint: flexion, extension, pronation, and supination. The forearm flexors include the biceps brachii, brachialis, and brachioradialis. The extensors are the **triceps brachii** and **anconeus**. The pronators are the **pronator teres** and the **pronator quadratus**, and the **supinator** is the only one that turns the forearm anteriorly. When the forearm faces anteriorly, it is supinated. When the forearm faces posteriorly, it is pronated.

The biceps brachii, brachialis, and brachioradialis flex the forearm. The two-headed **biceps brachii** crosses the shoulder and elbow joints to flex the forearm, also taking part in supinating the forearm at the radioulnar joints and flexing the arm at the shoulder joint. Deep to the biceps brachii, the **brachialis** provides additional power in flexing the forearm. Finally, the **brachioradialis** can flex the forearm quickly or help lift a load slowly. These muscles and their associated blood vessels and nerves form the **anterior compartment of the arm** (anterior flexor compartment of the arm) (Figure 4 and Table 3).

Table 3. Muscles That Move the Forearm

Movement	Target	Target motion direction	Prime mover	Origin	Insertion
Anterior muscles (flexion)					
Performs a bicep curl; also allows palm of hand to point toward body while flexing	Forearm	Flexion; supination	Biceps brachii	Coracoid process; tubercle above glenoid cavity	Radial tuberosity
	Forearm	Flexion	Brachialis	Front of distal humerus	Coronoid process of ulna
Assists and stabilizes elbow during bicep-curl motion	Forearm	Flexion	Brachioradialis	Lateral supracondylar ridge at distal end of humerus	Base of styloid process of radius
Posterior muscles (extension)					
Extends forearm, as during a punch	Forearm	Extension	Triceps brachii	Infraglenoid tubercle of scapula; posterior shaft of humerus; posterior humeral shaft distal to radial groove	Olecranon process of ulna
Assists in extending forearm; also allows forearm to extend away from body	Forearm	Extension; abduction	Anconeus	Lateral epicondyle of humerus	Lateral aspect of olecranon process of ulna
Anterior muscles (pronation)					
Turns hand palm-down	Forearm	Pronation	Pronator teres	Medial epicondyle of	Lateral radius

Table 3. Muscles That Move the Forearm					
Movement	Target	Target motion direction	Prime mover	Origin	Insertion
				humerus; coronoid process of ulna	
Assists in turning hand palm-down	Forearm	Pronation	Pronator quadratus	Distal portion of anterior ulnar shaft	Distal surface of anterior radius
Posterior muscles (supination)					
Tuns hand palm-up	Forearm	Supination	Supinator	Lateral epicondyle of humerus; proximal ulna	Proximal end of radius

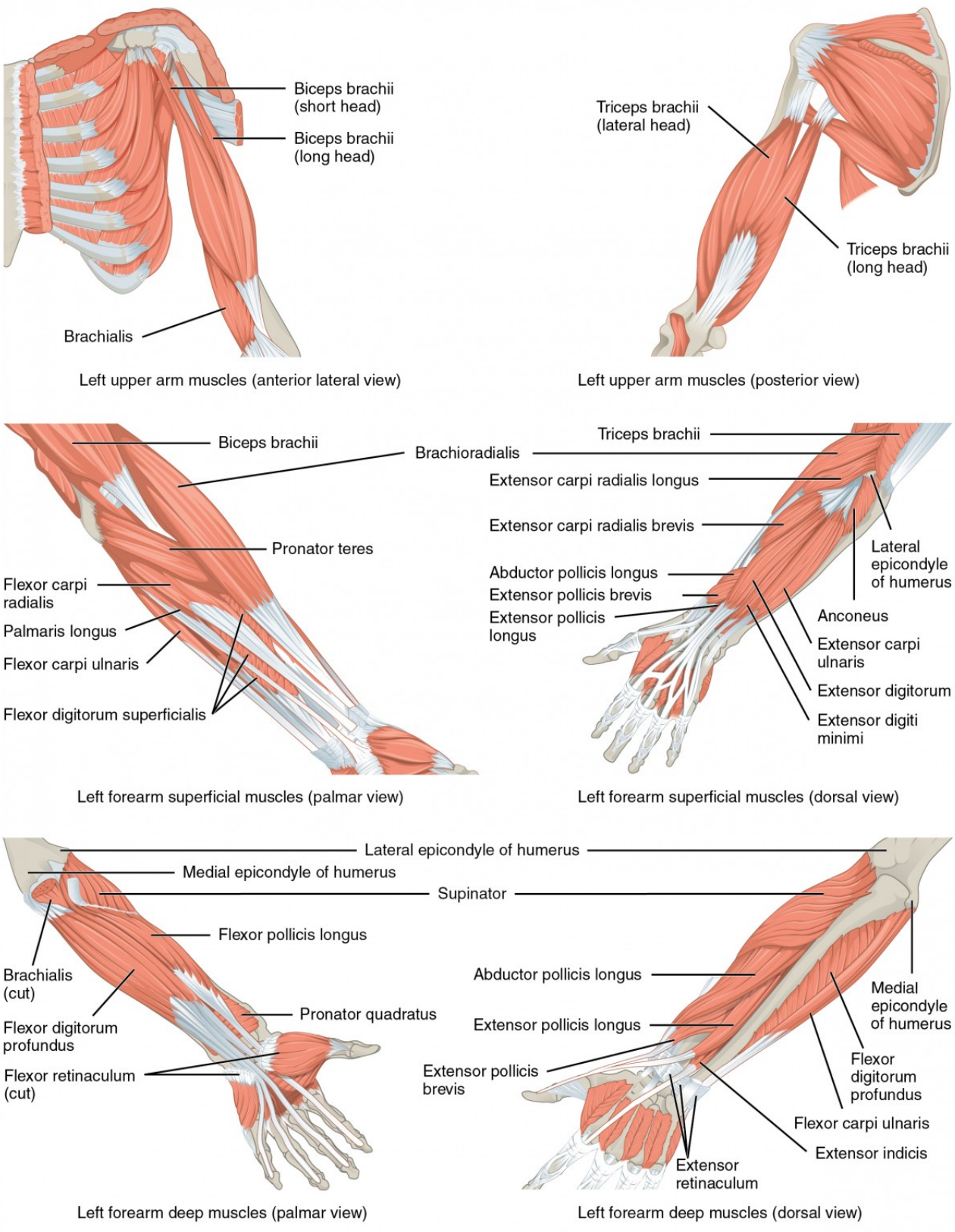


Figure 4. Muscles That Move the Forearm. *The muscles originating in the upper arm flex, extend, pronate, and supinate the forearm. The muscles originating in the forearm move the wrists, hands, and fingers.*

Muscles That Move the Wrist, Hand, and Fingers

Wrist, hand, and finger movements are facilitated by two groups of muscles. The forearm is the origin of the **extrinsic muscles of the hand**. The palm is the origin of the intrinsic muscles of the hand.

Muscles of the Arm That Move the Wrists, Hands, and Fingers

The muscles in the **anterior compartment of the forearm** (anterior flexor compartment of the forearm) originate on the humerus and insert onto different parts of the hand. These make up the bulk of the forearm. From lateral to medial, the **superficial anterior compartment of the forearm** includes the **flexor carpi radialis**, **palmaris longus**, **flexor carpi ulnaris**, and **flexor digitorum superficialis**. The flexor digitorum superficialis flexes the hand as well as the digits at the knuckles, which allows for rapid finger movements, as in typing or playing a musical instrument (see Table 4). However, poor ergonomics can irritate the tendons of these muscles as they slide back and forth with the carpal tunnel of the anterior wrist and pinch the median nerve, which also travels through the tunnel, causing Carpal Tunnel Syndrome. The **deep anterior compartment** produces flexion and bends fingers to make a fist. These are the **flexor pollicis longus** and the **flexor digitorum profundus**.

The muscles in the **superficial posterior compartment of the forearm** (superficial posterior extensor compartment of the forearm) originate on the humerus. These are the **extensor radialis longus**, **extensor carpi radialis brevis**,**extensor digitorum**, **extensor digiti minimi**, and the **extensor carpi ulnaris**.

The muscles of the **deep posterior compartment of the forearm** (deep posterior extensor compartment of the forearm) originate on the radius and ulna. These include the **abductor pollicis longus**, **extensor pollicis brevis**,**extensor pollicis longus**, and **extensor indicis** (see Table 4).

Table 4. Muscles That Move the Wrist, Hands, and Forearm

Movement	Target	Target motion direction	Prime mover	Origin	Insertion
Superficial anterior compartment of forearm					
Bends the wrist toward the body; it also tilts the hand to the side away from the body	Wrist; hand	Flexion; abduction	Flexor carpi radialis	Medial epicondyle of the humerus	Base of second and third metacarpals
Assists in bending the hand up toward the shoulder	Wrist	Flexion	Palmaris longus	Medial epicondyle of the humerus	Palmar aponeurosis; skin and fascia of palm
Assists in bending the hand up toward the shoulder; it also tilts the hand to the side away from the body and stabilizes the wrist	Wrist; hand	Flexion; abduction	Flexor carpi ulnaris	Medial epicondyle of the humerus, the olecranon process, and the posterior surface of the ulna	Pisiform, hamate bones, and base of fifth metacarpal
Bends the fingers to make a fist	Wrist; fingers 2–5	Flexion	Flexor digitorum superficialis	Medial epicondyle of the humerus, the coronoid process of the ulna, and	Middle phalanges of fingers 2–5

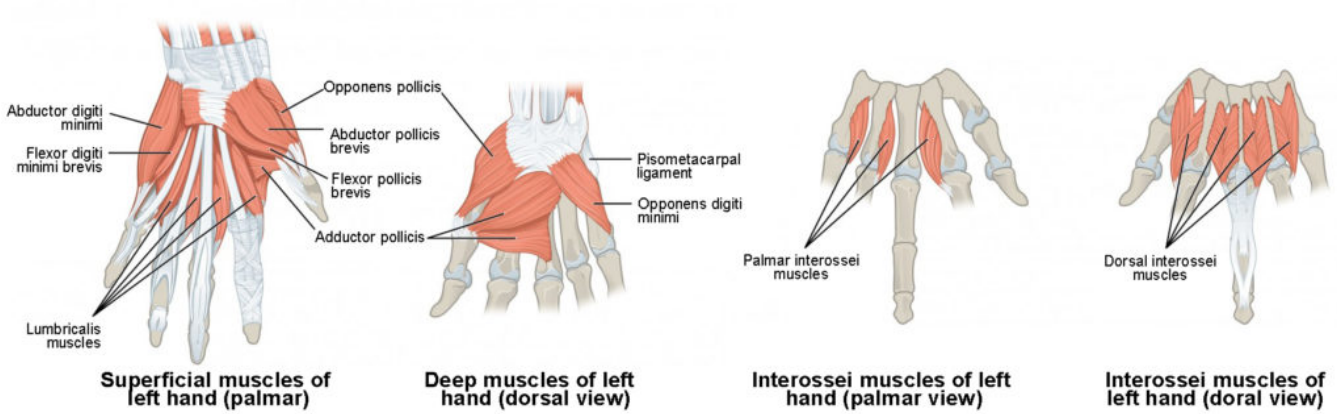
Table 4. Muscles That Move the Wrist, Hands, and Forearm					
Movement	Target	Target motion direction	Prime mover	Origin	Insertion
				the shaft of the radius	
Deep anterior compartment of forearm					
Bends the tip of the thumb	Thumb	Flexion	Flexor pollicis longus	Anterior surface of the radius and the interosseous membrane	Distal phalanx of thumb
Bends the fingers to make a fist; it also bends the wrist toward the body	Wrist; fingers	Flexion	Flexor digitorum profundus	Coronoid process, the anteromedial surface of the ulna, and the interosseous membrane	Distal phalanges of fingers 2–5
Superficial posterior compartment of forearm					
Straightens the wrist away from the body; it also tilts the hand to the side away from the body	Wrist	Extension; abduction	Extensor radialis longus	Lateral supracondylar ridge of the humerus	Base of second metacarpal
Assists the extensor radialis longus in extending and abducting the wrist; it also stabilizes the hand during finger flexion	Wrist	Extension; abduction	Extensor carpi radialis brevis	Lateral epicondyle of the humerus	Base of third metacarpal
Opens the fingers and moves them sideways away from the body	Wrist; fingers	Extension; abduction	Extensor digitorum	Lateral epicondyle of the humerus	Extensor expansions; distal phalanges of fingers
Extends the little finger	Little finger	Extension	Extensor digiti minimi	Lateral epicondyle of the humerus	Extensor expansion; distal phalanx of finger 5
Straightens the wrist away from the body; it also tilts the hand to the side toward the body	Wrist	Extension; abduction	Extensor carpi ulnaris	Lateral epicondyle of the humerus and the posterior of the ulna	Base of fifth metacarpal
Deep posterior compartment of forearm					

Table 4. Muscles That Move the Wrist, Hands, and Forearm					
Movement	Target	Target motion direction	Prime mover	Origin	Insertion
Moves the thumb sideways toward the body; it also extends the thumb and moves the hand sideways toward the body	Wrist; thumb	Thumb: abduction, extension; wrist: abduction	Abductor pollicis longus	Posterior surface of the radius and ulna and in the interosseous membrane	Base of first metacarpal; trapezium
Extends the thumb	Thumb	Extension	Extensor pollicis brevis	Dorsal shaft of the radius and ulna and in the interosseous membrane	Base of proximal phalanx of thumb
Extends the thumb	Thumb	Extension	Extensor pollicis longus	Dorsal shaft of the radius and ulna and in the interosseous membrane	Base of distal phalanx of thumb
Extends the index finger; it also straightens the wrist away from the body	Wrist; index finger	Extension	Extensor indicis	Posterior surface of the distal ulna and in the interosseous membrane	Tendon of extensor digitorum of finger

The tendons of the forearm muscles attach to the wrist and extend into the hand. Fibrous bands called **retinacula** sheath the tendons at the wrist. The **flexor retinaculum** extends over the palmar surface of the hand while the **extensor retinaculum** extends over the dorsal surface of the hand.

Intrinsic Muscles of the Hand

The **intrinsic muscles of the hand** both originate and insert within it (Figure 5). These muscles allow your fingers to also make precise movements for actions, such as typing or writing. These muscles are divided into three groups. The **thenar** muscles are on the radial aspect of the palm. The **hypothenar** muscles are on the medial aspect of the palm, and the **intermediate** muscles are midpalmar.



Superficial muscles of left hand (palmar) | Deep muscles of left hand (dorsal view) | Interossei muscles of left hand (palmar view) | Interossei muscles of left hand (doral view)

Figure 5. Intrinsic Muscles of the Hand. *The intrinsic muscles of the hand both originate and insert within the hand. These muscles provide the fine motor control of the fingers by flexing, extending, abducting, and adducting the more distal finger and thumb segments.*

The thenar muscles include the **abductor pollicis brevis**, **opponens pollicis**, **flexor pollicis brevis**, and the **adductor pollicis**. These muscles form the **thenar eminence**, the rounded contour of the base of the thumb, and all act on the thumb. The movements of the thumb play an integral role in most precise movements of the hand.

The hypothenar muscles include the **abductor digiti minimi**, **flexor digiti minimi brevis**, and the **opponens digiti minimi**. These muscles form the **hypothenar eminence**, the rounded contour of the little finger, and as such, they all act on the little finger. Finally, the intermediate muscles act on all the fingers and include the **lumbrical**, the **palmar interossei**, and the **dorsal interossei**.

Table 5. Muscles That Move the Wrist, Hands, and Forearm

Muscle	Movement	Target	Target motion direction	Prime mover	Origin	Insertion
Thenar muscles	Moves thumb toward body	Thumb	Abduction	Abductor pollicis brevis	Flexor retinaculum; nearby carpals	Lateral base of proximal phalanx of thumb
Thenar muscles	Moves thumb across palm toward body	Thumb	Opposition	Opponens pollicis	Flexor retinaculum; trapezium	Anterior of first metacarpal
Thenar muscles	Flexes thumb	Thumb	Flexion	Flexor pollicis brevis	Felxor retinaculum; trapezium	Lateral base of proximal phalanx of thumb
Thenar muscles	Moves thumb away from body	Thumb	Adduction	Adductor pollicis	Capitate bone; bases of metacarpals 2–4; front of metacarpal	Medial base of proximal phalanx of thumb
Hypothenar muscles	Moves little finger toward body	Little finger	Abduction	Abductor digiti minimi	Pisiform bone	Medial side of proximal phalanx of little finger
Hypothenar muscles	Flexes little finger	Little finger	Flexion	Flexor digiti minimi brevis	Hamate bone; flexor retinaculum	Medial side of proximal phalanx of little finger
Hypothenar muscles	Moves little finger across palm to touch thumb	Little finger	Opposition	Opponens digiti minimi	Hamate bone; flexor retinaculum	Medial side of proximal phalanx of little finger
Intermediate muscles	Flexes each finger at metacarpo-phalangeal	Fingers	Flexion	Lumbricals	Palm (lateral sides of tendons in flexor	Fingers 2–5 (lateral edges of extensional expansions on

Table 5. Muscles That Move the Wrist, Hands, and Forearm						
Muscle	Movement	Target	Target motion direction	Prime mover	Origin	Insertion
	joints; extends each finger at interphalangeal joints				digitorum profundus)	first phalanges)
Intermediate muscles	Adducts and flexes each finger at meacarpo-phalangeal joints; extends each finger at interphalangeal joints	Fingers	Adduction; flexion; extension	Palmar interossei	Side of each metacarpal that faces metacarpal 3 (absent from metacarpal 3)	Extensor expansion on first phalanx of each finger (except finger 3) on side facing finger 3
Intermediate muscles	Abducts and flexes the three middle fingers at metacarpo-phalangeal joints; extends the three middle fingers at interphalangeal joints	Fingers	Abduction; flexion; extension	Dorsal interossei	Sides of metacarpals	Both sides of finger 3; for each other finger, extensor expansion over first phalanx on side opposite finger 3

Self-Check Questions

Visit your course online to take a quiz to check your understanding of the Muscles of the Pectoral Girdle and Upper Limbs:

APPENDICULAR MUSCLES OF THE PELVIC GIRDLE AND LOWER LIMBS

Learning Objectives

- Identify the appendicular muscles of the pelvic girdle and lower limb
- Identify the movement and function of the pelvic girdle and lower limb

The appendicular muscles of the lower body position and stabilize the **pelvic girdle**, which serves as a foundation for the lower limbs. Comparatively, there is much more movement at the pectoral girdle than at the pelvic girdle. There is very little movement of the pelvic girdle because of its connection with the sacrum at the base of the axial skeleton. The pelvic girdle is less range of motion because it was designed to stabilize and support the body.

Muscles of the Thigh

What would happen if the pelvic girdle, which attaches the lower limbs to the torso, were capable of the same range of motion as the pectoral girdle? For one thing, walking would expend more energy if the heads of the femurs were not secured in the acetabula of the pelvis. The body's center of gravity is in the area of the pelvis. If the center of gravity were not to remain fixed, standing up would be difficult as well. Therefore, what the leg muscles lack in range of motion and versatility, they make up for in size and power, facilitating the body's stabilization, posture, and movement.

Gluteal Region Muscles That Move the Femur

Most muscles that insert on the femur (the thigh bone) and move it, originate on the pelvic girdle. The **psoas major** and **iliacus** make up the **iliopsoas group**. Some of the largest and most powerful muscles in the body are the gluteal muscles or **gluteal group**. The **gluteus maximus** is the largest; deep to the gluteus maximus is the **gluteus medius**, and deep to the gluteus medius is the **gluteus minimus**, the smallest of the trio (Figure 1 and Table 1).

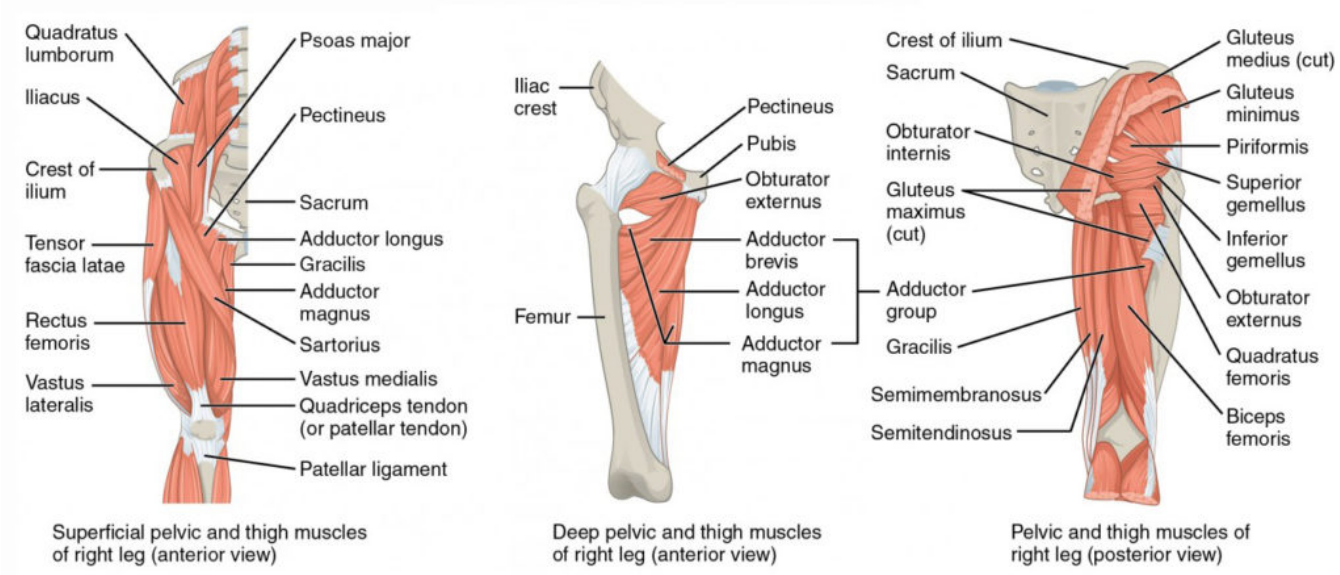


Figure 1. Hip and Thigh Muscles. *The large and powerful muscles of the hip that move the femur generally originate on the pelvic girdle and insert into the femur. The muscles that move the lower leg typically originate on the femur and insert into the bones of the knee joint. The anterior muscles of the femur extend the lower leg but also aid in flexing the thigh. The posterior muscles of the femur flex the lower leg but also aid in extending the thigh. A combination of gluteal and thigh muscles also adduct, abduct, and rotate the thigh and lower leg.*

Table 1. Gluteal Region Muscles That Move the Femur				
Movement	Target motion direction	Prime mover	Origin	Insertion
Iliopsoas group				

Table 1. Gluteal Region Muscles That Move the Femur				
Movement	Target motion direction	Prime mover	Origin	Insertion
raises the knee at the hip, as if performing a knee attack; it also assists the lateral rotators in twisting the thigh (and lower leg) outward, and assists with bending over and maintaining posture	thigh: flexion and lateral rotation; torso: flexion	psoas major	lumbar vertebrae (L1 through L5) and thoracic vertebra (T12)	lesser trochanter of femur
raises the knee at the hip, as if performing a knee attack; it also assists the lateral rotators in twisting the thigh (and lower leg) outward, and assists with bending over and maintaining posture	thigh: flexion and lateral rotation; torso: flexion	iliacus	iliac fossa, iliac crest, and lateral sacrum	lesser trochanter of femur
Gluteal group				
lowers the knee and moves the thigh back, as when getting ready to kick a ball	extension	gluteous maximus	dorsal ilium, sacrum, and coccyx	gluteal tuberosity of femur; iliotibial tract
opens the thigh, as when doing a split	abduction	gluteus medius	lateral surface of the ilium	greater trochanter of femur
brings the thighs back together	abduction	gluteus minimus	external surface of the ilium	greater trochanter of femur
assists with raising the knee at the hip and opening the thighs; it also maintains posture by stabilizing the iliotibial track, which connects to the knee	flexion; abduction	tensor fascia lata	anterior aspect of the iliac crest and the anterior superior iliac spine	iliotibial tract
Lateral rotators				
twists the thigh (and lower leg) outward; it also maintains posture by stabilizing the hip joint	lateral rotation	piriformis	anterolateral surface of the sacrum	greater trochanter of femur
twists the thigh (and lower leg) outward; it also maintains posture by stabilizing the hip joint	lateral rotation	obturator internus	inner surface of the obturator membrane, the greater sciatic notch, and the margins of the obturator foramen	greater trochanter in front of piriformis
twists thigh (and lower leg) outward; maintains posture by stabilizing hip joint	lateral rotation	obturator externus	outer surfaces of obturator membrane, pubic, and ischium;	trochanteric fossa of posterior femur

Table 1. Gluteal Region Muscles That Move the Femur				
Movement	Target motion direction	Prime mover	Origin	Insertion
			margins of obturator foramen	
twists the thigh (and lower leg) outward; it also maintains posture by stabilizing the hip joint	lateral rotation	superior gemellus	ischial spine	greater trochanter of femur
twists the thigh (and lower leg) outward; it also maintains posture by stabilizing the hip joint	lateral rotation	inferior gemellus	ischial tuberosity	greater trochanter of femur
twists the thigh (and lower leg) outward; it also maints posture by stabilizing the hip joint	lateral rotation	quatratus femoris	ischial tuberosity	trochanteric crest of femur
Adductors				
brings the thighs back together; it also assists with raising the knee	adduction; flexion	adductor longus	pubis near the pubic symphysis	linea aspera
brings the thighs back together; it also assists with raising the knee	adduction; flexion	adductor brevis	body of the pubis and in the inferior ramus of the pubis	linea aspera above adductor longus
brings the thighs back together; it also assists with raising the knee and moving the thigh back	adduction; flexion; extension	adductor magnus	ischial rami, the pubic rami, and the ischial tuberosity	linea aspera; adductor tubercle of femur
opens the thigh; with raising the knee and turning the thigh (and lower leg) inward	adduction; flexion; medial rotation	pectineus	pectineal line of the pubis	lesser trochanter to linea aspera of posterior aspect of femur

The **tensor fascia lata** is a thick, squarish muscle in the superior aspect of the lateral thigh. It acts as a synergist of the gluteus medius and iliopsoas in flexing and abducting the thigh. It also helps stabilize the lateral aspect of the knee by pulling on the **iliotibial tract** (band), making it taut. Deep to the gluteus maximus, the **piriformis**, **obturator internus**, **obturator externus**, **superior gemellus**, **inferior gemellus**, and **quadratus femoris** laterally rotate the femur at the hip.

The **adductor longus**, **adductor brevis**, and **adductor magnus** can both medially and laterally rotate the thigh depending on the placement of the foot. The adductor longus flexes the thigh, whereas the adductor magnus extends it. The **pectineus** adducts and flexes the femur at the hip as well. The pectineus is located in the **femoral triangle**, which is formed at the junction between the hip and the leg and also includes the femoral nerve, the femoral artery, the femoral vein, and the deep inguinal lymph nodes.

Thigh Muscles That Move the Femur, Tibia, and Fibula

Deep fascia in the thigh separates it into medial, anterior, and posterior compartments (see Figure 1 and Table 2). The muscles in the **medial compartment of the thigh** are responsible for adducting the femur at the hip. Along with

the adductor longus, adductor brevis, adductor magnus, and pectineus, the strap-like **gracilis** adducts the thigh in addition to flexing the leg at the knee.

Table 2. Thigh Muscles That Move the Femur, Tibia, and Fibula

Movement	Target	Target motion direction	Prime mover	Origin	Insertion
Medial compartment of thigh					
moves the back of the lower legs up toward the buttocks, as when kneeling; it also assists in opening the thighs	femur; tibia/ fibula	tibia/fibula: flexion; thigh: adduction	gracilis	inferior ramus, the body of the pubis, and the ischial ramus	medial surface of tibia
Anterior compartment of the thigh: Quadriceps femoris group					
moves the lower leg out in front of the body, as when kicking; it also assists in raising the knee	femur; tibia/ fibula	tibia/fibula: extension; thigh: flexion	rectus femoris	anterior inferior iliac spine and in the superior margin of the acetabulum	patella; tibial tuberosity
moves the lower leg out in front of the body, as when kicking	tibia/ fibula	extension	vastus lateralis	greater trochanter, the intertrochanteric line, and the linea aspera	patella; tibial tuberosity
moves the lower leg out in front of the body, as when kicking	tibia/ fibula	extension	vastus medialis	linea aspera and the intertrochanteric line	patella; tibial tuberosity
moves the lower leg out in front of the body, as when kicking	tibia/ fibula	extension	vastus intermedius	proximal femur shaft	patella; tibial tuberosity
moves the back of the lower legs up and back toward the buttocks, as when kneeling; it also assists in moving the thigh diagonally upward and outward as when mounting a bike	femur; tibia/ fibula	tibia: flexion; thigh: flexion, abduction, lateral rotation	sartorius	anterior superior iliac spine	medial aspect of proximal tibia
Posterior compartment of the thigh: Hamstring group					
moves the back of the lower leg up and back toward the buttocks, as when kneeling; it also moves the thigh down and back and twists the thigh (and lower leg) outward	femur; tibia/ fibula	tibia/fibula: flexion; thigh: extension, lateral rotation	biceps femoris	ischial tuberosity, linea aspera, and distal femur	head of fibula; lateral condyle of tibia
moves the back of the lower legs up toward the buttocks, as when kneeling; it also	femur; tibia/ fibula	tibia/fibula: flexion; thigh:	semitendinosus	ischial tuberosity	upper tibial shaft

Table 2. Thigh Muscles That Move the Femur, Tibia, and Fibula					
Movement	Target	Target motion direction	Prime mover	Origin	Insertion
moves the thigh down and back and twists the thigh (and lower leg) inward		extension, medial rotation			
moves the back of the lower legs up and back toward the buttocks, as when kneeling; it also moves the thigh down and back and twists the thigh (and lower leg) inward	femur; tibia/ fibula	tibia/fibula: flexion; thigh: extension, medial rotation	semi-membranosus	ischial tuberosity	medial condyle of tibia; lateral condyle of femur

The muscles of the **anterior compartment of the thigh** flex the thigh and extend the leg. This compartment contains the **quadriceps femoris group**, which actually comprises four muscles that extend and stabilize the knee. The **rectus femoris** is on the anterior aspect of the thigh, the **vastus lateralis** is on the lateral aspect of the thigh, the **vastus medialis** is on the medial aspect of the thigh, and the **vastus intermedius** is between the vastus lateralis and vastus medialis and deep to the rectus femoris. The tendon common to all four is the **quadriceps tendon** (patellar tendon), which inserts into the patella and continues below it as the **patellar ligament**. The patellar ligament attaches to the tibial tuberosity. In addition to the quadriceps femoris, the **sartorius** is a band-like muscle that extends from the anterior superior iliac spine to the medial side of the proximal tibia. This versatile muscle flexes the leg at the knee and flexes, abducts, and laterally rotates the leg at the hip. This muscle allows us to sit cross-legged.

The **posterior compartment of the thigh** includes muscles that flex the leg and extend the thigh. The three long muscles on the back of the knee are the **hamstring group**, which flexes the knee. These are the *biceps **femoris***,**semitendinosus**, and **semimembranosus**. The tendons of these muscles form the **popliteal fossa**, the diamond-shaped space at the back of the knee.

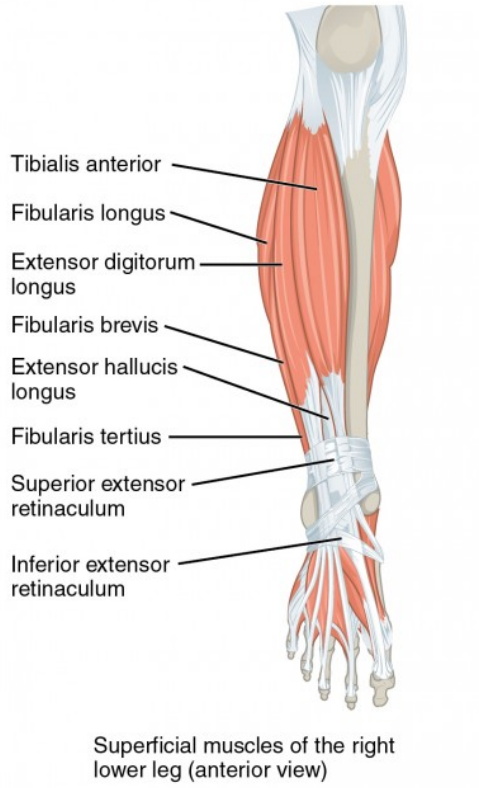
Muscles That Move the Feet and Toes

Similar to the thigh muscles, the muscles of the leg are divided by deep fascia into compartments, although the leg has three: anterior, lateral, and posterior (Figure 2 and Table 3).

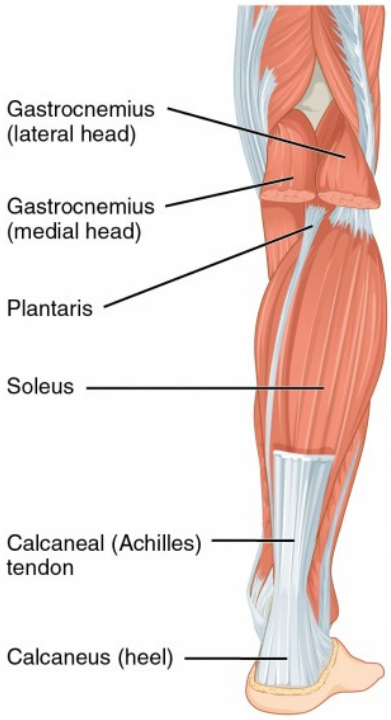
Table 3. Muscles That Move the Feet and Toes					
Movement	Target	Target motion direction	Prime mover	Origin	Insertion
Anterior compartment of the leg					
Raises the sole of the foot off the ground, as when preparing to foot-tap; bends the inside of the foot upwards, as when catching your balance while falling laterally toward the opposite side as the balancing foot	foot	dorsiflexion; inversion	tibialis anterior	lateral condyle and upper tibial shaft; interosseous membrane	interior surface of medial cuneiform; first metatarsal bone
raises the sole of the foot off the ground, as when	foot; big toe	foot: dorsiflexion;	extensor hallucis longus	anteromedial fibula shaft and	distal phalanx of big toe

Table 3. Muscles That Move the Feet and Toes					
Movement	Target	Target motion direction	Prime mover	Origin	Insertion
preparing to foot-tap; extends the big toe		big toe: extension		interosseous membrane	
raises the sole of the foot off the ground, as when preparing to foot-tap; extends the toes	foot; toes 2–5	foot: dorsiflexion; toes: extension	extensor digitorum longus	lateral condyle of the tibia, the proximal portion of the fibula, and the interosseous membrane	middle and distal phalanges of toes 2–5
Lateral compartment of the leg					
lowers the sole of the foot to the ground, as when foot-tapping or jumping; it also bends the inside of the foot downwards, as when catching your balance while falling laterally toward the same side as the balancing foot	foot	plantar flexion and eversion	fibularis longus	upper portion of the lateral fibula	first metatarsal; medial cuneiform
lowers the side of the foot to the ground, as when foot-tapping or jumping; it also bends the inside of the foot downward, as when catching your balance while falling laterally toward the same side as the balancing foot	foot	plantar flexion and eversion	fibularis (peroneus) brevis	distal fibula shaft	proximal end of fifth metatarsal
Posterior compartment of leg: Superficial muscles					
lowers the sole of the foot to the ground, as when foot-tapping or jumping; it also assists in moving the back of the lower legs up and back toward the buttocks	foot; tibia/ fibula	foot: plantar flexion; tibia/fibula: flexion	gastrocnemius	medial and lateral condyles of the femur	posterior calcaneus
lowers the sole of the foot the ground, as when foot-tapping or jumping; it also maintains posture while walking	foot	plantar flexion	soleus	superior tibia, fibula, and interosseous membrane	posterior calcaneus
lowers the sole of the foot to the ground, as when foot-tapping or jumping; it also assists in moving the back of the lower legs up and back toward the buttocks	foot; tibia/ fibula	foot: plantar flexion; tibia/fibula: flexion	plantaris	posterior femur above the lateral condyle	calcaneus or calcaneus tendon

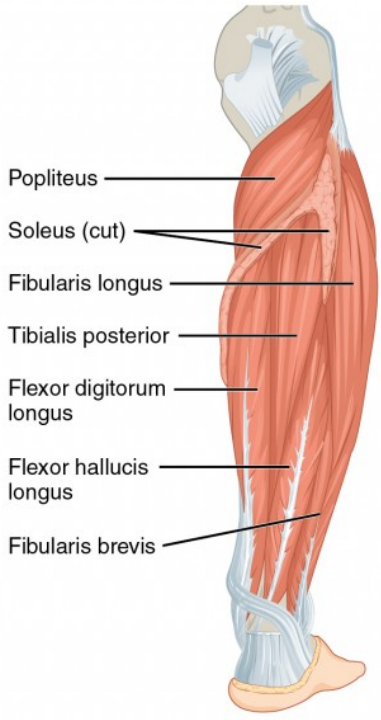
Table 3. Muscles That Move the Feet and Toes					
Movement	Target	Target motion direction	Prime mover	Origin	Insertion
lowers the sole of the foot to the ground, as when foot-tapping or jumping	foot	plantar flexion	tibialis posterior	superior tibia and fibula and in the interosseous membrane	several tarsals and metatarsals 2–4
Posterior compartment of the leg: Deep muscles					
moves the back of the lower legs up and back toward the buttocks; it also assists in rotation of the leg at the knee and thigh	tibia/ fibula	tibia/fibula: flexion; thigh and lower leg: medial and lateral rotation	popliteus	lateral condyle of the femur and the lateral meniscus	proximal tibia
lowers the sole of the foot to the ground, as when foot-tapping or jumping; it also bends the inside of the foot upward and flexes the toes	foot; toes 2–5	foot: plantar flexion and inversion; toes: flexion	flexor digitorum longus	posterior tibia	distal phalanges of toes 2–5
flexes the big toe	big toe; foot	big toe: flexion; foot: plantar flexion	flexor hallicis longus	midshaft of fibula; interosseous membrane	distal phalanx of big toe



Superficial muscles of the right lower leg (anterior view)



Superficial muscles of the right lower leg (posterior view)



Deep muscles of the right lower leg (posterior view)

Figure 2. Muscles of the Lower Leg. *The muscles of the anterior compartment of the lower leg are generally responsible for dorsiflexion, and the muscles of the posterior compartment of the lower leg are generally responsible for plantar flexion. The lateral and medial muscles in both compartments invert, evert, and rotate the foot.*

The muscles in the **anterior compartment of the leg**: the **tibialis anterior**, a long and thick muscle on the lateral surface of the tibia, the **extensor hallucis longus**, deep under it, and the **extensor digitorum longus**, lateral to it, all contribute to raising the front of the foot when they contract. The **fibularis tertius**, a small muscle that originates on the anterior surface of the fibula, is associated with the extensor digitorum longus and sometimes fused to it, but is not present in all people. Thick bands of connective tissue called the **superior extensor retinaculum** (transverse ligament of the ankle) and the **inferior extensor retinaculum**, hold the tendons of these muscles in place during dorsiflexion.

The **lateral compartment of the leg** includes two muscles: the **fibularis longus** (peroneus longus) and the **fibularis brevis** (peroneus brevis). The superficial muscles in the **posterior compartment of the leg** all insert onto the **calcaneal tendon** (Achilles tendon), a strong tendon that inserts into the calcaneal bone of the ankle. The muscles in this compartment are large and strong and keep humans upright. The most superficial and visible muscle of the calf is the **gastrocnemius**. Deep to the gastrocnemius is the wide, flat **soleus**. The **plantaris** runs obliquely between the two; some people may have two of these muscles, whereas no plantaris is observed in about seven percent of other cadaver dissections. The plantaris tendon is a desirable substitute for the fascia lata in hernia repair, tendon transplants, and repair of ligaments. There are four deep muscles in the posterior compartment of the leg as well: the **popliteus**, **flexor digitorum longus**, **flexor hallucis longus**, and **tibialis posterior**.

The foot also has intrinsic muscles, which originate and insert within it (similar to the intrinsic muscles of the hand). These muscles primarily provide support for the foot and its arch, and contribute to movements of the toes (Figure 3 and Table 4). The principal support for the longitudinal arch of the foot is a deep fascia called **plantar aponeurosis**, which runs from the calcaneus bone to the toes (inflammation of this tissue is the cause of “plantar fasciitis,” which can affect runners. The intrinsic muscles of the foot consist of two groups. The **dorsal group** includes only one muscle, the **extensor digitorum brevis**. The second group is the **plantar group**, which consists of four layers, starting with the most superficial.

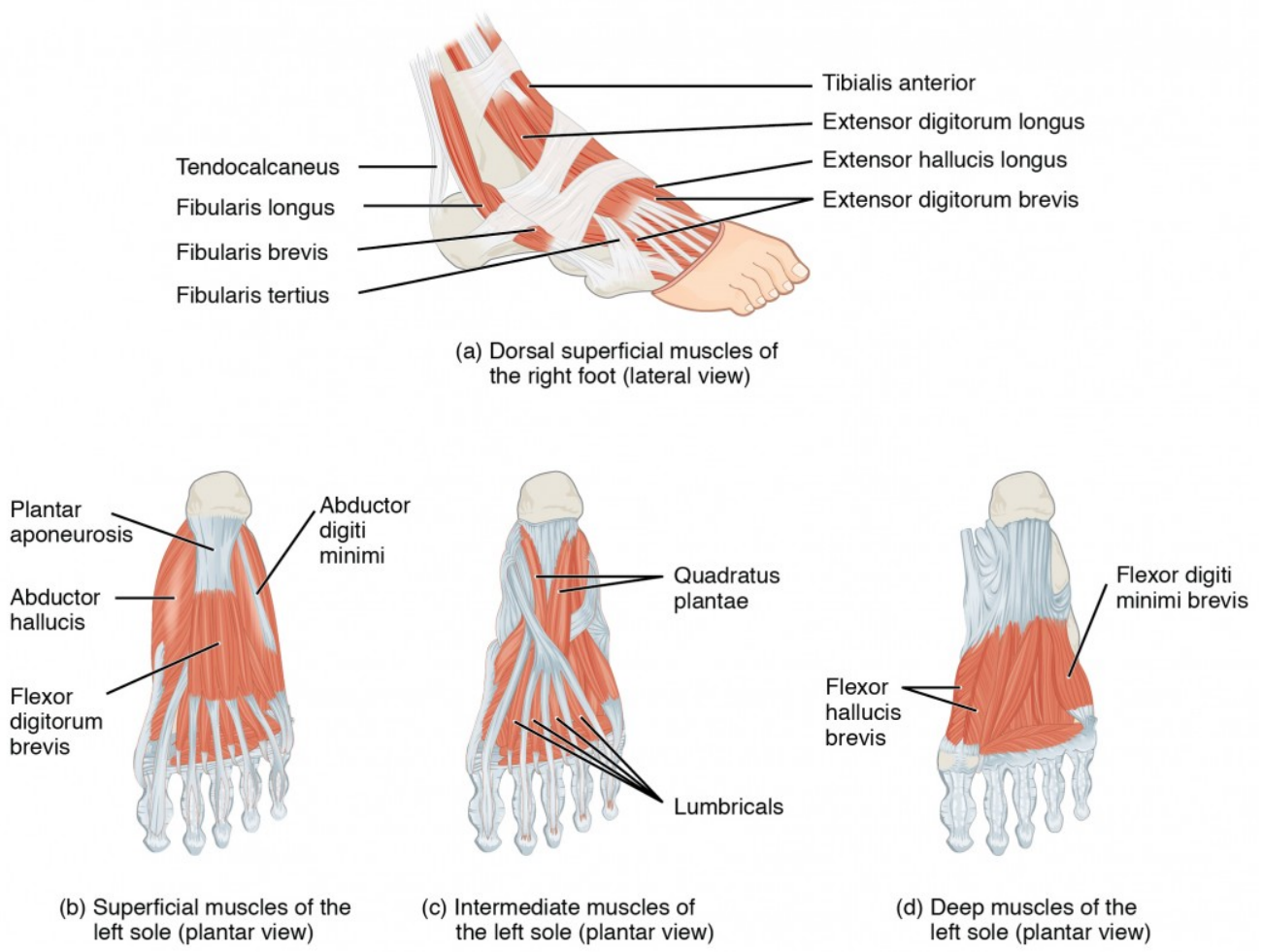


Figure 3. Intrinsic Muscles of the Foot. *The muscles along the dorsal side of the foot (a) generally extend the toes while the muscles of the plantar side of the foot (b, c, d) generally flex the toes. The plantar muscles exist in three layers, providing the foot the strength to counterbalance the weight of the body. In this diagram, these three layers are shown from a plantar view beginning with the bottom-most layer just under the plantar skin of the foot (b) and ending with the top-most layer (d) located just inferior to the foot and toe bones.*

Table 4. Intrinsic Muscles in the Foot					
Movement	**Target**	**Target motion direction**	**Prime mover**	**Origin**	**Insertion**
Dorsal group					
extends toes 2 through 5	toes 2–5	extension	extensor digitorum brevis	calcaneus; extensor retinaculum	base of proximal phalanx of big toe; extensor expansions on toes 2–5
Plantar group (layer 1)					
abducts and flexes the big toe	big toe	adduction; flexion	abductor hallucis	calcaneal tuberosity; flexor retinaculum	proximal phalanx of big toe

Table 4. Intrinsic Muscles in the Foot					
Movement	Target	Target motion direction	Prime mover	Origin	Insertion
flexes toes 2 through 4	middle toes	flexion	flexor digitorum brevis	calcaneal tuberosity	middle phalanx of toes 2–4
abducts and flexes the small toe	toe 5	abduction; flexion	abductor digiti minimi	calcaneal tuberosity	proximal phalanx of little toe
Plantar group (layer 2)					
assists in flexing toes 2 through 5	toes 2–5	flexion	quadratus plantae	medial and lateral sides of the calcaneus	tendon of flexor digitorum longus
extend toes 2 through 5 at the interphalangeal joints; they also flex the small toes at the metatarsophalangeal joints	toes 2–5	extension; flexion	lumbricals	tendons of the flexor digitorum longus	medial side of proximal phalanx of toes 2–5
Plantar group (layer 3)					
flexes the big toe	big toe	flexion	flexor hallucis brevis	lateral cuneiform and in the cuboid bones	base of proximal phalanx of big toe
adducts and flexes the big toe	big toe	adduction; flexion	adductor hallucis	bases of metatarsals 2 through 4, in the fibularis longus tendon sheath, and in the ligament across the metatarsophalangeal joints	base of proximal phalanx of big toe
flexes the small toe	little toe	flexion	flexor digiti minimi brevis	base of metatarsal 5 and in the tendon sheath of the fibularis longus	base of proximal phalanx of little toe
Plantar group (layer 4)					
abducts and flexes the middle toes at the metatarsophalangeal joints; it also extends the middle toes at the interphalangeal joints	middle toes	abduction; flexion; extension	dorsal interossei	sides of the metatarsals	both sides of toe 2; for each tother to, extensor expansion over first phalanx on side opposite toe 2

Table 4. Intrinsic Muscles in the Foot					
Movement	Target	Target motion direction	Prime mover	Origin	Insertion
abducts toes 3 through 5; it also flexes the proximal phalanges and extends the distal phalanges	small toes	abduction; flexion; extension	plantar interossei	side of each metatarsal that faces metatarsal 2 (absent from metatarsal 2)	extensor expansion on first phalanx of each toe (except toe 2) on side facing toe 2

Self-Check Questions

Visit your course online to take a quiz to check your understanding of the Appendicular Muscles of the Pelvic Girdle and Lower Limbs:

INTERACTIVE: VISIBLE BODY

Interactive Link
Download some of the Applications and find more information on the muscular system here: http://www.visiblebody.com/index.html

SELF CHECK: MUSCULAR ANATOMY

Interactive Link
Click on the link below to check your ability to identify each of the muscles: http://www.colorado.edu/intphys/iphy3415/models/index.html

LECTURE: WHOLE MUSCLE BEHAVIOR

Watch this video series by Wendy Riggs for a review of muscle behavior. In this series she covers muscle strength, the relationship between length and tension, flexibility, myofiber variation, motor units, and antagonistic groups.

Watch this video online: https://youtu.be/videoseries

SLIDES OF MUSCLES

Learning Objectives

- Be able to name and to identify the three types of muscle at the light and electron microscope levels, including distinctive features of each, such as the intercalated discs of cardiac muscle.
- Be able to describe and understand the structural basis of muscle striation at the light microscope and EM levels and the molecular level.
- Know the structural elements that harness muscle contraction (i.e., the shortening of myofibrils) to the movement of a body part (i.e., via connection to bone) as well as the mechanism by which muscle cells (skeletal, cardiac and smooth muscle) contract.
- Understand where stem cells are located in skeletal muscle and be able to identify their location at both the light and EM levels.
- Be familiar with the regenerative potential of each muscle type.

There are three major types of muscle, and their structure reflects their function. Skeletal and cardiac muscle cells are called striated muscle because of the very regular arrangement of their intracellular contractile units, sarcomeres, at the light microscope (LM) and electron microscope (EM) levels. This regular arrangement imparts a cross-striated (or striped) appearance. Such an arrangement is not seen in smooth muscle cells. Skeletal muscle is also called voluntary muscle, because its contraction is under conscious neural control. In contrast, cardiac and smooth muscles are called involuntary muscles because their contractions are either spontaneously generated or are under the control of the autonomic nervous system.

Each of these three types of muscle has a characteristic appearance in both cross and longitudinal sections. You should be able to recognize each type of muscle in both planes of section.

SKELETAL MUSCLE

A. Cytology of skeletal muscle cells

- **058L** *skeletal muscle H&E longitudinal* Webscope Imagescope
- **058Lex** *Skeletal muscle H&E longitudinal* Webscope Imagescope

- 058Thin *skeletal muscle H&E longitudinal* Webscope Imagescope
- 058T *Skeletal muscle H&E cross* Webscope Imagescope

In **longitudinal sections** of skeletal muscle (**Slide 58**, odd-numbered slide boxes), observe the following :

1. Nonbranching, cylindrical shape of the cell (also referred as muscle fiber). These cells are very long; you cannot see their ends.
2. Be sure you can identify the borders of the muscle cell. **You might see occasional nuclei which appear to be centrally located, but aren't. Why?** Again the answer to the question is in the plane of section. Cells with peripheral nuclei that are cut at an angle can appear to have centrally located nuclei. This is why it is important to look at other features of the cell to determine what exactly it is.
3. Peripheral position of the elongate nuclei just inside of the sarcolemma (plasma membrane). Note that each cell contains large numbers of nuclei.
4. **Cross striations** can be seen, and are due to the structure of the sarcomere. A sarcomere consists of the structures between two Z lines. You should recognize: **(Using your microscope and glass slides may help to see these fine structures)**
    1. The dark A band
    2. The lighter H zone which bisects the A band
    3. The light I band d. The dark Z line which bisects the I band.

    It is admittedly difficult to see the **Z line** and especially the **H zone** with the light microscope. However, they can be seen clearly on some areas of almost all slides, and it is just necessary to do some looking around for a favorable area on your slide. Here are some good examples showing cross striations: **#058L** Webscope **#058L** Webscope
5. A less regular longitudinal striping can sometimes be seen within the muscle fibers and is due to the bundling together of the thick and thin filaments into myofibrils, which are arranged parallel to the long axis of the cell. Note that sometimes the cross striations are not aligned all the way across the cell. This is because different myofibrils may not be aligned.In **transverse sections** of skeletal muscle cells (**slide 58**, even slide boxes), observe the**cylindrical shape** of the cells (fibers) and the **peripherally-located nuclei**. Note also the the cytoplasm of the muscle cells has a **stippled, punctate appearance** which is due to the bundling of thick and thin filaments into myofibrils as mentioned above. **What exactly is a muscle cell and what's the difference between a muscle fiber and a muscle fibril?** The basic units of muscle are the contractile proteins actin and myosin arranged in sarcomeres. Placed end to end, these sarcomeres form long bands called myofibrils. Within a skeletal muscle cell, the numerous myofibrils are separated by glycogen, mitochondria, and muscle triads (two terminal cisternae and a T tubule) and other organelles. Chances are, if you are looking at an electron micrograph of muscle tissue, you are looking at myofibrils. Groups of these fibrils form a muscle fiber, which is surrounded by endomysium. Muscle fiber and muscle cell are synonymous. Groups of individual cells that are surrounded by perimysium are known as fascicles and groups of these fascicles, surrounded by epimysium make up a muscle.

Perimuscular Connective Tissue

- 059-3 *forearm muscle Masson cross fetal* Webscope Imagescope Image
- 059-1 *forearm muscle H&E cross fetal* Webscope Imagescope Image

In **slide 59**, stained with **trichrome** (even slide boxes) or **H&E** (odd slide boxes), three layers of connective tissue sheaths are visible. This is a transverse section of an entire fetal forearm, and contains many elements in

ition to the muscle, such as *nerves* and *tendons*, both of which are, unfortunately, simlarly bundled into fascicles and therefore easily confused with muscle. So, make sure you're looking at the muscles Image Image

1. Endomysium – thin connective tissue sheath, consisting of basal lamina, some reticular fibers and capillaries around **each muscle fiber**. In fetal muscle, endomysium is not always clearly defined, so it is best to use the **trichrome-stained** slide (**slide 59-3**) to this –it is the connective tissue immediately surrounding the individual cells and **very delicate** perhaps visible only as a bluish tinge.
2. Perimysium – loose connective tissue sheath consisting of type I collagen fibers found around **fascicles** (bundles of muscle fibers). Note that the tissue in these specimens underwent some shrinkage during preparation so the separation between fascicles is somewhat exaggerated. Similarly, much of the perimysium has been damaged; however there are still some areas where it can be clearly seen (e.g. around many of the blood vessels found within the belly of the muscles).

3. Epimysium – the dense irregular connective tissue sheath around the **entire muscle** = deep fascia in gross anatomy; contains even larger blood vessels and nerves.

Three layers can be seen in **#059-3** Webscope Image

CARDIAC MUSCLE

- **057** *ventricle H&E* Webscope Imagescope
- **098-1** *Heart ventricle H&E* Webscope Imagescope
- **098N** *right wall Masson* Webscope Imagescope
- **305** *heart ventricle H&E* Webscope Imagescope (note: this slide NOT in glass slide collection)

Cardiac muscle will be studied in the wall of the ventricle of the heart. In comparison with skeletal muscle, note the following differences. Cardiac muscle cells branch and form a three-dimensional network. These branch points can sometimes be seen in your sections, and you should also note that the muscle fibers are less parallel than in skeletal muscle.

A. In longitudinal sections, observe:

1. Intercalated discs which are dark lines which cross the cell transversely. Look around in **slide 57 #057** Webscope or **slide 305** INDO 390 for lightly stained regions of the slide. There are artifactual transverse breaks in some of the muscle fibers, which are NOT intercalated discs. Intercalated discs are also fairly easy to find in the areas where muscle fibers are **longitudinally oriented** in **slide 98-1 #098-1** Webscope and/or **slide 98-N#098N** Webscope (be sure to look at both H&E and trichrome-stained sections).
2. The nucleus is **centrally located** in a fiber.
3. Longitudinal striping due to myofibrils can sometimes be seen.

B. In transverse sections, observe:

1. The myofibrils are coarse and give rise to the nonhomogeneous, punctate appearance of the sarcoplasm.
2. The nuclei are centrally-located. You won't see a nucleus in every fiber cross-section.
3. The extensive network of capillaries in the endomysium –heart muscle is ALWAYS beating and therefore always in demand of oxygen and nutrients delivered via the blood.

MAKE SURE YOU CAN DIFFERENTIATE BETWEEN CARDIAC AND SKELETAL MUSCLE IN BOTH LONGITUDINAL AND TRANSVERSE SECTIONS!

SMOOTH MUSCLE

- **029-1** *Small Intestine (simple columnar epithelium, simple squamous epithelium) H&E cross*Webscope Imagescope
- **169** *jejunum H&E cross* Webscope Imagescope
- **155** *gastro-esophageal junction H&E longitudinal* Webscope Imagescope
- **250-2** *vagina Masson* Webscope Imagescope
- **250-1** *vagina H&E* Webscope Imagescope

Smooth muscle may be studied using **slide #29 #029-1 smooth muscle** Webscope or **slide #169**, **#169** Webscope, both in the intestine. To find the muscle layer, look at the at slide at the lowest power (this is about the same as looking at the glass slide with the naked eye). The purple layer is largely the epithelium and the lamina propria filled with plasma cell and lymphocytes. Next to that you see a lighter region of connective tissue (the submucosa you looked at to see loose connective tissue and fibroblasts), then a darker pink region which is made up of the two layers of smooth muscle you want to look at. **Slide 29** is a **cross section** of the intestine, so the inner, circular layer of muscle will have cells oriented longitudinally (or, in places, the cells may

appear to be oriented more obliquely). Move further out to see the outer sheet of smooth muscle, which runs longitudinally along the intestine, and will therefore be seen in cross section.

Look at **slide #155,** which is a **longitudinal section** of the GI tract at the gastro-esophageal junction, to see more smooth muscle in various planes of section. The smooth muscle in the esophagus (the part lined with a stratified, non-keratinizing squamous epithelium) **#155** Webscope is organized in the "classic" inner circular and outer longitudinal arrangement. However, the stomach (the part lined by a columnar epithelium) **#155** Webscope has an inner oblique layer (seen mostly as longitudinal here), a very prominent middle circular layer, and a sometimes less obvious outer longitudinal layer. Don't worry knowing about the specific layers or being able to tell esophagus from stomach. However, you should definitely be able to identify smooth muscle in **any** plane of section (tranverse, longitudinal, or even oblique). In this particular slide, both the hematoxylin and eosin staining are quite intense, which should help you to see the cytoplasm more clearly, especially when the muscle is cut in cross section.

In longitudinally cut smooth muscle cells, observe the following points:

1. Cells are small and spindle-shaped (fusiform); this may be hard to appreciate because the cell membrane is indistinct.
2. Myofibirils and cross striation cannot be seen.
3. Nuclei are narrow, elongated and sometimes kinked or spiraling. They are centrally located.

In transversely cut smooth muscle cells, observe the following points:

1. The cell has a small diameter.
2. The nucleus is located centrally, but will not be seen in every cross section.
3. Myofibrils cannot be seen.
4. Cross-sectional diameters vary due to the spindle shape of the cells.

Now, look at **slide #250** and see if you can distinguish between small fascicles of smooth muscle and collagen fibers in the lamina propria (this task will be easier if you look first at the **trichrome-stained section**, which stains the muscle pink(ish) and the collagen blue) **#250-2** Webscope . It's more challenging to make this distinction in the **H&E-stained section #250-1** Webscope. You should note that smooth muscle is pink, wheras collagen is a bit more orange-red. Also, smooth muscle tissue is mostly **cellular** (and therefore more nuclei are present), whereas the connective tissue is mostly **extracellular** collagen fibers with fewer cells. The table below compares the differences in the morphology of the three types of muscle.

Major Histological Characteristics Of The Three Types Of Muscle As Seen With The Light Microscope

Skeletal Muscle	Cardiac Muscle	Smooth Muscle
Prominet cross- striations	Prominet cross- striations	No cross- striations
Fiber diameter large	Fiber diameter medium	Fiber diameter small
Nuclei usually peripheral	Central nucleus	Central nucleus
Unbranched	Branched	Unbranched
No intercalated discs	Intercalated discs	No intercalated discs
Longitudinal striation (myofibrils)	Longitudinal striation	No longitudinal striati

Electron Micrographs

- 37 Skeletal Muscle – Longitudinal Section ***low Magnification*** Webscope Imagescope

Skeletal Muscle (longitudinal section, low magnification). Find the skeletal muscle nuclei and note their peripheral location. Note the intimate contact between capillaries and muscle cells and be sure you can tell where one muscle cell or fiber stops and another begins (you can see parts of four fibers in this picture). Make sure you know which is the longitudinal axis of the cell. Identify sarcomeres, A bands, I bands, Z lines and H zones. Note that, as you saw at the LM level, the individual myofibrils do not line up perfectly across the fiber.

- 34 Skeletal muscle – Cross Section ***Low Magnification*** Webscope Imagescope

Skeletal Muscle (cross section, low magnification). Note location of muscle fiber nuclei. You can see cross sections of A bands (darker) and I bands (lighter) side by side in the same cell because of the fact that the myofibrils don't line up perfectly. Identify the approximate outline of a single myofibril.

- 32 Striated muscle – longitudinal section Webscope Imagescope

Skeletal Muscle (longitudinal section). Identify a sarcomere. Relate the sarcomeric structure seen in the LM to the structure seen here. Note that there is also lots of glycogen in the region between the two myofibrils in this picture, a storage form for glucose (which is metabolized to provide energy for muscle contraction). At the border of the I and A-bands, note triads consisting of a central T (transverse) tubule and flanking cisternae of the sarcoplasmic reticulum.

- 41 Cardiac muscle ***Intercalated Disc*** Webscope Imagescope

Cardiac Muscle (Intercalated Disc, longitudinal section). Note the somewhat irregular course of the intercalated disc. In this preparation, the I bands are very short, indicating that the sarcomere is in a contracted state. Review the types of junctions present in an intercalated disc and their functions.

- 43 Cardiac Muscle Webscope Imagescope

Cardiac Muscle (longitudinal section). Note central location of muscle nuclei. Note the "stacks" of mitochondria between myofibrils. Cardiac muscle is even richer than skeletal muscle in mitochondria (again, important for energy production). An intercalated disc is present in the upper left region of the picture.

- 207 Small intestine (Muscularis Externa) Webscope Imagescope

Study the orientation of the smooth muscle cells in the intestinal muscularis externa. The micrograph will help you understand the pattern, which arises from the inner circular layer and outer longitudinal layer of smooth muscle cells. Without the knowledge in which direction the intestinal epithelium is located, it is not possible to discriminate between the two sublayers of the muscularis externa.

- 44 Smooth muscle – Cross Section Webscope Imagescope

Smooth Muscle (cross section). Here you can see the filaments in cross-section, appearing as dots. Also, the dark areas, which are membrane-associated, are called dense plaques and are sites of filament attachment.

Review Questions

1. Why do some skeletal muscle cells seem wider than others?
   Answer:The plane of section is generally responsible for making some cells look larger than others. Some skeletal muscle cells on your slide may be sliced through the middle and appear quite large, while as other cells may just graze the section and appear much smaller. Also, some muscle cells are simply smaller or larger than others. They can range in size from 10 to 100 mm in width.
2. You might see occasional nuclei which appear to be centrally located, but aren't. Why?
   Answer:Again the answer to the question is in the plane of section. Cells with peripheral nuclei that are cut at an angle can appear to have centrally located nuclei. This is why it is important to look at other features of the cell to determine what exactly it is.
3. So what exactly is a muscle cell and what's the difference between a muscle fiber and a muscle fibril?
   Answer:The basic units of muscle are the contractile proteins actin and myosin arranged in sarcomeres. Placed end to end, these sarcomeres form long bands called myofibrils. Within a skeletal muscle cell, the numerous myofibrils are separated by glycogen, mitochondria, and muscle triads (two terminal cisternae and a T tubule) and other organelles. Chances are, if you are looking at an electron micrograph of muscle tissue, you are looking at myofibrils. Groups of these fibrils form a muscle fiber,

which is surrounded by endomysium. Muscle fiber and muscle cell are synonymous. Groups of individual cells that are surrounded by perimysium are known as fascicles and groups of these fascicles, surrounded by epimysium make up a muscle.

VIDEO: THE STERNUM

Watch this video online: https://youtu.be/711l2AJ6-Rc

ADDITIONAL LINKS

Interactive Links

- View and practice learning the Muscular System on the InnerBody website
- Play Muscular System Games
- Consider purchasing the Virtual Human app.

GLOSSARY: THE MUSCULAR SYSTEM

abduct: move away from midline in the sagittal plane

abductor digiti minimi: muscle that abducts the little finger

abductor pollicis brevis: muscle that abducts the thumb

abductor pollicis longus: muscle that inserts into the first metacarpal

abductor: moves the bone away from the midline

adductor brevis: muscle that adducts and medially rotates the thigh

adductor longus: muscle that adducts, medially rotates, and flexes the thigh

adductor magnus: muscle with an anterior fascicle that adducts, medially rotates and flexes the thigh, and a posterior fascicle that assists in thigh extension

adductor pollicis: muscle that adducts the thumb

adductor: moves the bone toward the midline

agonist: (also, prime mover) muscle whose contraction is responsible for producing a particular motion

anal triangle: posterior triangle of the perineum that includes the anus

anconeus: small muscle on the lateral posterior elbow that extends the forearm

antagonist: muscle that opposes the action of an agonist

anterior compartment of the arm: (anterior flexor compartment of the arm) the biceps brachii, brachialis, brachioradialis, and their associated blood vessels and nerves

anterior compartment of the forearm: (anterior flexor compartment of the forearm) deep and superficial muscles that originate on the humerus and insert into the hand

anterior compartment of the leg: region that includes muscles that dorsiflex the foot

anterior compartment of the thigh: region that includes muscles that flex the thigh and extend the leg

anterior scalene: a muscle anterior to the middle scalene

appendicular: of the arms and legs

axial: of the trunk and head

belly: bulky central body of a muscle

bi: two

biceps brachii: two-headed muscle that crosses the shoulder and elbow joints to flex the forearm while assisting in supinating it and flexing the arm at the shoulder

biceps femoris: hamstring muscle

bipennate: pennate muscle that has fascicles that are located on both sides of the tendon

brachialis: muscle deep to the biceps brachii that provides power in flexing the forearm.

brachioradialis: muscle that can flex the forearm quickly or help lift a load slowly

brevis: short

buccinator: muscle that compresses the cheek

calcaneal tendon: (also, Achilles tendon) strong tendon that inserts into the calcaneal bone of the ankle

caval opening: opening in the diaphragm that allows the inferior vena cava to pass through; foramen for the vena cava

circular: (also, sphincter) fascicles that are concentrically arranged around an opening

compressor urethrae: deep perineal muscle in women

convergent: fascicles that extend over a broad area and converge on a common attachment site

coracobrachialis: muscle that flexes and adducts the arm

corrugator supercilii: prime mover of the eyebrows

deep anterior compartment: flexor pollicis longus, flexor digitorum profundus, and their associated blood vessels and nerves

deep posterior compartment of the forearm: (deep posterior extensor compartment of the forearm) the abductor pollicis longus, extensor pollicis brevis, extensor pollicis longus, extensor indicis, and their associated blood vessels and nerves

deep transverse perineal: deep perineal muscle in men

deglutition: swallowing

deltoid: shoulder muscle that abducts the arm as well as flexes and medially rotates it, and extends and laterally rotates it

diaphragm: skeletal muscle that separates the thoracic and abdominal cavities and is dome-shaped at rest

digastric: muscle that has anterior and posterior bellies and elevates the hyoid bone and larynx when one swallows; it also depresses the mandible

dorsal group: region that includes the extensor digitorum brevis

dorsal interossei: muscles that abduct and flex the three middle fingers at the metacarpophalangeal joints and extend them at the interphalangeal joints

epicranial aponeurosis: (also, galea aponeurosis) flat broad tendon that connects the frontalis and occipitalis

erector spinae group: large muscle mass of the back; primary extensor of the vertebral column

extensor carpi radialis brevis: muscle that extends and abducts the hand at the wrist

extensor carpi ulnaris: muscle that extends and adducts the hand

extensor digiti minimi: muscle that extends the little finger

extensor digitorum brevis: muscle that extends the toes

extensor digitorum longus: muscle that is lateral to the tibialis anterior

extensor digitorum: muscle that extends the hand at the wrist and the phalanges

extensor hallucis longus: muscle that is partly deep to the tibialis anterior and extensor digitorum longus

extensor indicis: muscle that inserts onto the tendon of the extensor digitorum of the index finger

extensor pollicis brevis: muscle that inserts onto the base of the proximal phalanx of the thumb

extensor pollicis longus: muscle that inserts onto the base of the distal phalanx of the thumb

extensor radialis longus: muscle that extends and abducts the hand at the wrist

extensor retinaculum: band of connective tissue that extends over the dorsal surface of the hand

extensor: muscle that increases the angle at the joint

external intercostal: superficial intercostal muscles that raise the rib cage

external oblique: superficial abdominal muscle with fascicles that extend inferiorly and medially

extrinsic eye muscles: originate outside the eye and insert onto the outer surface of the white of the eye, and create eyeball movement

extrinsic muscles of the hand: muscles that move the wrists, hands, and fingers and originate on the arm

fascicle: muscle fibers bundled by perimysium into a unit

femoral triangle: region formed at the junction between the hip and the leg and includes the pectineus, femoral nerve, femoral artery, femoral vein, and deep inguinal lymph nodes

fibularis brevis: (also, peroneus brevis) muscle that plantar flexes the foot at the ankle and everts it at the intertarsal joints

fibularis longus: (also, peroneus longus) muscle that plantar flexes the foot at the ankle and everts it at the intertarsal joints

fibularis tertius: small muscle that is associated with the extensor digitorum longus

fixator: synergist that assists an agonist by preventing or reducing movement at another joint, thereby stabilizing the origin of the agonist

flexion: movement that decreases the angle of a joint

flexor carpi radialis: muscle that flexes and abducts the hand at the wrist

flexor carpi ulnaris: muscle that flexes and adducts the hand at the wrist

flexor digiti minimi brevis: muscle that flexes the little finger

flexor digitorum longus: muscle that flexes the four small toes

flexor digitorum profundus: muscle that flexes the phalanges of the fingers and the hand at the wrist

flexor digitorum superficialis: muscle that flexes the hand and the digits

flexor hallucis longus: muscle that flexes the big toe

flexor pollicis brevis: muscle that flexes the thumb

flexor pollicis longus: muscle that flexes the distal phalanx of the thumb

flexor retinaculum: band of connective tissue that extends over the palmar surface of the hand

flexor: muscle that decreases the angle at the joint

frontalis: front part of the occipitofrontalis muscle

fusiform: muscle that has fascicles that are spindle-shaped to create large bellies

gastrocnemius: most superficial muscle of the calf

genioglossus: muscle that originates on the mandible and allows the tongue to move downward and forward

geniohyoid: muscle that depresses the mandible, and raises and pulls the hyoid bone anteriorly

gluteal group: muscle group that extends, flexes, rotates, adducts, and abducts the femur

gluteus maximus: largest of the gluteus muscles that extends the femur

gluteus medius: muscle deep to the gluteus maximus that abducts the femur at the hip

gluteus minimus: smallest of the gluteal muscles and deep to the gluteus medius

gracilis: muscle that adducts the thigh and flexes the leg at the knee

hamstring group: three long muscles on the back of the leg

hyoglossus: muscle that originates on the hyoid bone to move the tongue downward and flatten it

hypothenar eminence: rounded contour of muscle at the base of the little finger

hypothenar: group of muscles on the medial aspect of the palm

iliacus: muscle that, along with the psoas major, makes up the iliopsoas

iliococcygeus: muscle that makes up the levator ani along with the pubococcygeus

iliocostalis cervicis: muscle of the iliocostalis group associated with the cervical region

iliocostalis group: laterally placed muscles of the erector spinae

iliocostalis lumborum: muscle of the iliocostalis group associated with the lumbar region

iliocostalis thoracis: muscle of the iliocostalis group associated with the thoracic region

iliopsoas group: muscle group consisting of iliacus and psoas major muscles, that flexes the thigh at the hip, rotates it laterally, and flexes the trunk of the body onto the hip

iliotibial tract: muscle that inserts onto the tibia; made up of the gluteus maximus and connective tissues of the tensor fasciae latae

inferior extensor retinaculum: cruciate ligament of the ankle

inferior gemellus: muscle deep to the gluteus maximus on the lateral surface of the thigh that laterally rotates the femur at the hip

infrahyoid muscles: anterior neck muscles that are attached to, and inferior to the hyoid bone

infraspinatus: muscle that laterally rotates the arm

innermost intercostal: the deepest intercostal muscles that draw the ribs together

insertion: end of a skeletal muscle that is attached to the structure (usually a bone) that is moved when the muscle contracts

intercostal muscles: muscles that span the spaces between the ribs

intermediate: group of midpalmar muscles

internal intercostal: muscles the intermediate intercostal muscles that draw the ribs together

internal oblique: flat, intermediate abdominal muscle with fascicles that run perpendicular to those of the external oblique

intrinsic muscles of the hand: muscles that move the wrists, hands, and fingers and originate in the palm

ischiococcygeus: muscle that assists the levator ani and pulls the coccyx anteriorly

lateral compartment of the leg: region that includes the fibularis (peroneus) longus and the fibularis (peroneus) brevis and their associated blood vessels and nerves

lateral pterygoid: muscle that moves the mandible from side to side

lateralis: to the outside

latissimus dorsi: broad, triangular axial muscle located on the inferior part of the back

levator ani: pelvic muscle that resists intra-abdominal pressure and supports the pelvic viscera

linea alba: white, fibrous band that runs along the midline of the trunk

longissimus capitis: muscle of the longissimus group associated with the head region

longissimus cervicis: muscle of the longissimus group associated with the cervical region

longissimus group: intermediately placed muscles of the erector spinae

longissimus thoracis: muscle of the longissimus group associated with the thoracic region

longus: long

lumbrical: muscle that flexes each finger at the metacarpophalangeal joints and extend each finger at the interphalangeal joints

masseter: main muscle for chewing that elevates the mandible to close the mouth

mastication: chewing

maximus: largest

medial compartment of the thigh: a region that includes the adductor longus, adductor brevis, adductor magnus, pectineus, gracilis, and their associated blood vessels and nerves

medial pterygoid: muscle that moves the mandible from side to side

medialis: to the inside

medius: medium

middle scalene: longest scalene muscle, located between the anterior and posterior scalenes

minimus: smallest

multifidus: muscle of the lumbar region that helps extend and laterally flex the vertebral column

multipennate: pennate muscle that has a tendon branching within it

mylohyoid: muscle that lifts the hyoid bone and helps press the tongue to the top of the mouth

oblique: at an angle

obturator externus: muscle deep to the gluteus maximus on the lateral surface of the thigh that laterally rotates the femur at the hip

obturator internus: muscle deep to the gluteus maximus on the lateral surface of the thigh that laterally rotates the femur at the hip

occipitalis: posterior part of the occipitofrontalis muscle

occipitofrontalis: muscle that makes up the scalp with a frontal belly and an occipital belly

omohyoid: muscle that has superior and inferior bellies and depresses the hyoid bone

opponens digiti minimi: muscle that brings the little finger across the palm to meet the thumb

opponens pollicis: muscle that moves the thumb across the palm to meet another finger

orbicularis oculi: circular muscle that closes the eye

orbicularis oris: circular muscle that moves the lips

origin: end of a skeletal muscle that is attached to another structure (usually a bone) in a fixed position

palatoglossus: muscle that originates on the soft palate to elevate the back of the tongue

palmar interossei: muscles that abduct and flex each finger at the metacarpophalangeal joints and extend each finger at the interphalangeal joints

palmaris longus: muscle that provides weak flexion of the hand at the wrist

parallel: fascicles that extend in the same direction as the long axis of the muscle

patellar ligament: extension of the quadriceps tendon below the patella

pectineus: muscle that abducts and flexes the femur at the hip

pectoral girdle: shoulder girdle, made up of the clavicle and scapula

pectoralis major: thick, fan-shaped axial muscle that covers much of the superior thorax

pectoralis minor: muscle that moves the scapula and assists in inhalation

pelvic diaphragm: muscular sheet that comprises the levator ani and the ischiococcygeus

pelvic girdle: hips, a foundation for the lower limb

pennate: fascicles that are arranged differently based on their angles to the tendon

perineum: diamond-shaped region between the pubic symphysis, coccyx, and ischial tuberosities

piriformis: muscle deep to the gluteus maximus on the lateral surface of the thigh that laterally rotates the femur at the hip

plantar aponeurosis: muscle that supports the longitudinal arch of the foot

plantar group: four-layered group of intrinsic foot muscles

plantaris: muscle that runs obliquely between the gastrocnemius and the soleus

popliteal fossa: diamond-shaped space at the back of the knee

popliteus: muscle that flexes the leg at the knee and creates the floor of the popliteal fossa

posterior compartment of the leg: region that includes the superficial gastrocnemius, soleus, and plantaris, and the deep popliteus, flexor digitorum longus, flexor hallucis longus, and tibialis posterior

posterior compartment of the thigh: region that includes muscles that flex the leg and extend the thigh

posterior scalene: smallest scalene muscle, located posterior to the middle scalene

prime mover: (also, agonist) principle muscle involved in an action

pronator quadratus: pronator that originates on the ulna and inserts on the radius

pronator teres: pronator that originates on the humerus and inserts on the radius

psoas major: muscle that, along with the iliacus, makes up the iliopsoas

pubococcygeus: muscle that makes up the levator ani along with the iliococcygeus

quadratus femoris: muscle deep to the gluteus maximus on the lateral surface of the thigh that laterally rotates the femur at the hip

quadratus lumborum: posterior part of the abdominal wall that helps with posture and stabilization of the body

quadriceps femoris group: four muscles, that extend and stabilize the knee

quadriceps tendon: (also, patellar tendon) tendon common to all four quadriceps muscles, inserts into the patella

rectus abdominis: long, linear muscle that extends along the middle of the trunk

rectus femoris: quadricep muscle on the anterior aspect of the thigh

rectus sheaths: tissue that makes up the linea alba

rectus: straight

retinacula: fibrous bands that sheath the tendons at the wrist

rhomboid major: muscle that attaches the vertebral border of the scapula to the spinous process of the thoracic vertebrae

rhomboid minor: muscle that attaches the vertebral border of the scapula to the spinous process of the thoracic vertebrae

rotator cuff: (also, musculotendinous cuff) the circle of tendons around the shoulder joint

sartorius: band-like muscle that flexes, abducts, and laterally rotates the leg at the hip

scalene muscles: flex, laterally flex, and rotate the head; contribute to deep inhalation

segmental muscle group: interspinales and intertransversarii muscles that bring together the spinous and transverse processes of each consecutive vertebra

semimembranosus: hamstring muscle

semispinalis capitis: transversospinales muscle associated with the head region

semispinalis cervicis: transversospinales muscle associated with the cervical region

semispinalis thoracis: transversospinales muscle associated with the thoracic region

semitendinosus: hamstring muscle

serratus anterior: large and flat muscle that originates on the ribs and inserts onto the scapula

soleus: wide, flat muscle deep to the gastrocnemius

sphincter urethrovaginalis: deep perineal muscle in women

spinalis capitis: muscle of the spinalis group associated with the head region

spinalis cervicis: muscle of the spinalis group associated with the cervical region

spinalis group: medially placed muscles of the erector spinae

spinalis thoracis: muscle of the spinalis group associated with the thoracic region

splenius capitis: neck muscle that inserts into the head region

splenius cervicis: neck muscle that inserts into the cervical region

splenius: posterior neck muscles; includes the splenius capitis and splenius cervicis

sternocleidomastoid: major muscle that laterally flexes and rotates the head

sternohyoid: muscle that depresses the hyoid bone

sternothyroid: muscle that depresses the larynx’s thyroid cartilage

styloglossus: muscle that originates on the styloid bone, and allows upward and backward motion of the tongue

stylohyoid: muscle that elevates the hyoid bone posteriorly

subclavius: muscle that stabilizes the clavicle during movement

subscapularis: muscle that originates on the anterior scapula and medially rotates the arm

superficial anterior compartment of the forearm: flexor carpi radialis, palmaris longus, flexor carpi ulnaris, flexor digitorum superficialis, and their associated blood vessels and nerves

superficial posterior compartment of the forearm: extensor radialis longus, extensor carpi radialis brevis, extensor digitorum, extensor digiti minimi, extensor carpi ulnaris, and their associated blood vessels and nerves

superior extensor retinaculum: transverse ligament of the ankle

superior gemellus: muscle deep to the gluteus maximus on the lateral surface of the thigh that laterally rotates the femur at the hip

supinator: muscle that moves the palm and forearm anteriorly

suprahyoid muscles: neck muscles that are superior to the hyoid bone

supraspinatus: muscle that abducts the arm

synergist: muscle whose contraction helps a prime mover in an action

temporalis: muscle that retracts the mandible

tendinous intersections: three transverse bands of collagen fibers that divide the rectus abdominis into segments

tensor fascia lata: muscle that flexes and abducts the thigh

teres major: muscle that extends the arm and assists in adduction and medial rotation of it

teres minor: muscle that laterally rotates and extends the arm

thenar eminence: rounded contour of muscle at the base of the thumb

thenar: group of muscles on the lateral aspect of the palm

thyrohyoid: muscle that depresses the hyoid bone and elevates the larynx's thyroid cartilage

tibialis anterior: muscle located on the lateral surface of the tibia

tibialis posterior: muscle that plantar flexes and inverts the foot

transversospinales: muscles that originate at the transverse processes and insert at the spinous processes of the vertebrae

transversus abdominis: deep layer of the abdomen that has fascicles arranged transversely around the abdomen

trapezius: muscle that stabilizes the upper part of the back

triceps brachii: three-headed muscle that extends the forearm

tri: three

unipennate: pennate muscle that has fascicles located on one side of the tendon

urogenital triangle: anterior triangle of the perineum that includes the external genitals

vastus intermedius: quadricep muscle that is between the vastus lateralis and vastus medialis and is deep to the rectus femoris

vastus lateralis: quadricep muscle on the lateral aspect of the thigh

vastus medialis: quadricep muscle on the medial aspect of the thigh

PRACTICE TEST: THE MUSCULAR SYSTEM

Review the material from this module by completing the practice in course online.

MODULE 13: THE NERVOUS SYSTEM

INTRODUCTION TO THE NERVOUS SYSTEM

Learning Objectives

- Relate the developmental processes of the embryonic nervous system to the adult structures
- Name the major regions of the adult nervous system
- Locate regions of the cerebral cortex on the basis of anatomical landmarks common to all human brains
- Describe the regions of the spinal cord in cross-section
- List the cranial nerves in order of anatomical location and provide the central and peripheral connections
- List the spinal nerves by vertebral region and by which nerve plexus each supplies

The nervous system is responsible for controlling much of the body, both through somatic (voluntary) and autonomic (involuntary) functions. The structures of the nervous system must be described in detail to understand how many of these functions are possible. There is a physiological concept known as localization of function that states that certain structures are specifically responsible for prescribed functions. It is an underlying concept in all of anatomy and physiology, but the nervous system illustrates the concept very well.

Figure 1. Human Nervous System. *The ability to balance like an acrobat combines functions throughout the nervous system. The central and peripheral divisions coordinate control of the body using the senses of balance, body position, and touch on the soles of the feet. (credit: Rhett Sutphin)*

Fresh, unstained nervous tissue can be described as gray or white matter, and within those two types of tissue it can be very hard to see any detail. However, as specific regions and structures have been described, they were related to specific functions. Understanding these structures and the functions they perform requires a detailed description of the anatomy of the nervous system, delving deep into what the central and peripheral structures are.

The place to start this study of the nervous system is the beginning of the individual human life, within the womb. The embryonic development of the nervous system allows for a simple framework on which progressively more complicated structures can be built. With this framework in place, a thorough investigation of the nervous system is possible.

THE EMBRYOLOGIC PERSPECTIVE

Learning Objectives

- Describe the growth and differentiation of the neural tube
- Relate the different stages of development to the adult structures of the central nervous system
- Explain the expansion of the ventricular system of the adult brain from the central canal of the neural tube
- Describe the connections of the diencephalon and cerebellum on the basis of patterns of embryonic development

The brain is a complex organ composed of gray parts and white matter, which can be hard to distinguish. Starting from an embryologic perspective allows you to understand more easily how the parts relate to each other. The embryonic nervous system begins as a very simple structure—essentially just a straight line, which then gets increasingly complex. Looking at the development of the nervous system with a couple of early snapshots makes it easier to understand the whole complex system. Many structures that appear to be adjacent in the adult brain are not connected, and the connections that exist may seem arbitrary. But there is an underlying order to the system that comes from how different parts develop. By following the developmental pattern, it is possible to learn what the major regions of the nervous system are.

The Neural Tube

To begin, a sperm cell and an egg cell fuse to become a fertilized egg. The fertilized egg cell, or zygote, starts dividing to generate the cells that make up an entire organism. Sixteen days after fertilization, the developing embryo's cells belong to one of three germ layers that give rise to the different tissues in the body. The endoderm, or inner tissue, is responsible for generating the lining tissues of various spaces within the body, such as the mucosae of the digestive and respiratory systems. The mesoderm, or middle tissue, gives rise to most of the muscle and connective tissues. Finally the ectoderm, or outer tissue, develops into the integumentary system (the skin) and the nervous system.

It is probably not difficult to see that the outer tissue of the embryo becomes the outer covering of the body. But how is it responsible for the nervous system? As the embryo develops, a portion of the ectoderm differentiates into a specialized region of neuroectoderm, which is the precursor for the tissue of the nervous system. Molecular signals induce cells in this region to differentiate into the neuroepithelium, forming a **neural plate**. The cells then begin to change shape, causing the tissue to buckle and fold inward (Figure 1).

A **neural groove** forms, visible as a line along the dorsal surface of the embryo. The ridge-like edge on either side of the neural groove is referred as the **neural fold**. As the neural folds come together and converge, the underlying structure forms into a tube just beneath the ectoderm called the **neural tube**. Cells from the neural folds then separate from the ectoderm to form a cluster of cells referred to as the **neural crest**, which runs lateral to the neural tube. The neural crest migrates away from the nascent, or embryonic, central nervous system (CNS) that will form along the neural groove and develops into several parts of the peripheral nervous system (PNS), including the enteric nervous tissue. Many tissues that are not part of the nervous system also arise from the neural crest, such as craniofacial cartilage and bone, and melanocytes.

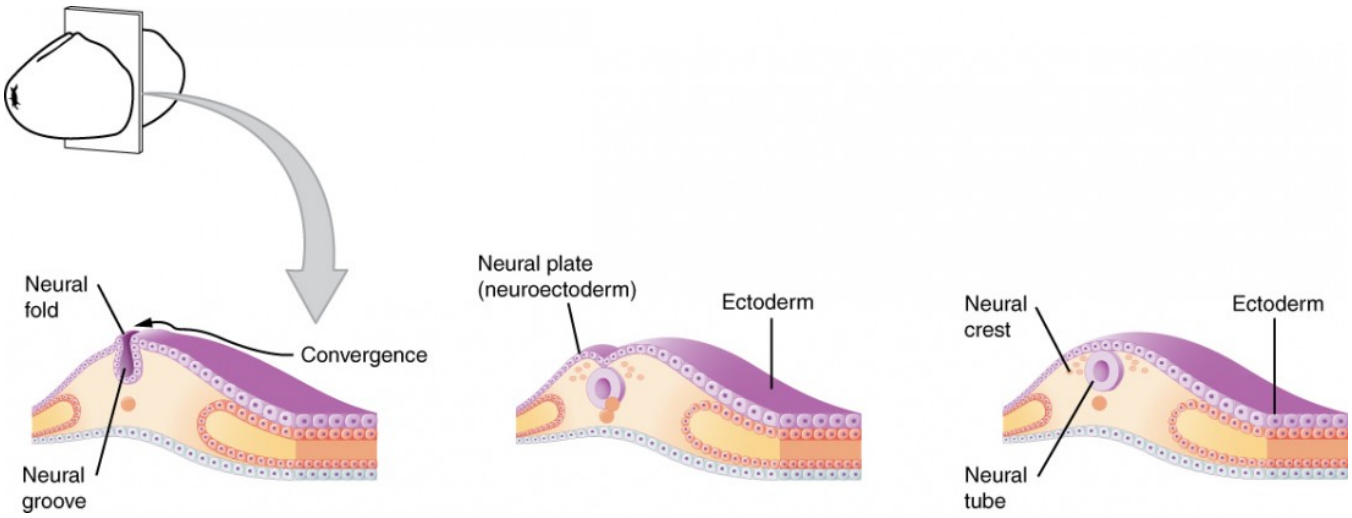


Figure 1. Early Embryonic Development of Nervous System *The neuroectoderm begins to fold inward to form the neural groove. As the two sides of the neural groove converge, they form the neural tube, which lies beneath the ectoderm. The anterior end of the neural tube will develop into the brain, and the posterior portion will become the spinal cord. The neural crest develops into peripheral structures.*

At this point, the early nervous system is a simple, hollow tube. It runs from the anterior end of the embryo to the posterior end. Beginning at 25 days, the anterior end develops into the brain, and the posterior portion becomes the spinal cord. This is the most basic arrangement of tissue in the nervous system, and it gives rise to the more complex structures by the fourth week of development.

Primary Vesicles

As the anterior end of the neural tube starts to develop into the brain, it undergoes a couple of enlargements; the result is the production of sac-like vesicles. Similar to a child's balloon animal, the long, straight neural tube begins to take on a new shape. Three vesicles form at the first stage, which are called **primary vesicles**.

These vesicles are given names that are based on Greek words, the main root word being *enkephalon*, which means "brain" (en- = "inside"; kephalon = "head"). The prefix to each generally corresponds to its position along the length of the developing nervous system. The **prosencephalon** (pros- = "in front") is the forward-most vesicle, and the term can be loosely translated to mean **forebrain**. The **mesencephalon** (mes- = "middle") is the next vesicle, which can be called the **midbrain**. The third vesicle at this stage is the **rhombencephalon**. The first part of this word is also the root of the word rhombus, which is a geometrical figure with four sides of equal length (a square is a rhombus with 90° angles). Whereas prosencephalon and mesencephalon translate into the English words forebrain and midbrain, there is not a word for "four-sided-figure-brain." However, the third vesicle can be called the **hindbrain**. One way of thinking about how the brain is arranged is to use these three regions—forebrain, midbrain, and hindbrain—which are based on the primary vesicle stage of development (Figure 2a).

Secondary Vesicles

The brain continues to develop, and the vesicles differentiate further (see Figure 2b). The three primary vesicles become five **secondary vesicles**. The prosencephalon enlarges into two new vesicles called the **telencephalon** and the **diencephalon**.

The telecephalon will become the cerebrum. The diencephalon gives rise to several adult structures; two that will be important are the thalamus and the hypothalamus. In the embryonic diencephalon, a structure known as the eye cup develops, which will eventually become the retina, the nervous tissue of the eye called the retina. This is a rare example of nervous tissue developing as part of the CNS structures in the embryo, but becoming a peripheral structure in the fully formed nervous system.

The mesencephalon does not differentiate into any finer divisions. The midbrain is an established region of the brain at the primary vesicle stage of development and remains that way. The rest of the brain develops around it and constitutes a large percentage of the mass of the brain. Dividing the brain into forebrain, midbrain, and hindbrain is useful in considering its developmental pattern, but the midbrain is a small proportion of the entire brain, relatively speaking.

The rhombencephalon develops into the **metencephalon** and **myelencephalon**. The metencephalon corresponds to the adult structure known as the pons and also gives rise to the cerebellum. The cerebellum (from the Latin meaning "little brain") accounts for about 10 percent of the mass of the brain and is an important structure in itself. The most significant connection between the cerebellum and the rest of the brain is at the pons, because the pons and cerebellum develop out of the same vesicle. The myelencephalon corresponds to the adult structure known as the medulla oblongata. The structures that come from the mesencephalon and rhombencephalon, except for the cerebellum, are collectively considered the **brain stem**, which specifically includes the midbrain, pons, and medulla.

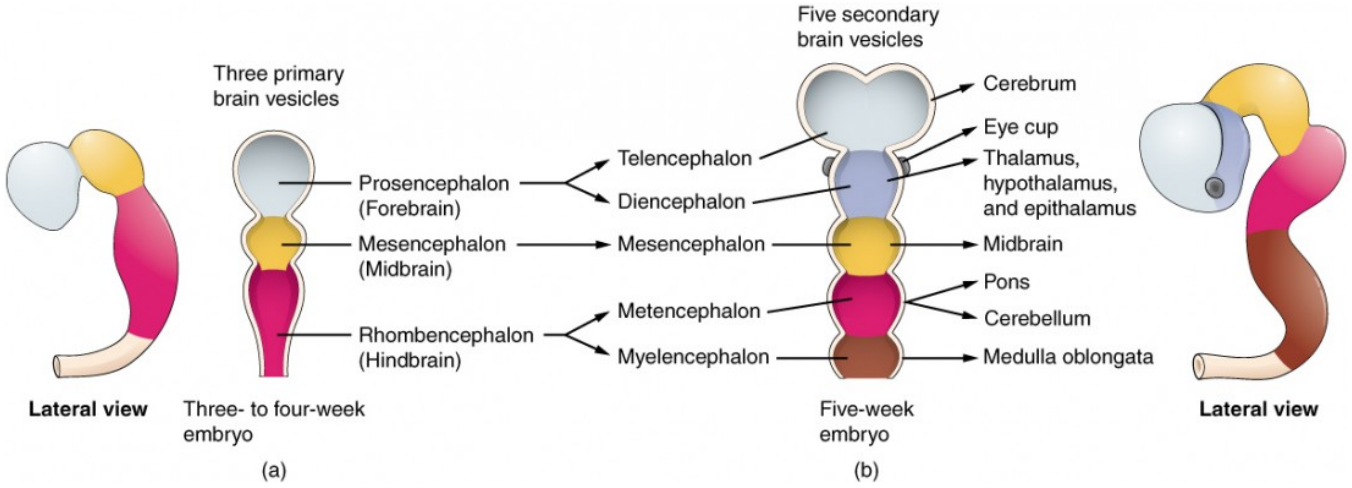


Figure 2. Primary and Secondary Vesicle Stages of Development *The embryonic brain develops complexity through enlargements of the neural tube called vesicles; (a) The primary vesicle stage has three regions, and (b) the secondary vesicle stage has five regions.*

Watch this animation to examine the development of the brain, starting with the neural tube. As the anterior end of the neural tube develops, it enlarges into the primary vesicles that establish the forebrain, midbrain, and hindbrain. Those structures continue to develop throughout the rest of embryonic development and into adolescence. They are the basis of the structure of the fully developed adult brain. How would you describe the difference in the relative sizes of the three regions of the brain when comparing the early (25th embryonic day) brain and the adult brain?

Spinal Cord Development

While the brain is developing from the anterior neural tube, the spinal cord is developing from the posterior neural tube. However, its structure does not differ from the basic layout of the neural tube. It is a long, straight cord with a small, hollow space down the center. The neural tube is defined in terms of its anterior versus posterior portions, but it also has a dorsal–ventral dimension. As the neural tube separates from the rest of the ectoderm, the side closest to the surface is dorsal, and the deeper side is ventral. As the spinal cord develops, the cells making up the wall of the neural tube proliferate and differentiate into the neurons and glia of the spinal cord. The dorsal tissues will be associated with sensory functions, and the ventral tissues will be associated with motor functions.

Relating Embryonic Development to the Adult Brain

Embryonic development can help in understanding the structure of the adult brain because it establishes a framework on which more complex structures can be built. First, the neural tube establishes the anterior–posterior

dimension of the nervous system, which is called the **neuraxis**. The embryonic nervous system in mammals can be said to have a standard arrangement. Humans (and other primates, to some degree) make this complicated by standing up and walking on two legs. The anterior–posterior dimension of the neuraxis overlays the superior–inferior dimension of the body. However, there is a major curve between the brain stem and forebrain, which is called the **cephalic flexure**. Because of this, the neuraxis starts in an inferior position—the end of the spinal cord—and ends in an anterior position, the front of the cerebrum. If this is confusing, just imagine a four-legged animal standing up on two legs. Without the flexure in the brain stem, and at the top of the neck, that animal would be looking straight up instead of straight in front (Figure 3).

In summary, the primary vesicles help to establish the basic regions of the nervous system: forebrain, midbrain, and hindbrain. These divisions are useful in certain situations, but they are not equivalent regions. The midbrain is small compared with the hindbrain and particularly the forebrain. The secondary vesicles go on to establish the major regions of the adult nervous system that will be followed in this text. The telencephalon is the cerebrum, which is the major portion of the human brain.

The diencephalon continues to be referred to by this Greek name, because there is no better term for it (*dia–* = "through"). The diencephalon is between the cerebrum and the rest of the nervous system and can be described as the region through which all projections have to pass between the cerebrum and everything else.

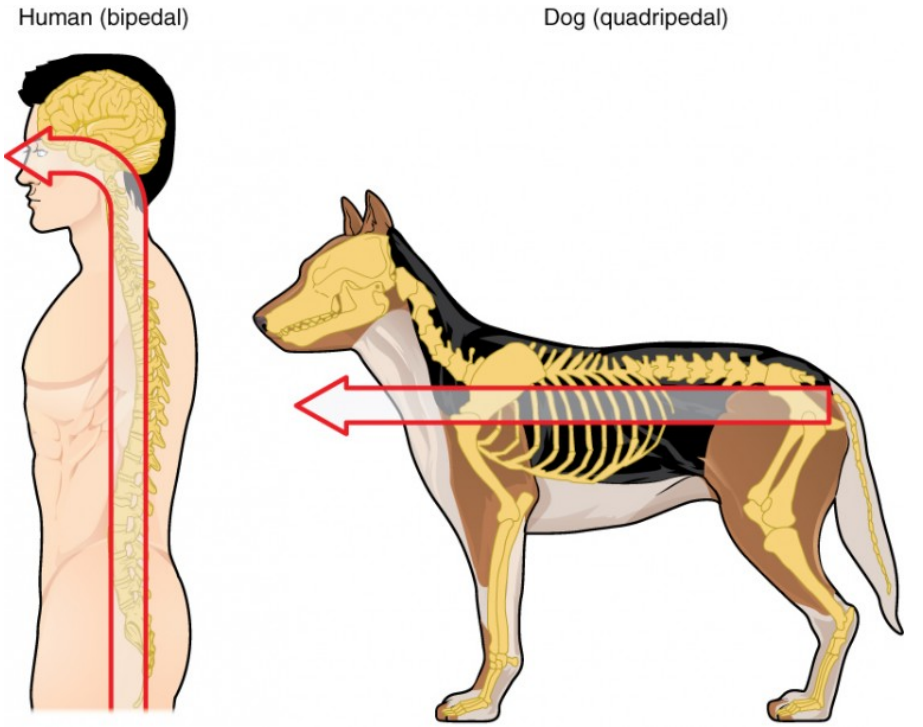


Figure 3. Human Neuraxis *The mammalian nervous system is arranged with the neural tube running along an anterior to posterior axis, from nose to tail for a four-legged animal like a dog. Humans, as two-legged animals, have a bend in the neuraxis between the brain stem and the diencephalon, along with a bend in the neck, so that the eyes and the face are oriented forward.*

The brain stem includes the midbrain, pons, and medulla, which correspond to the mesencephalon, metencephalon, and myelencephalon. The cerebellum, being a large portion of the brain, is considered a separate region. Table 1 connects the different stages of development to the adult structures of the CNS.

One other benefit of considering embryonic development is that certain connections are more obvious because of how these adult structures are related. The retina, which began as part of the diencephalon, is primarily connected to the diencephalon. The eyes are just inferior to the anterior-most part of the cerebrum, but the optic nerve extends back to the thalamus as the optic tract, with branches into a region of the hypothalamus.

There is also a connection of the optic tract to the midbrain, but the mesencephalon is adjacent to the diencephalon, so that is not difficult to imagine. The cerebellum originates out of the metencephalon, and its largest white matter connection is to the pons, also from the metencephalon. There are connections between the cerebellum and both the medulla and midbrain, which are adjacent structures in the secondary vesicle stage of development. In the adult brain, the cerebellum seems close to the cerebrum, but there is no direct connection between them.

Another aspect of the adult CNS structures that relates to embryonic development is the ventricles—open spaces within the CNS where cerebrospinal fluid circulates. They are the remnant of the hollow center of the neural tube. The four ventricles and the tubular spaces associated with them can be linked back to the hollow center of the embryonic brain (see Table 1).

Table 1. Stages of Embryonic Development				
Neural tube	Primary vesicle stage	Secondary vesicle stage	Adult structures	Ventricles
Anterior neural tube	Prosencephalon	Telencephalon	Cerebrum	Lateral ventricles
Anterior neural tube	Prosencephalon	Diencephalon	Diencephalon	Third ventricle
Anterior neural tube	Mesencephalon	Mesencephalon	Midbrain	Cerebral aqueduct
Anterior neural tube	Rhombencephalon	Metencephalon	Pons cerebellum	Fourth ventricle
Anterior neural tube	Rhombencephalon	Myelencephalon	Medulla	Fourth ventricle
Posterior neural tube			Spinal cord	Central canal

Disorders of the Nervous System

Early formation of the nervous system depends on the formation of the neural tube. A groove forms along the dorsal surface of the embryo, which becomes deeper until its edges meet and close off to form the tube. If this fails to happen, especially in the posterior region where the spinal cord forms, a developmental defect called spina bifida occurs. The closing of the neural tube is important for more than just the proper formation of the nervous system. The surrounding tissues are dependent on the correct development of the tube. The connective tissues surrounding the CNS can be involved as well. There are three classes of this disorder: occulta, meningocele, and myelomeningocele (Figure 4).

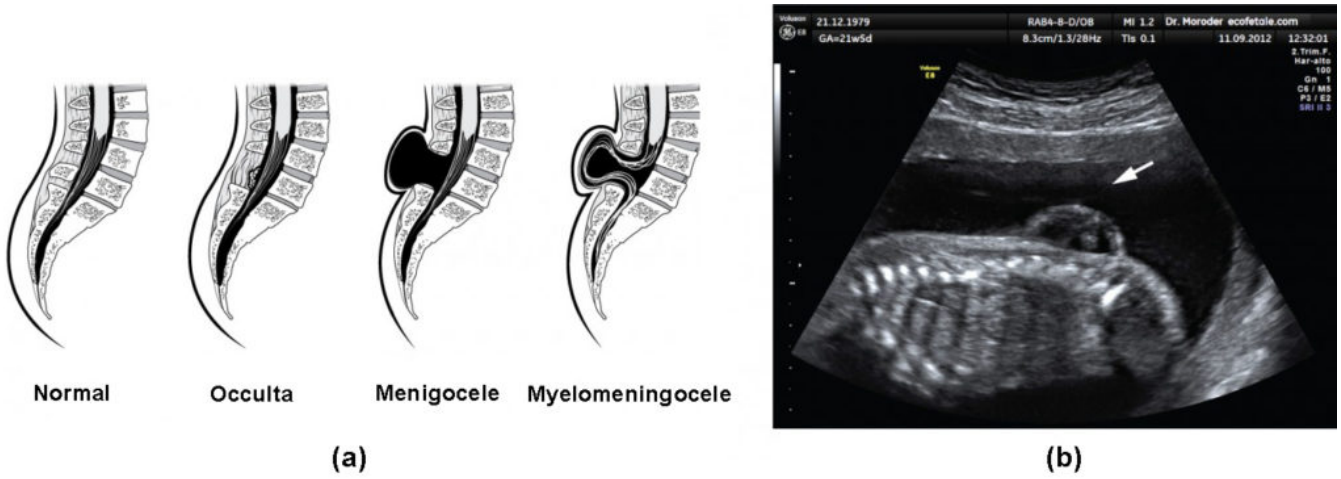


Figure 4. Spinal Bifida *(a) Spina bifida is a birth defect of the spinal cord caused when the neural tube does not completely close, but the rest of development continues. The result is the emergence of meninges and neural tissue through the vertebral column. (b) Fetal myelomeningocele is evident in this ultrasound taken at 21 weeks.*

The first type, spina bifida occulta, is the mildest because the vertebral bones do not fully surround the spinal cord, but the spinal cord itself is not affected. No functional differences may be noticed, which is what the word occulta means; it is hidden spina bifida.

The other two types both involve the formation of a cyst—a fluid-filled sac of the connective tissues that cover the spinal cord called the meninges. “Meningocele” means that the meninges protrude through the spinal column but nerves may not be involved and few symptoms are present, though complications may arise later in life.

“Myelomeningocele” means that the meninges protrude and spinal nerves are involved, and therefore severe neurological symptoms can be present.

Often surgery to close the opening or to remove the cyst is necessary. The earlier that surgery can be performed, the better the chances of controlling or limiting further damage or infection at the opening. For many children with meningocele, surgery will alleviate the pain, although they may experience some functional loss. Because the myelomeningocele form of spina bifida involves more extensive damage to the nervous tissue, neurological damage may persist, but symptoms can often be handled. Complications of the spinal cord may present later in life, but overall life expectancy is not reduced.

Watch this video to learn about the white matter in the cerebrum that develops during childhood and adolescence. This is a composite of MRI images taken of the brains of people from 5 years of age through 20 years of age, demonstrating how the cerebrum changes. As the color changes to blue, the ratio of gray matter to white matter changes. The caption for the video describes it as “less gray matter,” which is another way of saying “more white matter.” If the brain does not finish developing until approximately 20 years of age, can teenagers be held responsible for behaving badly?

THE CENTRAL NERVOUS SYSTEM

Learning Objectives

- Name the major regions of the adult brain
- Describe the connections between the cerebrum and brain stem through the diencephalon, and from those regions into the spinal cord
- Recognize the complex connections within the subcortical structures of the basal nuclei
- Explain the arrangement of gray and white matter in the spinal cord

The brain and the spinal cord are the central nervous system, and they represent the main organs of the nervous system. The spinal cord is a single structure, whereas the adult brain is described in terms of four major regions: the cerebrum, the diencephalon, the brain stem, and the cerebellum. A person’s conscious experiences are based on neural activity in the brain. The regulation of homeostasis is governed by a specialized region in the brain. The coordination of reflexes depends on the integration of sensory and motor pathways in the spinal cord.

The Cerebrum

The iconic gray mantle of the human brain, which appears to make up most of the mass of the brain, is the **cerebrum** (Figure 1). The wrinkled portion is the **cerebral cortex**, and the rest of the structure is beneath that outer covering. There is a large separation between the two sides of the cerebrum called the **longitudinal fissure**. It separates the cerebrum into two distinct halves, a right and left **cerebral hemisphere**. Deep within the cerebrum, the white matter of the **corpus callosum** provides the major pathway for communication between the two hemispheres of the cerebral cortex.

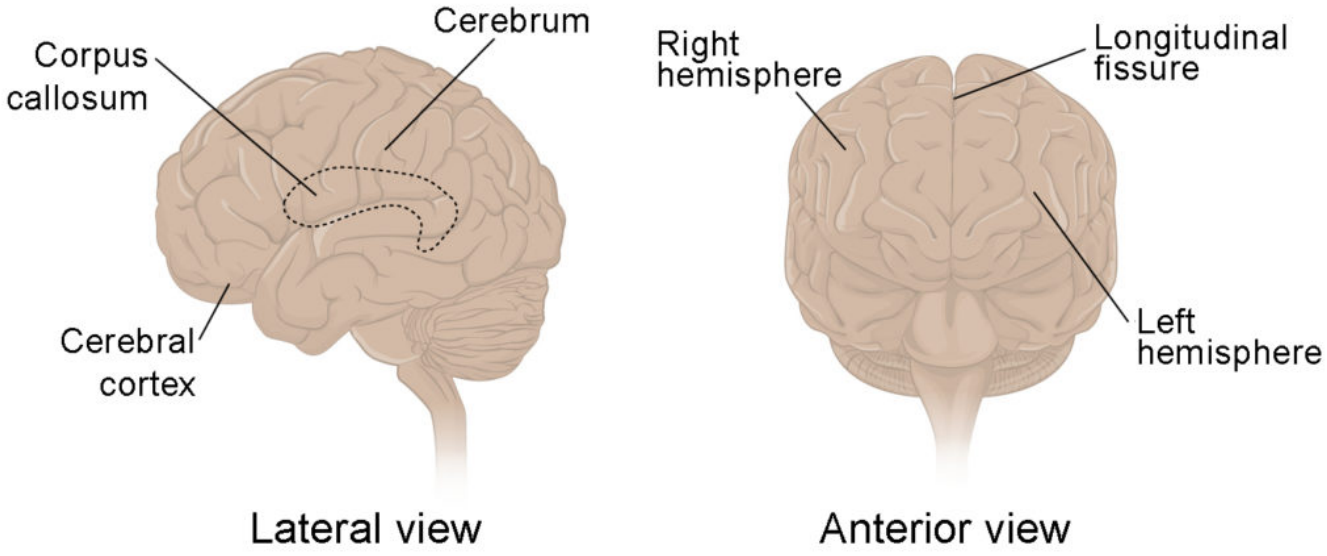


Figure 1. *This figure shows the lateral view on the left panel and anterior view on the right panel of the brain. The major parts including the cerebrum are labeled.*

Many of the higher neurological functions, such as memory, emotion, and consciousness, are the result of cerebral function. The complexity of the cerebrum is different across vertebrate species. The cerebrum of the most primitive vertebrates is not much more than the connection for the sense of smell. In mammals, the cerebrum comprises the outer gray matter that is the cortex (from the Latin word meaning “bark of a tree”) and several deep nuclei that belong to three important functional groups. The **basal nuclei** are responsible for cognitive processing, the most important function being that associated with planning movements. The **basal forebrain** contains nuclei that are important in learning and memory. The **limbic cortex** is the region of the cerebral cortex that is part of the **limbic system**, a collection of structures involved in emotion, memory, and behavior.

Cerebral Cortex

The cerebrum is covered by a continuous layer of gray matter that wraps around either side of the forebrain—the cerebral cortex. This thin, extensive region of wrinkled gray matter is responsible for the higher functions of the nervous system. A **gyrus** (plural = *gyri*) is the ridge of one of those wrinkles, and a **sulcus** (plural = *sulci*) is the groove between two gyri. The pattern of these folds of tissue indicates specific regions of the cerebral cortex. The head is limited by the size of the birth canal, and the brain must fit inside the cranial cavity of the skull. Extensive folding in the cerebral cortex enables more gray matter to fit into this limited space. If the gray matter of the cortex were peeled off of the cerebrum and laid out flat, its surface area would be roughly equal to one square meter. The folding of the cortex maximizes the amount of gray matter in the cranial cavity. During embryonic development, as the telencephalon expands within the skull, the brain goes through a regular course of growth that results in everyone’s brain having a similar pattern of folds.

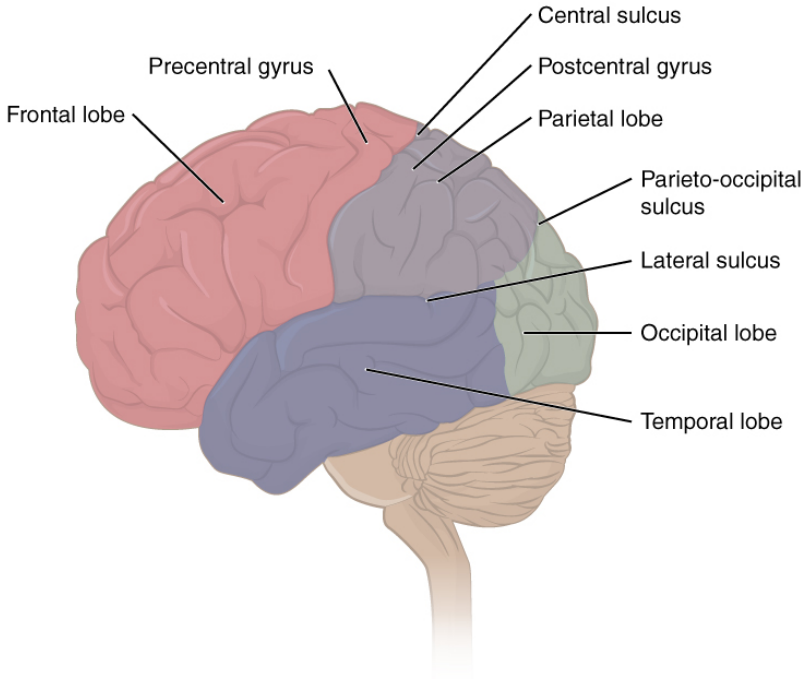


Figure 2. Lobes of the Cerebral Cortex. *The cerebral cortex is divided into four lobes. Extensive folding increases the surface area available for cerebral functions.*

The surface of the brain can be mapped on the basis of the locations of large gyri and sulci. Using these landmarks, the cortex can be separated into four major regions, or lobes (Figure 2).

The **lateral sulcus** that separates the **temporal lobe** from the other regions is one such landmark. Superior to the lateral sulcus are the **parietal lobe** and **frontal lobe**, which are separated from each other by the **central sulcus**. The posterior region of the cortex is the **occipital lobe**, which has no obvious anatomical border between it and the parietal or temporal lobes on the lateral surface of the brain. From the medial surface, an obvious landmark separating the parietal and occipital lobes is called the **parieto-occipital sulcus**. The fact that there is no obvious anatomical border between these lobes is consistent with the functions of these regions being interrelated.

Different regions of the cerebral cortex can be associated with particular functions, a concept known as localization of function. In the early 1900s, a German neuroscientist named Korbinian Brodmann performed an extensive study of the microscopic anatomy—the cytoarchitecture—of the cerebral cortex and divided the cortex into 52 separate regions on the basis of the histology of the cortex. His work resulted in a system of classification known as **Brodmann's areas**, which is still used today to describe the anatomical distinctions within the cortex (Figure 3). The results from Brodmann's work on the anatomy align very well with the functional differences within the cortex. Areas 17 and 18 in the occipital lobe are responsible for primary visual perception. That visual information is complex, so it is processed in the temporal and parietal lobes as well. The temporal lobe is associated with primary auditory sensation, known as Brodmann's areas 41 and 42 in the superior temporal lobe.

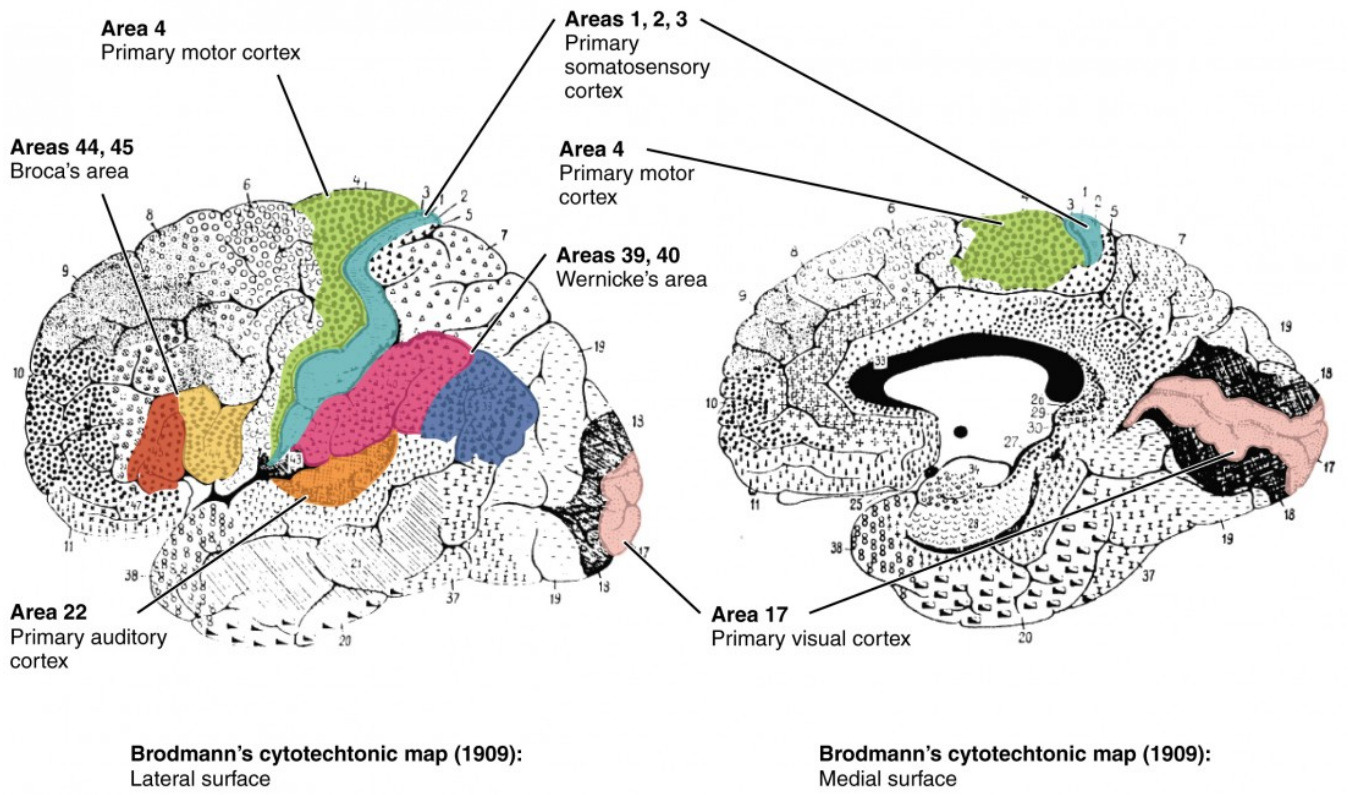


Figure 3. Brodmann's Areas of the Cerebral Cortex. *Brodmann mapping of functionally distinct regions of the cortex was based on its cytoarchitecture at a microscopic level.*

Because regions of the temporal lobe are part of the limbic system, memory is an important function associated with that lobe. Memory is essentially a sensory function; memories are recalled sensations such as the smell of Mom's baking or the sound of a barking dog. Even memories of movement are really the memory of sensory feedback from those movements, such as stretching muscles or the movement of the skin around a joint. Structures in the temporal lobe are responsible for establishing long-term memory, but the ultimate location of those memories is usually in the region in which the sensory perception was processed. The main sensation associated with the parietal lobe is **somatosensation**, meaning the general sensations associated with the body.

Posterior to the central sulcus is the **postcentral gyrus**, the primary somatosensory cortex, which is identified as Brodmann's areas 1, 2, and 3. All of the tactile senses are processed in this area, including touch, pressure,

tickle, pain, itch, and vibration, as well as more general senses of the body such as **proprioception** and **kinesthesia**, which are the senses of body position and movement, respectively.

Anterior to the central sulcus is the frontal lobe, which is primarily associated with motor functions. The **precentral gyrus** is the primary motor cortex. Cells from this region of the cerebral cortex are the upper motor neurons that instruct cells in the spinal cord to move skeletal muscles.

Anterior to this region are a few areas that are associated with planned movements. The **premotor area** is responsible for thinking of a movement to be made. The **frontal eye fields** are important in eliciting eye movements and in attending to visual stimuli. **Broca's area** is responsible for the production of language, or controlling movements responsible for speech; in the vast majority of people, it is located only on the left side. Anterior to these regions is the **prefrontal lobe**, which serves cognitive functions that can be the basis of personality, short-term memory, and consciousness. The prefrontal lobotomy is an outdated mode of treatment for personality disorders (psychiatric conditions) that profoundly affected the personality of the patient.

Subcortical Structures

Beneath the cerebral cortex are sets of nuclei known as **subcortical nuclei** that augment cortical processes. The nuclei of the basal forebrain serve as the primary location for acetylcholine production, which modulates the overall activity of the cortex, possibly leading to greater attention to sensory stimuli. Alzheimer's disease is associated with a loss of neurons in the basal forebrain.

The **hippocampus** and **amygdala** are medial-lobe structures that, along with the adjacent cortex, are involved in long-term memory formation and emotional responses. The basal nuclei are a set of nuclei in the cerebrum responsible for comparing cortical processing with the general state of activity in the nervous system to influence the likelihood of movement taking place. For example, while a student is sitting in a classroom listening to a lecture, the basal nuclei will keep the urge to jump up and scream from actually happening. (The basal nuclei are also referred to as the basal ganglia, although that is potentially confusing because the term ganglia is typically used for peripheral structures.)

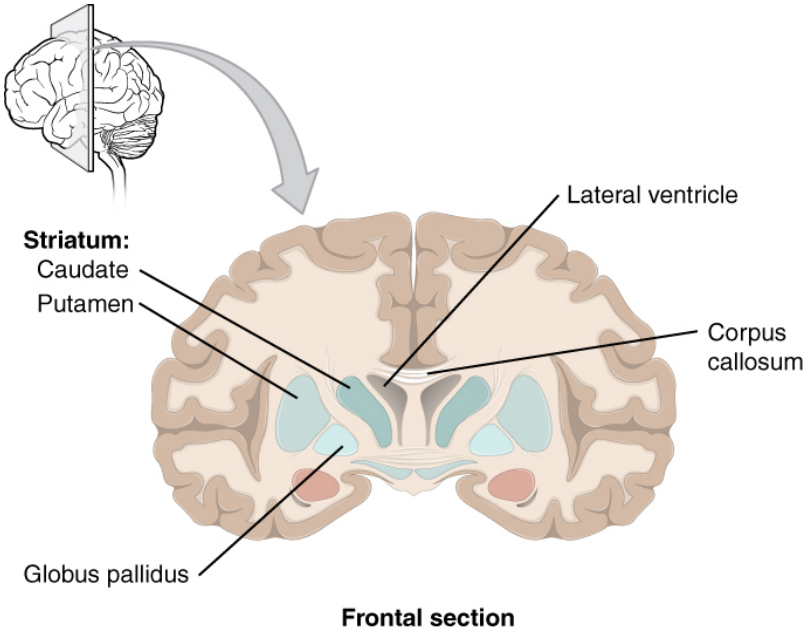


Figure 4. Frontal Section of Cerebral Cortex and Basal Nuclei. *The major components of the basal nuclei, shown in a frontal section of the brain, are the caudate (just lateral to the lateral ventricle), the putamen (inferior to the caudate and separated by the large white-matter structure called the internal capsule), and the globus pallidus (medial to the putamen).*

The major structures of the basal nuclei that control movement are the **caudate**, **putamen**, and **globus pallidus**, which are located deep in the cerebrum. The caudate is a long nucleus that follows the basic C-shape of the cerebrum from the frontal lobe, through the parietal and occipital lobes, into the temporal lobe. The putamen is mostly deep in the anterior regions of the frontal and parietal lobes. Together, the caudate and putamen are called the **striatum**. The globus pallidus is a layered nucleus that lies just medial to the putamen; they are called the lenticular nuclei because they look like curved pieces fitting together like lenses. The globus pallidus has two subdivisions, the external and internal segments, which are lateral and medial, respectively. These nuclei are depicted in a frontal section of the brain in Figure 4.

The basal nuclei in the cerebrum are connected with a few more nuclei in the brain stem that together act as a functional group that forms a motor pathway. Two streams of information processing take place in the basal nuclei. All input to the basal nuclei is from the cortex into the striatum (Figure 5).

The **direct pathway** is the projection of axons from the striatum to the globus pallidus internal segment (GPi) and the **substantia nigra pars reticulata** (SNr). The GPi/SNr then projects to the thalamus, which projects back to the cortex. The **indirect pathway** is the projection of axons from the striatum to the globus pallidus external segment (GPe), then to the subthalamic nucleus (STN), and finally to GPi/SNr. The two streams both target the GPi/SNr, but one has a direct projection and the other goes through a few intervening nuclei. The direct pathway causes the **disinhibition** of the thalamus (inhibition of one cell on a target cell that then inhibits the first cell), whereas the indirect pathway causes, or reinforces, the normal inhibition of the thalamus. The thalamus then can either excite the cortex (as a result of the direct pathway) or fail to excite the cortex (as a result of the indirect pathway).

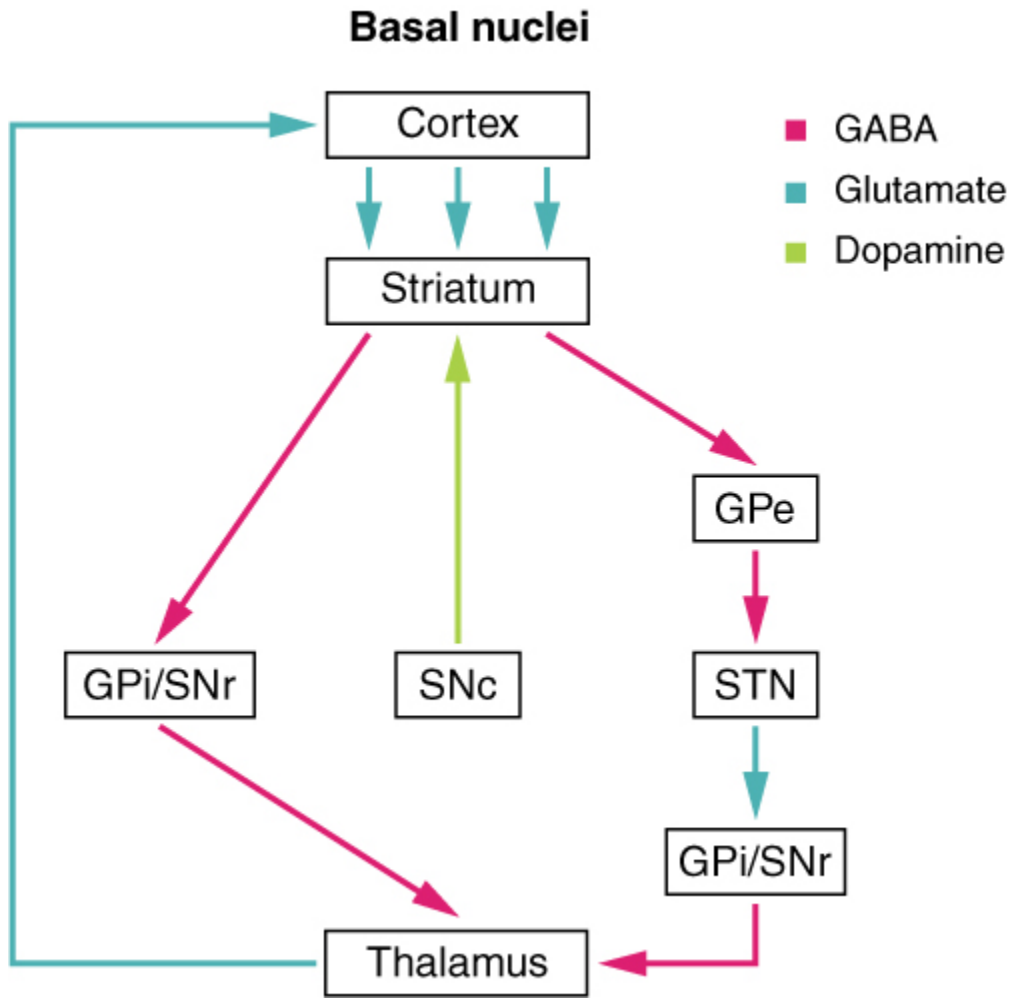


Figure 5. Connections of Basal Nuclei. *Input to the basal nuclei is from the cerebral cortex, which is an excitatory connection releasing glutamate as a neurotransmitter. This input is to the striatum, or the caudate and putamen. In the direct pathway, the striatum projects to the internal segment of the globus pallidus and the substantia nigra pars reticulata (GPi/SNr). This is an inhibitory pathway, in which GABA is released at the synapse, and the target cells are hyperpolarized and less likely to fire. The output from the basal nuclei is to the thalamus, which is an inhibitory projection using GABA.*

The switch between the two pathways is the **substantia nigra pars compacta**, which projects to the striatum and releases the neurotransmitter dopamine. Dopamine receptors are either excitatory (D1-type receptors) or inhibitory (D2-type receptors). The direct pathway is activated by dopamine, and the indirect pathway is inhibited by dopamine.

When the substantia nigra pars compacta is firing, it signals to the basal nuclei that the body is in an active state, and movement will be more likely. When the substantia nigra pars compacta is silent, the body is in a passive state, and movement is inhibited. To illustrate this situation, while a student is sitting listening to a lecture, the substantia nigra pars compacta would be silent and the student less likely to get up and walk around. Likewise, while the professor is lecturing, and walking around at the front of the classroom, the professor's substantia nigra pars compacta would be active, in keeping with his or her activity level.

Watch this video to learn about the basal nuclei (also known as the basal ganglia), which have two pathways that process information within the cerebrum.

Watch this video online: https://youtu.be/J56CFExkHgE

As shown in this video, the direct pathway is the shorter pathway through the system that results in increased activity in the cerebral cortex and increased motor activity. The direct pathway is described as resulting in "disinhibition" of the thalamus. What does disinhibition mean? What are the two neurons doing individually to cause this?

Everyday Connections: The Myth of Left Brain/Right Brain

There is a persistent myth that people are "right-brained" or "left-brained," which is an oversimplification of an important concept about the cerebral hemispheres. There is some lateralization of function, in which the left side of the brain is devoted to language function and the right side is devoted to spatial and nonverbal reasoning. Whereas these functions are predominantly associated with those sides of the brain, there is no monopoly by either side on these functions. Many pervasive functions, such as language, are distributed globally around the cerebrum. Some of the support for this misconception has come from studies of split brains.

A drastic way to deal with a rare and devastating neurological condition (intractable epilepsy) is to separate the two hemispheres of the brain. After sectioning the corpus callosum, a split-brained patient will have trouble producing verbal responses on the basis of sensory information processed on the right side of the cerebrum, leading to the idea that the left side is responsible for language function. However, there are well-documented cases of language functions lost from damage to the right side of the brain.

The deficits seen in damage to the left side of the brain are classified as aphasia, a loss of speech function; damage on the right side can affect the use of language. Right-side damage can result in a loss of ability to understand figurative aspects of speech, such as jokes, irony, or metaphors. Nonverbal aspects of speech can be affected by damage to the right side, such as facial expression or body language, and right-side damage can lead to a "flat affect" in speech, or a loss of emotional expression in speech—sounding like a robot when talking.

The Diencephalon

The diencephalon is the one region of the adult brain that retains its name from embryologic development. The etymology of the word diencephalon translates to "through brain." It is the connection between the cerebrum and the rest of the nervous system, with one exception. The rest of the brain, the spinal cord, and the PNS all send information to the cerebrum through the diencephalon. Output from the cerebrum passes through the diencephalon. The single exception is the system associated with **olfaction**, or the sense of smell, which connects directly with the cerebrum. In the earliest vertebrate species, the cerebrum was not much more than olfactory bulbs that received peripheral information about the chemical environment (to call it smell in these organisms is imprecise because they lived in the ocean). The diencephalon is deep beneath the cerebrum and constitutes the walls of the third ventricle. The diencephalon can be described as any region of the brain with "thalamus" in its name. The two major regions of the diencephalon are the thalamus itself and the hypothalamus (Figure 6). There are other structures, such as the **epithalamus**, which contains the pineal gland, or the **subthalamus**, which includes the subthalamic nucleus that is part of the basal nuclei.

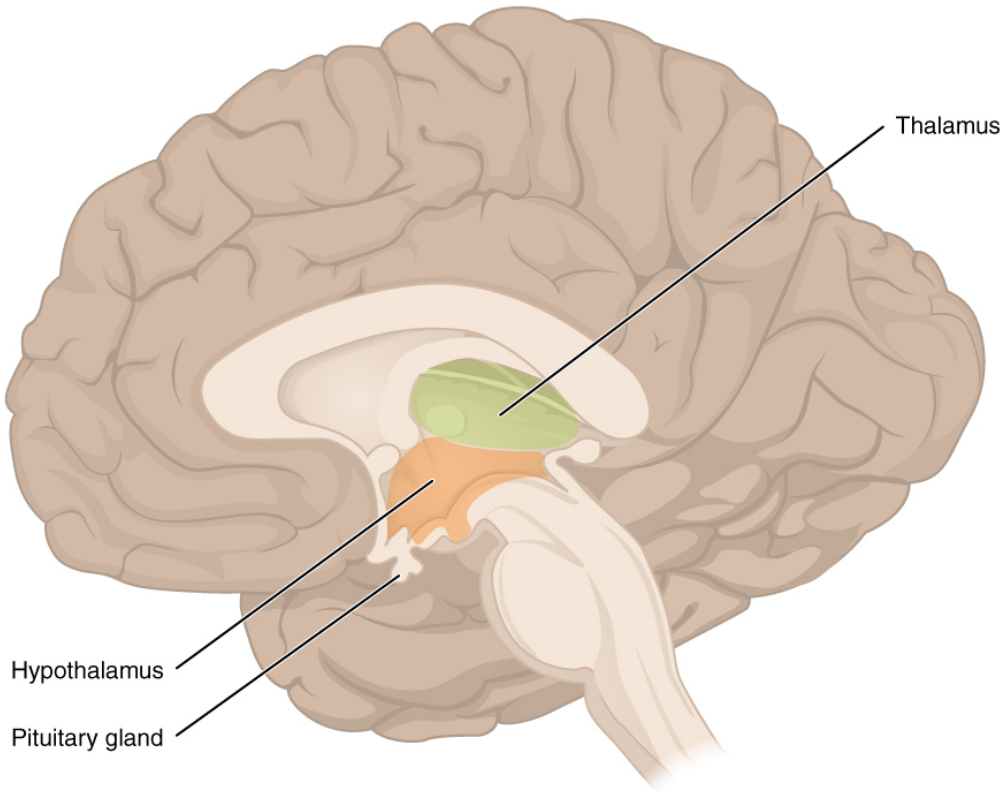


Figure 6. The Diencephalon. *The diencephalon is composed primarily of the thalamus and hypothalamus, which together define the walls of the third ventricle. The thalami are two elongated, ovoid structures on either side of the midline that make contact in the middle. The hypothalamus is inferior and anterior to the thalamus, culminating in a sharp angle to which the pituitary gland is attached.*

Thalamus

The **thalamus** is a collection of nuclei that relay information between the cerebral cortex and the periphery, spinal cord, or brain stem. All sensory information, except for the sense of smell, passes through the thalamus before processing by the cortex. Axons from the peripheral sensory organs, or intermediate nuclei, synapse in the thalamus, and thalamic neurons project directly to the cerebrum. It is a requisite synapse in any sensory pathway, except for olfaction. The thalamus does not just pass the information on, it also processes that information. For example, the portion of the thalamus that receives visual information will influence what visual stimuli are important, or what receives attention. The cerebrum also sends information down to the thalamus, which usually communicates motor commands. This involves interactions with the cerebellum and other nuclei in the brain stem. The cerebrum interacts with the basal nuclei, which involves connections with the thalamus. The primary output of the basal nuclei is to the thalamus, which relays that output to the cerebral cortex. The cortex also sends information to the thalamus that will then influence the effects of the basal nuclei.

Hypothalamus

Inferior and slightly anterior to the thalamus is the **hypothalamus**, the other major region of the diencephalon. The hypothalamus is a collection of nuclei that are largely involved in regulating homeostasis. The hypothalamus is the executive region in charge of the autonomic nervous system and the endocrine system through its regulation of the anterior pituitary gland. Other parts of the hypothalamus are involved in memory and emotion as part of the limbic system.

Brain Stem

The midbrain and hindbrain (composed of the pons and the medulla) are collectively referred to as the brain stem (Figure 7). The structure emerges from the ventral surface of the forebrain as a tapering cone that connects the brain to the spinal cord. Attached to the brain stem, but considered a separate region of the adult brain, is the cerebellum. The midbrain coordinates sensory representations of the visual, auditory, and somatosensory perceptual spaces. The pons is the main connection with the cerebellum. The pons and the medulla regulate several crucial functions, including the cardiovascular and respiratory systems and rates.

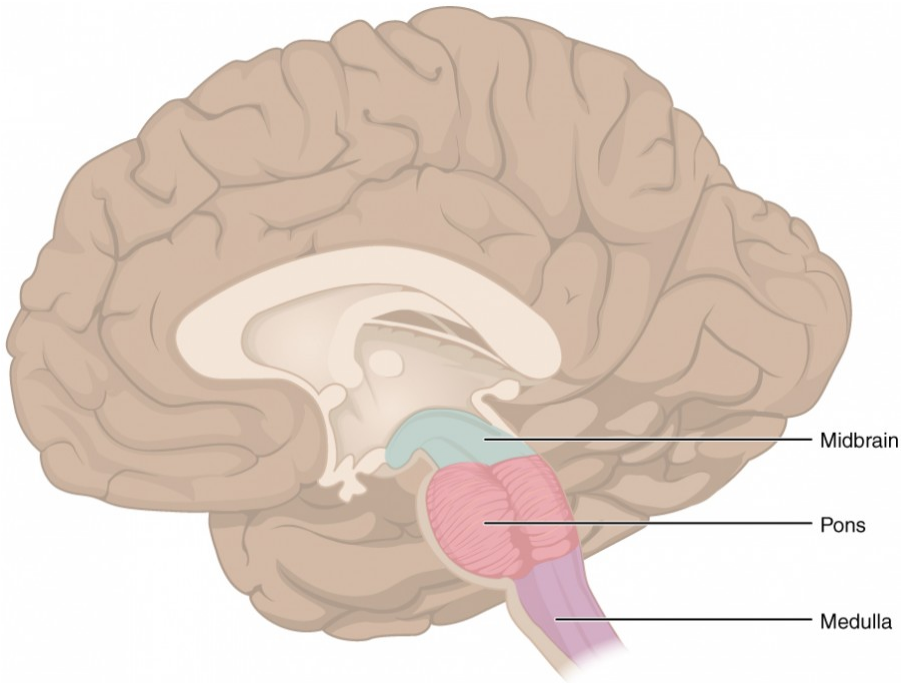


Figure 7. The Brain Stem. *The brain stem comprises three regions: the midbrain, the pons, and the medulla.*

The cranial nerves connect through the brain stem and provide the brain with the sensory input and motor output associated with the head and neck, including most of the special senses. The major ascending and descending pathways between the spinal cord and brain, specifically the cerebrum, pass through the brain stem.

Midbrain

One of the original regions of the embryonic brain, the midbrain is a small region between the thalamus and pons. It is separated into the **tectum** and **tegmentum**, from the Latin words for roof and floor, respectively. The cerebral aqueduct passes through the center of the midbrain, such that these regions are the roof and floor of that canal. The tectum is composed of four bumps known as the colliculi (singular = colliculus), which means “little hill” in Latin. The **inferior colliculus** is the inferior pair of these enlargements and is part of the auditory brain stem pathway. Neurons of the inferior colliculus project to the thalamus, which then sends auditory information to the cerebrum for the conscious perception of sound. The **superior colliculus** is the superior pair and combines sensory information about visual space, auditory space, and somatosensory space. Activity in the superior colliculus is related to orienting the eyes to a sound or touch stimulus. If you are walking along the sidewalk on campus and you hear chirping, the superior colliculus coordinates that information with your awareness of the visual location of the tree right above you. That is the correlation of auditory and visual maps. If you suddenly feel something wet fall on your head, your superior colliculus integrates that with the auditory and visual maps and you know that the chirping bird just relieved itself on you. You want to look up to see the culprit, but do not. The tegmentum is continuous with the gray matter of the rest of the brain stem. Throughout the midbrain, pons, and medulla, the tegmentum contains the nuclei that receive and send information through the cranial nerves, as well as regions that regulate important functions such as those of the cardiovascular and respiratory systems.

Pons

The word pons comes from the Latin word for bridge. It is visible on the anterior surface of the brain stem as the thick bundle of white matter attached to the cerebellum. The pons is the main connection between the cerebellum and the brain stem. The bridge-like white matter is only the anterior surface of the pons; the gray matter beneath that is a continuation of the tegmentum from the midbrain. Gray matter in the tegmentum region of the pons contains neurons receiving descending input from the forebrain that is sent to the cerebellum.

Medulla

The medulla is the region known as the myelencephalon in the embryonic brain. The initial portion of the name, "myel," refers to the significant white matter found in this region—especially on its exterior, which is continuous with the white matter of the spinal cord. The tegmentum of the midbrain and pons continues into the medulla because this gray matter is responsible for processing cranial nerve information. A diffuse region of gray matter throughout the brain stem, known as the **reticular formation**, is related to sleep and wakefulness, such as general brain activity and attention.

The Cerebellum

The **cerebellum**, as the name suggests, is the "little brain." It is covered in gyri and sulci like the cerebrum, and looks like a miniature version of that part of the brain (Figure 8). The cerebellum is largely responsible for comparing information from the cerebrum with sensory feedback from the periphery through the spinal cord. It accounts for approximately 10 percent of the mass of the brain.

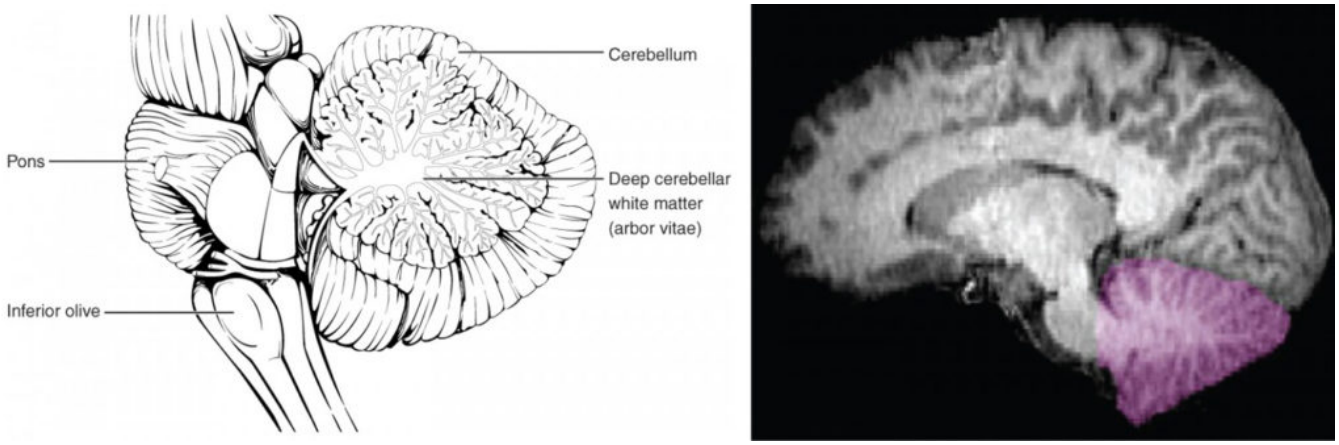


Figure 8. The Cerebellum. *The cerebellum is situated on the posterior surface of the brain stem. Descending input from the cerebellum enters through the large white matter structure of the pons. Ascending input from the periphery and spinal cord enters through the fibers of the inferior olive. Output goes to the midbrain, which sends a descending signal to the spinal cord.*

Descending fibers from the cerebrum have branches that connect to neurons in the pons. Those neurons project into the cerebellum, providing a copy of motor commands sent to the spinal cord. Sensory information from the periphery, which enters through spinal or cranial nerves, is copied to a nucleus in the medulla known as the **inferior olive**. Fibers from this nucleus enter the cerebellum and are compared with the descending commands from the cerebrum. If the primary motor cortex of the frontal lobe sends a command down to the spinal cord to initiate walking, a copy of that instruction is sent to the cerebellum. Sensory feedback from the muscles and joints, proprioceptive information about the movements of walking, and sensations of balance are sent to the cerebellum through the inferior olive and the cerebellum compares them. If walking is not coordinated, perhaps because the ground is uneven or a strong wind is blowing, then the cerebellum sends out a corrective command to compensate for the difference between the original cortical command and the sensory feedback. The output of the cerebellum is into the midbrain, which then sends a descending input to the spinal cord to correct the messages going to skeletal muscles.

The Spinal Cord

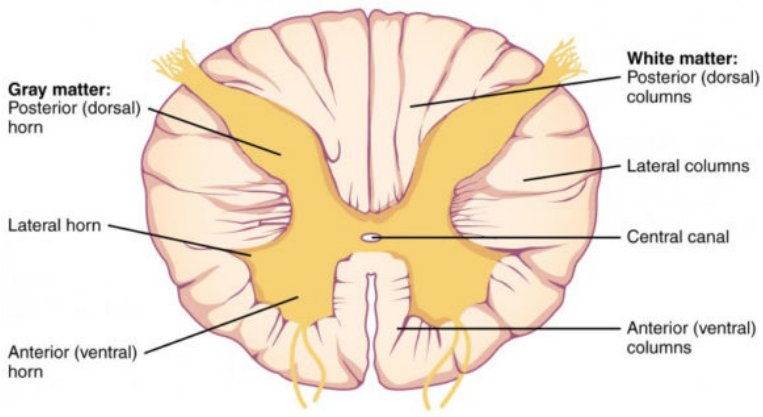
The description of the CNS is concentrated on the structures of the brain, but the spinal cord is another major organ of the system. Whereas the brain develops out of expansions of the neural tube into primary and then secondary vesicles, the spinal cord maintains the tube structure and is only specialized into certain regions. As the spinal cord continues to develop in the newborn, anatomical features mark its surface. The anterior midline is marked by the **anterior median fissure**, and the posterior midline is marked by the **posterior median sulcus**. Axons enter the posterior side through the **dorsal (posterior) nerve root**, which marks the **posterolateral sulcus** on either side. The axons emerging from the anterior side do so through the **ventral (anterior) nerve root**. Note that it is common to see the terms dorsal (dorsal = "back") and ventral (ventral = "belly") used interchangeably with posterior and anterior, particularly in reference to nerves and the structures of the spinal cord. You should learn to be comfortable with both.

On the whole, the posterior regions are responsible for sensory functions and the anterior regions are associated with motor functions. This comes from the initial development of the spinal cord, which is divided into the **basal plate** and the **alar plate**. The basal plate is closest to the ventral midline of the neural tube, which will become the anterior face of the spinal cord and gives rise to motor neurons. The alar plate is on the dorsal side of the neural tube and gives rise to neurons that will receive sensory input from the periphery. The length of the spinal cord is divided into regions that correspond to the regions of the vertebral column. The name of a spinal cord region corresponds to the level at which spinal nerves pass through the intervertebral foramina.

Immediately adjacent to the brain stem is the cervical region, followed by the thoracic, then the lumbar, and finally the sacral region. The spinal cord is not the full length of the vertebral column because the spinal cord does not grow significantly longer after the first or second year, but the skeleton continues to grow. The nerves that emerge from the spinal cord pass through the intervertebral formina at the respective levels. As the vertebral column grows, these nerves grow with it and result in a long bundle of nerves that resembles a horse's tail and is named the **cauda equina**. The sacral spinal cord is at the level of the upper lumbar vertebral bones. The spinal nerves extend from their various levels to the proper level of the vertebral column.

Gray Horns

In cross-section, the gray matter of the spinal cord has the appearance of an ink-blot test, with the spread of the gray matter on one side replicated on the other—a shape reminiscent of a bulbous capital "H." As shown in Figure 9, the gray matter is subdivided into regions that are referred to as horns. The **posterior horn** is responsible for sensory processing. The **anterior horn** sends out motor signals to the skeletal muscles. The **lateral horn**, which is only found in the thoracic, upper lumbar, and sacral regions, is the central component of the sympathetic division of the autonomic nervous system. Some of the largest neurons of the spinal cord are the multipolar motor neurons in the anterior horn. The fibers that cause contraction of skeletal muscles are the axons of these neurons. The motor neuron that causes contraction of the big toe, for example, is located in the sacral spinal cord. The axon that has to reach all the way to the belly of that muscle may be a meter in length. The neuronal cell body that maintains that long fiber must be quite large, possibly several hundred micrometers in diameter, making it one of the largest cells in the body.



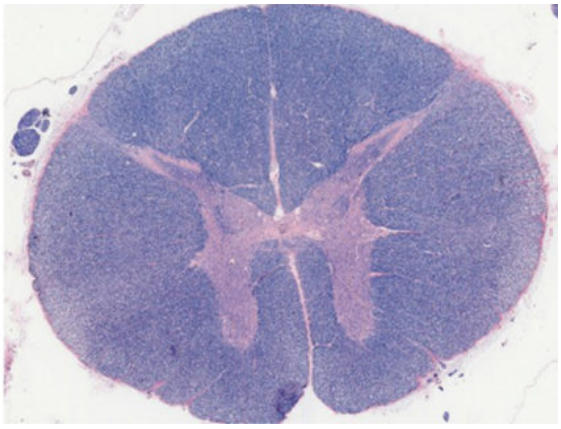


Figure 9. Cross-section of Spinal Cord. *The cross-section of a thoracic spinal cord segment shows the posterior, anterior, and lateral horns of gray matter, as well as the posterior, anterior, and lateral columns of white matter. LM × 40. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

White Columns

Just as the gray matter is separated into horns, the white matter of the spinal cord is separated into columns. **Ascending tracts** of nervous system fibers in these columns carry sensory information up to the brain, whereas **descending tracts** carry motor commands from the brain. Looking at the spinal cord longitudinally, the columns extend along its length as continuous bands of white matter. Between the two posterior horns of gray matter are the **posterior columns**. Between the two anterior horns, and bounded by the axons of motor neurons emerging from that gray matter area, are the **anterior columns**. The white matter on either side of the spinal cord, between the posterior horn and the axons of the anterior horn neurons, are the **lateral columns**. The posterior columns are composed of axons of ascending tracts. The anterior and lateral columns are composed of many different groups of axons of both ascending and descending tracts—the latter carrying motor commands down from the brain to the spinal cord to control output to the periphery.

Watch this video to learn about the gray matter of the spinal cord that receives input from fibers of the dorsal (posterior) root and sends information out through the fibers of the ventral (anterior) root.

Watch this video online: https://youtu.be/LwuV5JbgCNk

As discussed in this video, these connections represent the interactions of the CNS with peripheral structures for both sensory and motor functions. The cervical and lumbar spinal cords have enlargements as a result of larger populations of neurons. What are these enlargements responsible for?

Disorders of the Basal Nuclei

Parkinson's disease is a disorder of the basal nuclei, specifically of the substantia nigra, that demonstrates the effects of the direct and indirect pathways. Parkinson's disease is the result of neurons in the substantia nigra pars compacta dying. These neurons release dopamine into the striatum. Without that modulatory influence, the basal nuclei are stuck in the indirect pathway, without the direct pathway being activated. The direct pathway is responsible for increasing cortical movement commands. The increased activity of the indirect pathway results in the hypokinetic disorder of Parkinson's disease. Parkinson's disease is neurodegenerative, meaning that neurons die that cannot be replaced, so there is no cure for the disorder. Treatments for Parkinson's disease are aimed at increasing dopamine levels in the striatum. Currently, the most common way of doing that is by providing the amino acid L-DOPA, which is a precursor to the neurotransmitter dopamine and can cross the blood-brain barrier. With levels of the precursor elevated, the remaining cells of the substantia nigra pars compacta can make more neurotransmitter and have a greater effect. Unfortunately, the patient will become less responsive to L-DOPA treatment as time progresses, and it can cause increased dopamine levels elsewhere in the brain, which are associated with psychosis or schizophrenia.

Visit this site for a thorough explanation of Parkinson's disease.

Compared with the nearest evolutionary relative, the chimpanzee, the human has a brain that is huge. At a point in the past, a common ancestor gave rise to the two species of humans and chimpanzees. That evolutionary history is long and is still an area of intense study. But something happened to increase the size of the human brain relative to the chimpanzee. Read this article in which the author explores the current understanding of why this happened. According to one hypothesis about the expansion of brain size, what tissue might have been sacrificed so energy was available to grow our larger brain? Based on what you know about that tissue and nervous tissue, why would there be a trade-off between them in terms of energy use?

CIRCULATION AND THE CENTRAL NERVOUS SYSTEM

Learning Objectives

- Describe the vessels that supply the CNS with blood
- Name the components of the ventricular system and the regions of the brain in which each is located
- Explain the production of cerebrospinal fluid and its flow through the ventricles
- Explain how a disruption in circulation would result in a stroke

The CNS is crucial to the operation of the body, and any compromise in the brain and spinal cord can lead to severe difficulties. The CNS has a privileged blood supply, as suggested by the blood-brain barrier. The function of the tissue in the CNS is crucial to the survival of the organism, so the contents of the blood cannot simply pass into the central nervous tissue. To protect this region from the toxins and pathogens that may be traveling through the blood stream, there is strict control over what can move out of the general systems and into the brain and spinal cord. Because of this privilege, the CNS needs specialized structures for the maintenance of circulation. This begins with a unique arrangement of blood vessels carrying fresh blood into the CNS. Beyond the supply of blood, the CNS filters that blood into cerebrospinal fluid (CSF), which is then circulated through the cavities of the brain and spinal cord called ventricles.

Blood Supply to the Brain

A lack of oxygen to the CNS can be devastating, and the cardiovascular system has specific regulatory reflexes to ensure that the blood supply is not interrupted. There are multiple routes for blood to get into the CNS, with specializations to protect that blood supply and to maximize the ability of the brain to get an uninterrupted perfusion.

Arterial Supply

The major artery carrying recently oxygenated blood away from the heart is the aorta. The very first branches off the aorta supply the heart with nutrients and oxygen. The next branches give rise to the **common carotid arteries**, which further branch into the **internal carotid arteries**. The external carotid arteries supply blood to the tissues on the surface of the cranium. The bases of the common carotids contain stretch receptors that immediately respond to the drop in blood pressure upon standing. The **orthostatic reflex** is a reaction to this change in body position, so that blood pressure is maintained against the increasing effect of gravity (orthostatic means "standing up"). Heart rate increases—a reflex of the sympathetic division of the autonomic nervous system—and this raises blood pressure.

The internal carotid artery enters the cranium through the **carotid canal** in the temporal bone. A second set of vessels that supply the CNS are the **vertebral arteries**, which are protected as they pass through the neck region by the transverse foramina of the cervical vertebrae. The vertebral arteries enter the cranium through the **foramen magnum** of the occipital bone.

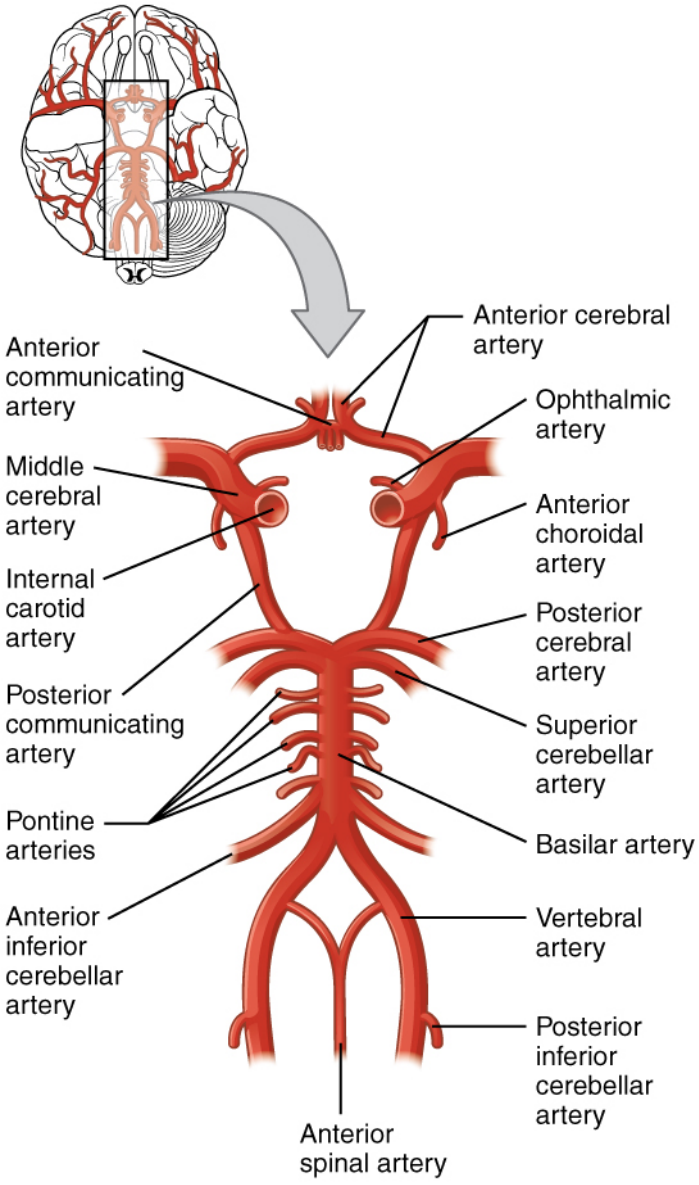


Figure 1. Circle of Willis. *The blood supply to the brain enters through the internal carotid arteries and the vertebral arteries, eventually giving rise to the circle of Willis.*

Branches off the left and right vertebral arteries merge into the **anterior spinal artery** supplying the anterior aspect of the spinal cord, found along the anterior median fissure. The two vertebral arteries then merge into the **basilar artery**, which gives rise to branches to the brain stem and cerebellum. The left and right internal carotid arteries and branches of the basilar artery all become the **circle of Willis**, a confluence of arteries that can maintain perfusion of the brain even if narrowing or a blockage limits flow through one part (Figure 1).

Watch this animation to see how blood flows to the brain and passes through the circle of Willis before being distributed through the cerebrum. The circle of Willis is a specialized arrangement of arteries that ensure constant perfusion of the cerebrum even in the event of a blockage of one of the arteries in the circle. The animation shows the normal direction of flow through the circle of Willis to the middle cerebral artery. Where would the blood come from if there were a blockage just posterior to the middle cerebral artery on the left?

Venous Return

After passing through the CNS, blood returns to the circulation through a series of **dural sinuses** and veins (Figure 2). The **superior sagittal sinus** runs in the groove of the longitudinal fissure, where it absorbs CSF from the meninges. The superior sagittal sinus drains to the confluence of sinuses, along with the **occipital sinuses** and **straight sinus**, to then drain into the **transverse sinuses**. The transverse sinuses connect to the **sigmoid sinuses**, which then connect to the **jugular veins**. From there, the blood continues toward the heart to be pumped to the lungs for reoxygenation.

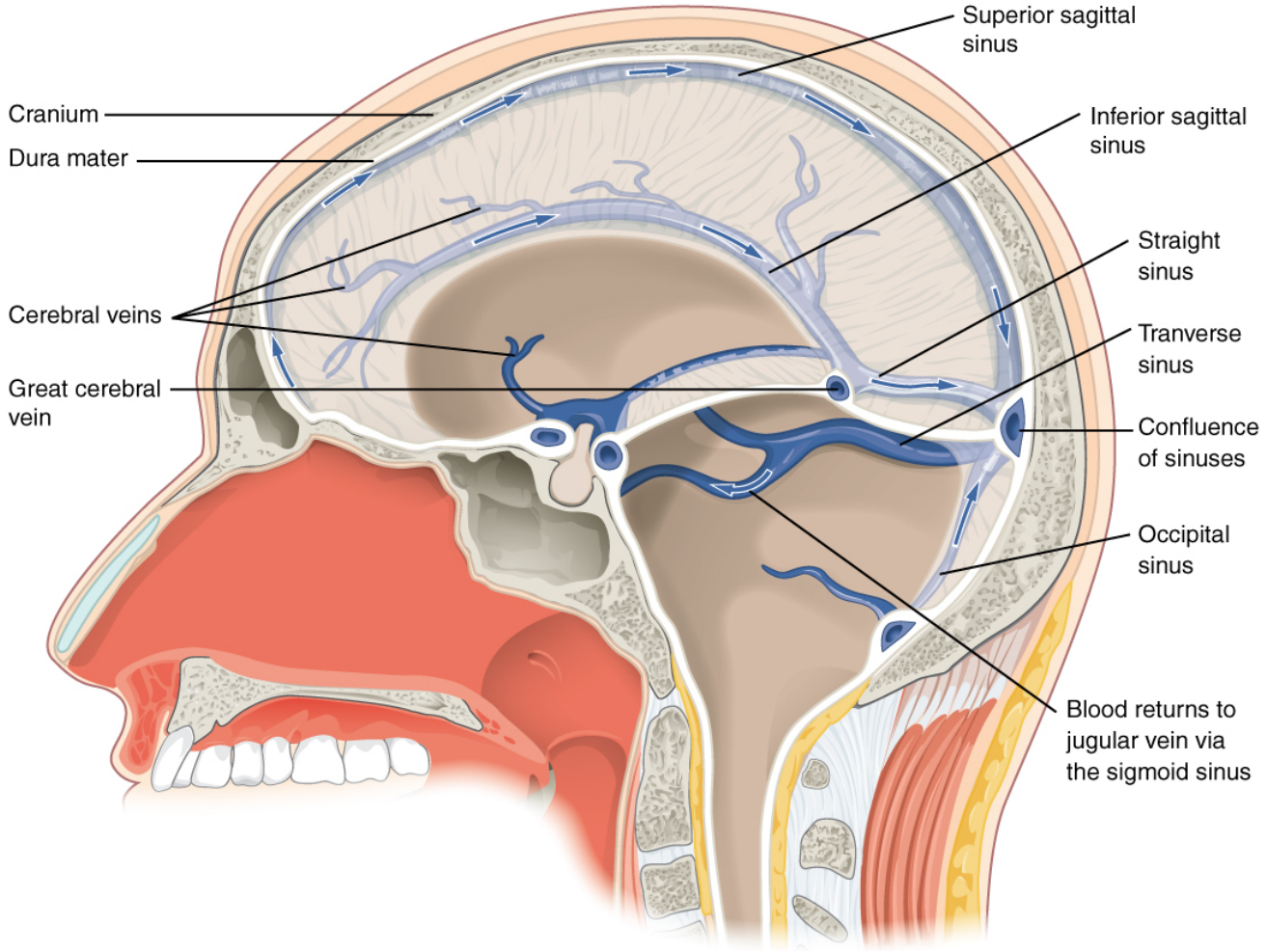


Figure 2. Dural Sinuses and Veins. *Blood drains from the brain through a series of sinuses that connect to the jugular veins.*

Protective Coverings of the Brain and Spinal Cord

The outer surface of the CNS is covered by a series of membranes composed of connective tissue called the **meninges**, which protect the brain. The **dura mater** is a thick fibrous layer and a strong protective sheath over the entire brain and spinal cord. It is anchored to the inner surface of the cranium and vertebral cavity. The **arachnoid mater** is a membrane of thin fibrous tissue that forms a loose sac around the CNS. Beneath the arachnoid is a thin, filamentous mesh called the **arachnoid trabeculae**, which looks like a spider web, giving this layer its name. Directly adjacent to the surface of the CNS is the **pia mater**, a thin fibrous membrane that follows the convolutions of gyri and sulci in the cerebral cortex and fits into other grooves and indentations (Figure 3).

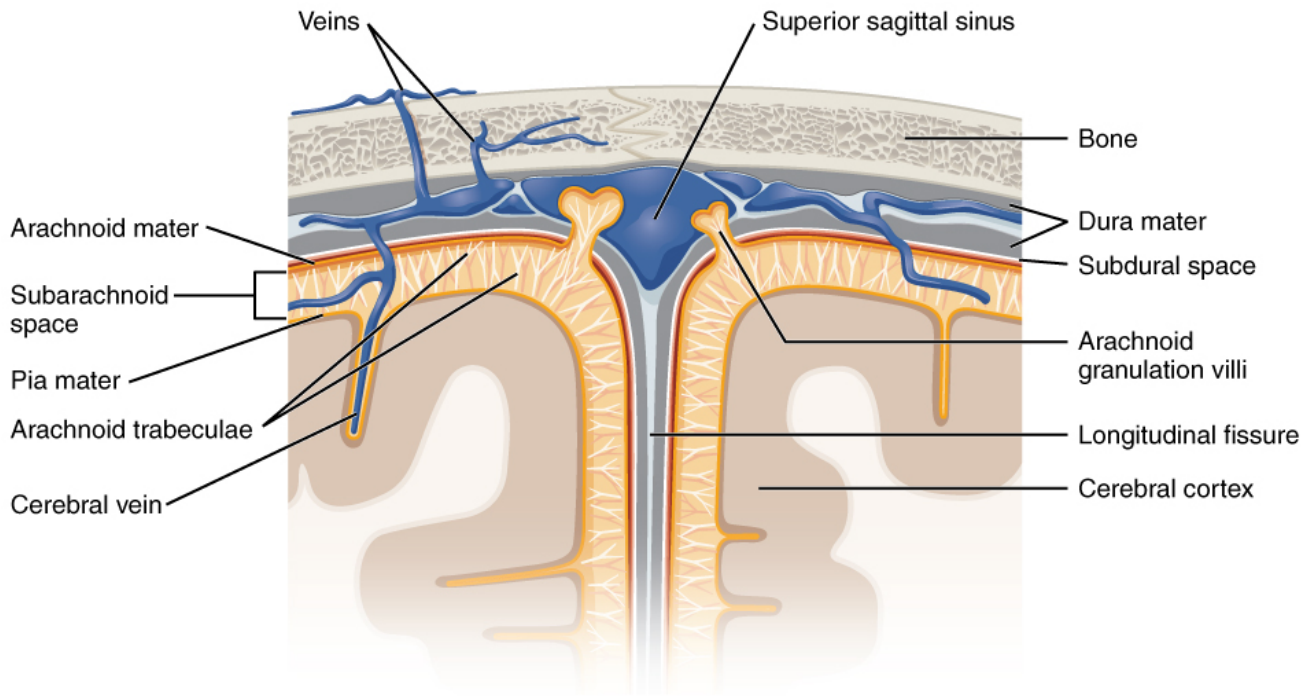


Figure 3. Meningeal Layers of Superior Sagittal Sinus. *The layers of the meninges in the longitudinal fissure of the superior sagittal sinus are shown, with the dura mater adjacent to the inner surface of the cranium, the pia mater adjacent to the surface of the brain, and the arachnoid and subarachnoid space between them. An arachnoid villus is shown emerging into the dural sinus to allow CSF to filter back into the blood for drainage.*

Dura Mater

Like a thick cap covering the brain, the dura mater is a tough outer covering. The name comes from the Latin for "tough mother" to represent its physically protective role. It encloses the entire CNS and the major blood vessels that enter the cranium and vertebral cavity. It is directly attached to the inner surface of the bones of the cranium and to the very end of the vertebral cavity. There are infoldings of the dura that fit into large crevasses of the brain. Two infoldings go through the midline separations of the cerebrum and cerebellum; one forms a shelf-like tent between the occipital lobes of the cerebrum and the cerebellum, and the other surrounds the pituitary gland. The dura also surrounds and supports the venous sinuses.

Arachnoid Mater

The middle layer of the meninges is the arachnoid, named for the spider-web–like trabeculae between it and the pia mater. The arachnoid defines a sac-like enclosure around the CNS. The trabeculae are found in the **subarachnoid space**, which is filled with circulating CSF. The arachnoid emerges into the dural sinuses as the **arachnoid granulations**, where the CSF is filtered back into the blood for drainage from the nervous system. The subarachnoid space is filled with circulating CSF, which also provides a liquid cushion to the brain and spinal cord. Similar to clinical blood work, a sample of CSF can be withdrawn to find chemical evidence of neuropathology or metabolic traces of the biochemical functions of nervous tissue.

Pia Mater

The outer surface of the CNS is covered in the thin fibrous membrane of the pia mater. It is thought to have a continuous layer of cells providing a fluid-impermeable membrane. The name pia mater comes from the Latin for "tender mother," suggesting the thin membrane is a gentle covering for the brain. The pia extends into every convolution of the CNS, lining the inside of the sulci in the cerebral and cerebellar cortices. At the end of the spinal cord, a thin filament extends from the inferior end of CNS at the upper lumbar region of the vertebral column to the sacral end of the vertebral column. Because the spinal cord does not extend through the lower

lumbar region of the vertebral column, a needle can be inserted through the dura and arachnoid layers to withdraw CSF. This procedure is called a **lumbar puncture** and avoids the risk of damaging the central tissue of the spinal cord. Blood vessels that are nourishing the central nervous tissue are between the pia mater and the nervous tissue.

Disorders of the Meninges

Meningitis is an inflammation of the meninges, the three layers of fibrous membrane that surround the CNS. Meningitis can be caused by infection by bacteria or viruses. The particular pathogens are not special to meningitis; it is just an inflammation of that specific set of tissues from what might be a broader infection. Bacterial meningitis can be caused by *Streptococcus*, *Staphylococcus*, or the tuberculosis pathogen, among many others. Viral meningitis is usually the result of common enteroviruses (such as those that cause intestinal disorders), but may be the result of the herpes virus or West Nile virus. Bacterial meningitis tends to be more severe.

The symptoms associated with meningitis can be fever, chills, nausea, vomiting, light sensitivity, soreness of the neck, or severe headache. More important are the neurological symptoms, such as changes in mental state (confusion, memory deficits, and other dementia-type symptoms). A serious risk of meningitis can be damage to peripheral structures because of the nerves that pass through the meninges. Hearing loss is a common result of meningitis.

The primary test for meningitis is a lumbar puncture. A needle inserted into the lumbar region of the spinal column through the dura mater and arachnoid membrane into the subarachnoid space can be used to withdraw the fluid for chemical testing. Fatality occurs in 5 to 40 percent of children and 20 to 50 percent of adults with bacterial meningitis. Treatment of bacterial meningitis is through antibiotics, but viral meningitis cannot be treated with antibiotics because viruses do not respond to that type of drug. Fortunately, the viral forms are milder.

Watch this video that describes the procedure known as the lumbar puncture, a medical procedure used to sample the CSF. Because of the anatomy of the CNS, it is a relative safe location to insert a needle. Why is the lumbar puncture performed in the lower lumbar area of the vertebral column?

The Ventricular System

Cerebrospinal fluid (CSF) circulates throughout and around the CNS. In other tissues, water and small molecules are filtered through capillaries as the major contributor to the interstitial fluid. In the brain, CSF is produced in special structures to perfuse through the nervous tissue of the CNS and is continuous with the interstitial fluid. Specifically, CSF circulates to remove metabolic wastes from the interstitial fluids of nervous tissues and return them to the blood stream. The **ventricles** are the open spaces within the brain where CSF circulates. In some of these spaces, CSF is produced by filtering of the blood that is performed by a specialized membrane known as a choroid plexus. The CSF circulates through all of the ventricles to eventually emerge into the subarachnoid space where it will be reabsorbed into the blood.

The Ventricles

There are four ventricles within the brain, all of which developed from the original hollow space within the neural tube, the **central canal**. The first two are named the **lateral ventricles** and are deep within the cerebrum. These ventricles are connected to the **third ventricle** by two openings called the **interventricular foramina**. The third ventricle is the space between the left and right sides of the diencephalon, which opens into the **cerebral aqueduct** that passes through the midbrain. The aqueduct opens into the **fourth ventricle**, which is the space between the cerebellum and the pons and upper medulla (Figure 4).

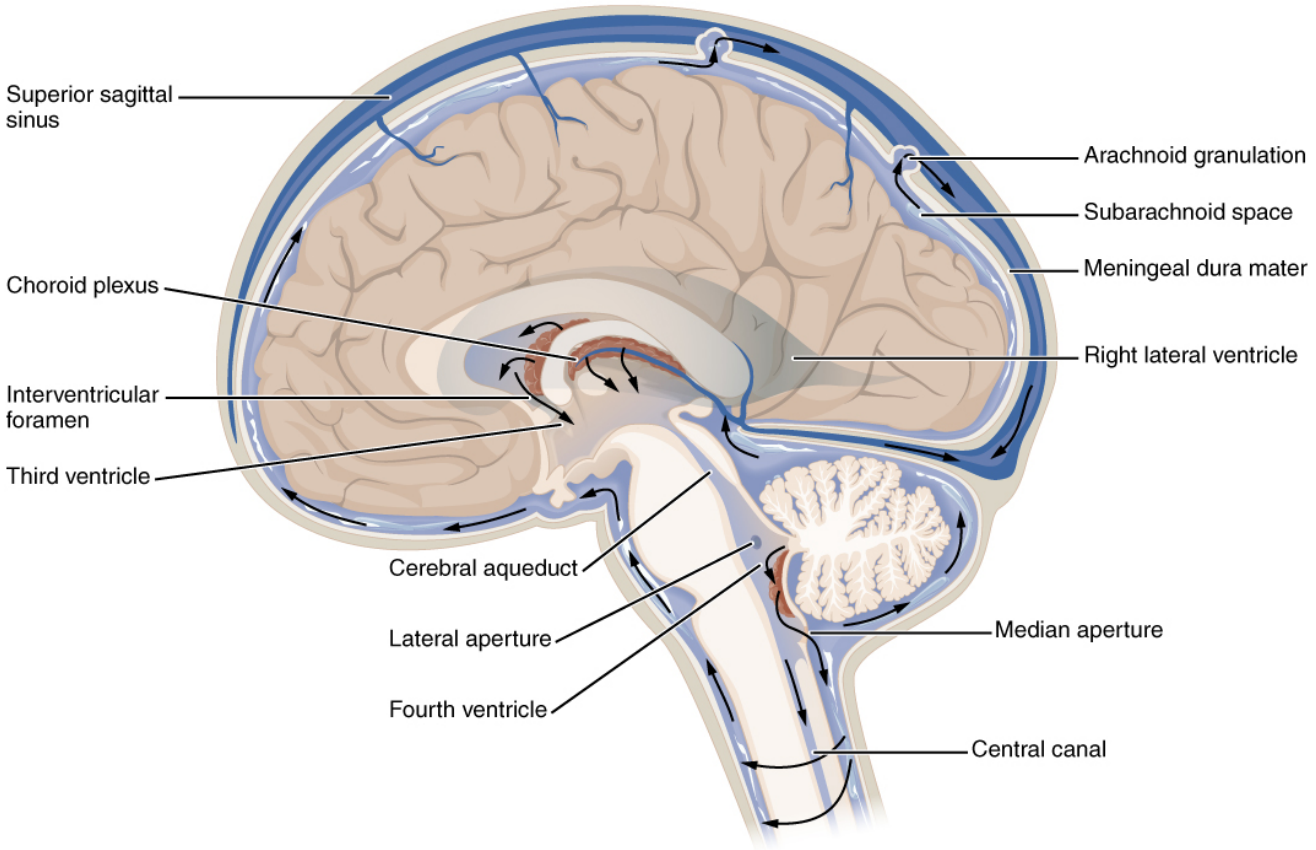


Figure 4. Cerebrospinal Fluid Circulation. *The choroid plexus in the four ventricles produce CSF, which is circulated through the ventricular system and then enters the subarachnoid space through the median and lateral apertures. The CSF is then reabsorbed into the blood at the arachnoid granulations, where the arachnoid membrane emerges into the dural sinuses.*

As the telencephalon enlarges and grows into the cranial cavity, it is limited by the space within the skull. The telencephalon is the most anterior region of what was the neural tube, but cannot grow past the limit of the frontal bone of the skull. Because the cerebrum fits into this space, it takes on a C-shaped formation, through the frontal, parietal, occipital, and finally temporal regions.

The space within the telencephalon is stretched into this same C-shape. The two ventricles are in the left and right sides, and were at one time referred to as the first and second ventricles. The interventricular foramina connect the frontal region of the lateral ventricles with the third ventricle. The third ventricle is the space bounded by the medial walls of the hypothalamus and thalamus. The two thalami touch in the center in most brains as the massa intermedia, which is surrounded by the third ventricle. The cerebral aqueduct opens just inferior to the epithalamus and passes through the midbrain. The tectum and tegmentum of the midbrain are the roof and floor of the cerebral aqueduct, respectively. The aqueduct opens up into the fourth ventricle. The floor of the fourth ventricle is the dorsal surface of the pons and upper medulla (that gray matter making a continuation of the tegmentum of the midbrain). The fourth ventricle then narrows into the central canal of the spinal cord.

The ventricular system opens up to the subarachnoid space from the fourth ventricle. The single **median aperture** and the pair of **lateral apertures** connect to the subarachnoid space so that CSF can flow through the ventricles and around the outside of the CNS. Cerebrospinal fluid is produced within the ventricles by a type of specialized membrane called a **choroid plexus**. Ependymal cells (one of the types of glial cells described in the introduction to the nervous system) surround blood capillaries and filter the blood to make CSF. The fluid is a clear solution with a limited amount of the constituents of blood. It is essentially water, small molecules, and electrolytes. Oxygen and carbon dioxide are dissolved into the CSF, as they are in blood, and can diffuse between the fluid and the nervous tissue.

Cerebrospinal Fluid Circulation

The choroid plexuses are found in all four ventricles. Observed in dissection, they appear as soft, fuzzy structures that may still be pink, depending on how well the circulatory system is cleared in preparation of the tissue. The CSF is produced from components extracted from the blood, so its flow out of the ventricles is tied to the pulse of cardiovascular circulation. From the lateral ventricles, the CSF flows into the third ventricle, where more CSF is produced, and then through the cerebral aqueduct into the fourth ventricle where even more CSF is produced.

A very small amount of CSF is filtered at any one of the plexuses, for a total of about 500 milliliters daily, but it is continuously made and pulses through the ventricular system, keeping the fluid moving. From the fourth ventricle, CSF can continue down the central canal of the spinal cord, but this is essentially a cul-de-sac, so more of the fluid leaves the ventricular system and moves into the subarachnoid space through the median and lateral apertures. Within the subarachnoid space, the CSF flows around all of the CNS, providing two important functions.

Watch this animation that shows the flow of CSF through the brain and spinal cord, and how it originates from the ventricles and then spreads into the space within the meninges, where the fluids then move into the venous sinuses to return to the cardiovascular circulation. What are the structures that produce CSF and where are they found? How are the structures indicated in this animation?

As with elsewhere in its circulation, the CSF picks up metabolic wastes from the nervous tissue and moves it out of the CNS. It also acts as a liquid cushion for the brain and spinal cord. By surrounding the entire system in the subarachnoid space, it provides a thin buffer around the organs within the strong, protective dura mater. The arachnoid granulations are outpocketings of the arachnoid membrane into the dural sinuses so that CSF can be reabsorbed into the blood, along with the metabolic wastes. From the dural sinuses, blood drains out of the head and neck through the jugular veins, along with the rest of the circulation for blood, to be reoxygenated by the lungs and wastes to be filtered out by the kidneys (Table 1).

Table 1. Components of CSF Circulation

	Lateral ventricles	Third ventricle	Cerebral aqueduct	Fourth ventricle	Central canal	Subarachnoid space
Location in CNS	Cerebrum	Diencephalon	Midbrain	Between pons/upper medulla and cerebellum	Spinal cord	External to entire CNS
Blood vessel structure	Choroid plexus	Choroid plexus	None	Choroid plexus	None	Arachnoid granulations

Disorders of the Central Nervous System

The supply of blood to the brain is crucial to its ability to perform many functions. Without a steady supply of oxygen, and to a lesser extent glucose, the nervous tissue in the brain cannot keep up its extensive electrical activity. These nutrients get into the brain through the blood, and if blood flow is interrupted, neurological function is compromised. The common name for a disruption of blood supply to the brain is a stroke. It is caused by a blockage to an artery in the brain. The blockage is from some type of embolus: a blood clot, a fat embolus, or an air bubble. When the blood cannot travel through the artery, the surrounding tissue that is deprived starves and dies.

Strokes will often result in the loss of very specific functions. A stroke in the lateral medulla, for example, can cause a loss in the ability to swallow. Sometimes, seemingly unrelated functions will be lost because they are dependent on structures in the same region. Along with the swallowing in the previous example, a stroke in that region could affect sensory functions from the face or extremities because important white matter pathways also pass through the lateral medulla. Loss of blood flow to specific regions of the cortex can lead to

the loss of specific higher functions, from the ability to recognize faces to the ability to move a particular region of the body. Severe or limited memory loss can be the result of a temporal lobe stroke.

Related to strokes are transient ischemic attacks (TIAs), which can also be called “mini-strokes.” These are events in which a physical blockage may be temporary, cutting off the blood supply and oxygen to a region, but not to the extent that it causes cell death in that region. While the neurons in that area are recovering from the event, neurological function may be lost. Function can return if the area is able to recover from the event. Recovery from a stroke (or TIA) is strongly dependent on the speed of treatment. Often, the person who is present and notices something is wrong must then make a decision.

The mnemonic **FAST** helps people remember what to look for when someone is dealing with sudden losses of neurological function. If someone complains of feeling “funny,” check these things quickly:

- **Face**: Look at the person’s face. Does he or she have problems moving **F**ace muscles and making regular facial expressions?
- **Arms**: Ask the person to raise his or her **A**rms above the head. Can the person lift one arm but not the other?
- **Speech**: Has the person’s **S**peech changed? Is he or she slurring words or having trouble saying things?
- **Time**: If any of these things have happened, then it is **T**ime to call for help.

Sometimes, treatment with blood-thinning drugs can alleviate the problem, and recovery is possible. If the tissue is damaged, the amazing thing about the nervous system is that it is adaptable. With physical, occupational, and speech therapy, victims of strokes can recover, or more accurately relearn, functions.

THE PERIPHERAL NERVOUS SYSTEM

Learning Objectives

- Describe the structures found in the PNS
- Distinguish between somatic and autonomic structures, including the special peripheral structures of the enteric nervous system
- Name the twelve cranial nerves and explain the functions associated with each
- Describe the sensory and motor components of spinal nerves and the plexuses that they pass through

The PNS is not as contained as the CNS because it is defined as everything that is not the CNS. Some peripheral structures are incorporated into the other organs of the body. In describing the anatomy of the PNS, it is necessary to describe the common structures, the nerves and the ganglia, as they are found in various parts of the body. Many of the neural structures that are incorporated into other organs are features of the digestive system; these structures are known as the **enteric nervous system** and are a special subset of the PNS.

Ganglia

A ganglion is a group of neuron cell bodies in the periphery. Ganglia can be categorized, for the most part, as either sensory ganglia or autonomic ganglia, referring to their primary functions. The most common type of sensory ganglion is a **dorsal (posterior) root ganglion**. These ganglia are the cell bodies of neurons with axons that are sensory endings in the periphery, such as in the skin, and that extend into the CNS through the dorsal nerve root. The ganglion is an enlargement of the nerve root. Under microscopic inspection, it can be seen to include the cell bodies of the neurons, as well as bundles of fibers that are the posterior nerve root (Figure 1). The cells of the dorsal root ganglion are unipolar cells, classifying them by shape. Also, the small round nuclei of satellite cells can be seen surrounding—as if they were orbiting—the neuron cell bodies.

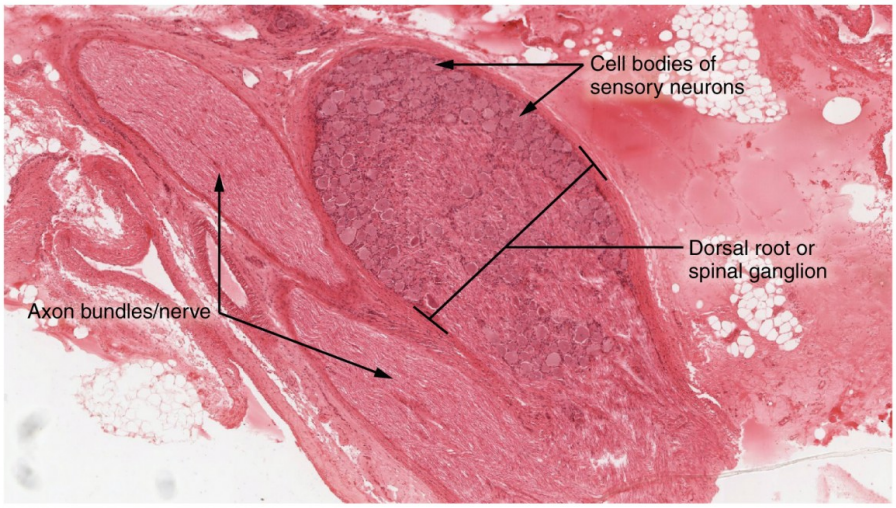


Figure 1. Dorsal Root Ganglion. *The cell bodies of sensory neurons, which are unipolar neurons by shape, are seen in this photomicrograph. Also, the fibrous region is composed of the axons of these neurons that are passing through the ganglion to be part of the dorsal nerve root (tissue source: canine). LM × 40. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

Another type of sensory ganglion is a **cranial nerve ganglion**. This is analogous to the dorsal root ganglion, except that it is associated with a **cranial nerve** instead of a **spinal nerve**. The roots of cranial nerves are within the cranium, whereas the ganglia are outside the skull. For example, the **trigeminal ganglion** is superficial to the temporal bone whereas its associated nerve is attached to the mid-pons region of the brain stem. The neurons of cranial nerve ganglia are also unipolar in shape with associated satellite cells. The other major category of ganglia are those of the autonomic nervous system, which is divided into the sympathetic and parasympathetic nervous systems.

The **sympathetic chain ganglia** constitute a row of ganglia along the vertebral column that receive central input from the lateral horn of the thoracic and upper lumbar spinal cord. Superior to the chain ganglia are three **paravertebral ganglia** in the cervical region. Three other autonomic ganglia that are related to the sympathetic chain are the **prevertebral ganglia**, which are located outside of the chain but have similar functions. They are referred to as prevertebral because they are anterior to the vertebral column. The neurons of these autonomic ganglia are multipolar in shape, with dendrites radiating out around the cell body where synapses from the spinal cord neurons are made. The neurons of the chain, paravertebral,

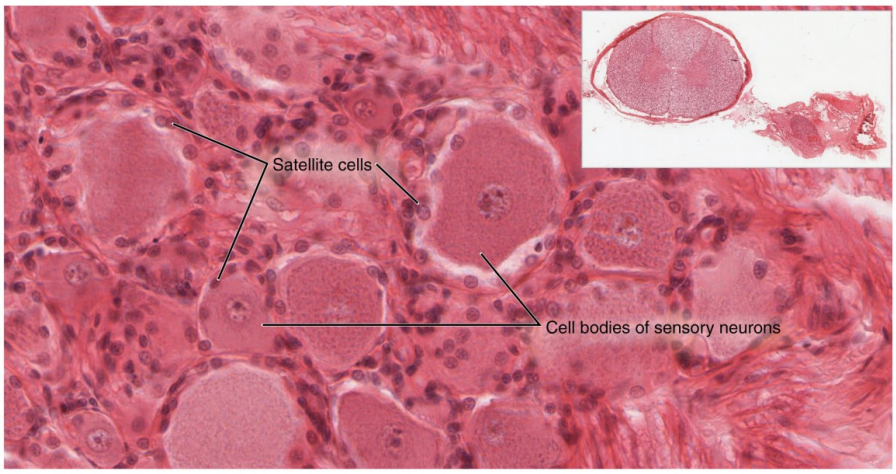


Figure 2. Spinal Cord and Root Ganglion. *The slide includes both a cross-section of the lumbar spinal cord and a section of the dorsal root ganglion (see also Figure 1) (tissue source: canine). LM × 1600. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

and prevertebral ganglia then project to organs in the head and neck, thoracic, abdominal, and pelvic cavities to regulate the sympathetic aspect of homeostatic mechanisms.

Another group of autonomic ganglia are the **terminal ganglia** that receive input from cranial nerves or sacral spinal nerves and are responsible for regulating the parasympathetic aspect of homeostatic mechanisms. These two sets of ganglia, sympathetic and parasympathetic, often project to the same organs—one input from the chain ganglia and one input from a terminal ganglion—to regulate the overall function of an organ. For example, the heart receives two inputs such as these; one increases heart rate, and the other decreases it.

The terminal ganglia that receive input from cranial nerves are found in the head and neck, as well as the thoracic and upper abdominal cavities, whereas the terminal ganglia that receive sacral input are in the lower abdominal and pelvic cavities. Terminal ganglia below the head and neck are often incorporated into the wall of the target organ as a **plexus**. A plexus, in a general sense, is a network of fibers or vessels. This can apply to nervous tissue (as in this instance) or structures containing blood vessels (such as a choroid plexus). For example, the **enteric plexus** is the extensive network of axons and neurons in the wall of the small and large intestines. The enteric plexus is actually part of the enteric nervous system, along with the **gastric plexuses** and the **esophageal plexus**. Though the enteric nervous system receives input originating from central neurons of the autonomic nervous system, it does not require CNS input to function. In fact, it operates independently to regulate the digestive system.

View the University of Michigan WebScope to explore the tissue sample in greater detail. If you zoom in on the dorsal root ganglion, you can see smaller satellite glial cells surrounding the large cell bodies of the sensory neurons. From what structure do satellite cells derive during embryologic development?

Nerves

Bundles of axons in the PNS are referred to as nerves. These structures in the periphery are different than the central counterpart, called a tract. Nerves are composed of more than just nervous tissue. They have connective tissues invested in their structure, as well as blood vessels supplying the tissues with nourishment. The outer surface of a nerve is a surrounding layer of fibrous connective tissue called the **epineurium**. Within the nerve, axons are further bundled into **fascicles**, which are each surrounded by their own layer of fibrous connective tissue called **perineurium**. Finally, individual axons are surrounded by loose connective tissue called the **endoneurium** (Figure 3).

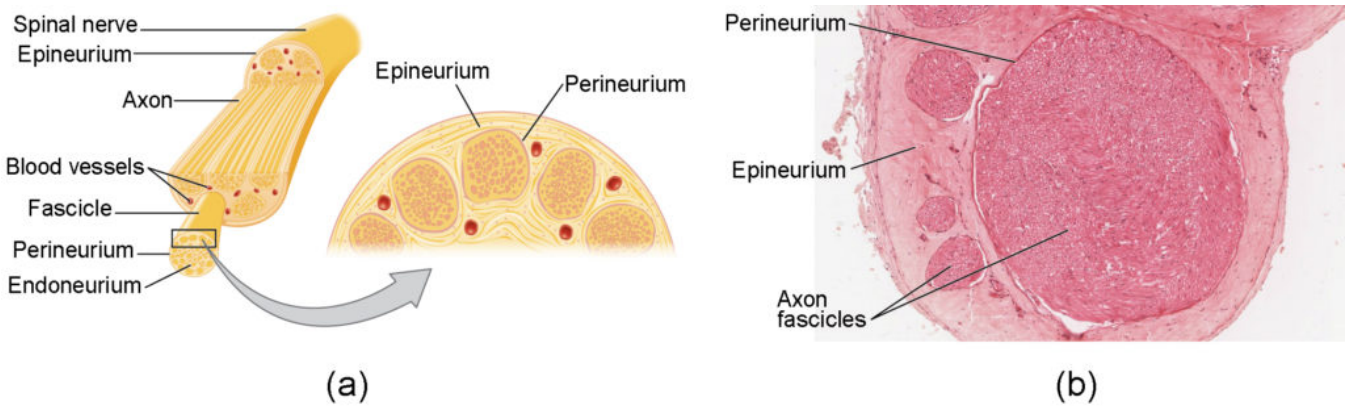


Figure 3. Nerve Structure. *The structure of a nerve is organized by the layers of connective tissue on the outside, around each fascicle, and surrounding the individual nerve fibers (tissue source: simian). LM × 40. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

These three layers are similar to the connective tissue sheaths for muscles. Nerves are associated with the region of the CNS to which they are connected, either as cranial nerves connected to the brain or spinal nerves connected to the spinal cord.

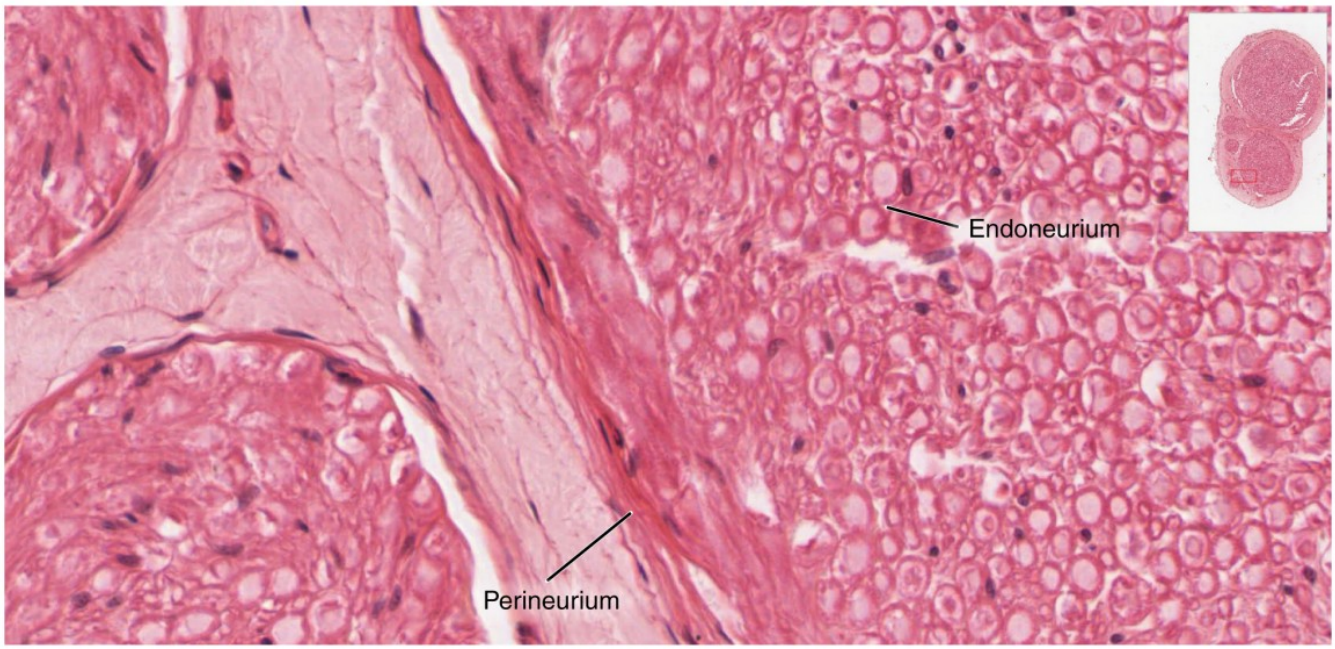


Figure 4. Close-Up of Nerve Trunk. *Zoom in on this slide of a nerve trunk to examine the endoneurium, perineurium, and epineurium in greater detail (tissue source: simian). LM × 1600. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

View the University of Michigan WebScope to explore the tissue sample in greater detail. With what structures in a skeletal muscle are the endoneurium, perineurium, and epineurium comparable?

Cranial Nerves

The nerves attached to the brain are the cranial nerves, which are primarily responsible for the sensory and motor functions of the head and neck (one of these nerves targets organs in the thoracic and abdominal cavities as part of the parasympathetic nervous system). There are twelve cranial nerves, which are designated CNI through CNXII for “Cranial Nerve,” using Roman numerals for 1 through 12. They can be classified as sensory nerves, motor nerves, or a combination of both, meaning that the axons in these nerves originate out of sensory ganglia external to the cranium or motor nuclei within the brain stem. Sensory axons enter the brain to synapse in a nucleus. Motor axons connect to skeletal muscles of the head or neck. Three of the nerves are solely composed of sensory fibers; five are strictly motor; and the remaining four are mixed nerves.

Learning the cranial nerves is a tradition in anatomy courses, and students have always used mnemonic devices to remember the nerve names. A traditional mnemonic is the rhyming couplet, “On Old Olympus’ Towering Tops/ A Finn And German Viewed Some Hops,” in which the initial letter of each word corresponds to the initial letter in the name of each nerve. The names of the nerves have changed over the years to reflect current usage and more accurate naming. An exercise to help learn this sort of information is to generate a mnemonic using words that have personal significance. The names of the cranial nerves are listed in Table 1 along with a brief description of their function, their source (sensory ganglion or motor nucleus), and their target (sensory nucleus or skeletal muscle).

Figure 5 shows where the nerves are located in the brain. The **olfactory nerve** and **optic nerve** are responsible for the sense of smell and vision, respectively. The **oculomotor nerve** is responsible for eye movements by controlling four of the **extraocular muscles**. It is also responsible for lifting the upper eyelid when the eyes point up, and for pupillary constriction. The **trochlear nerve** and the **abducens nerve** are both responsible for eye movement, but do so by controlling different extraocular muscles. The **trigeminal nerve** is responsible for cutaneous sensations of the face and controlling the muscles of mastication. The **facial nerve** is responsible for the muscles involved in facial expressions, as well as part of the sense of taste and the production of saliva. The **vestibulocochlear nerve** is responsible for the senses of hearing and balance. The **glossopharyngeal nerve** is responsible for controlling muscles in the oral cavity and upper throat, as well as part of the sense of taste and the production of saliva. The **vagus nerve** is responsible for contributing to homeostatic control of the organs of the thoracic and upper abdominal cavities. The **spinal accessory nerve** is responsible for controlling the muscles of the neck, along with cervical spinal nerves. The **hypoglossal nerve** is responsible for controlling the muscles of the lower throat and tongue.

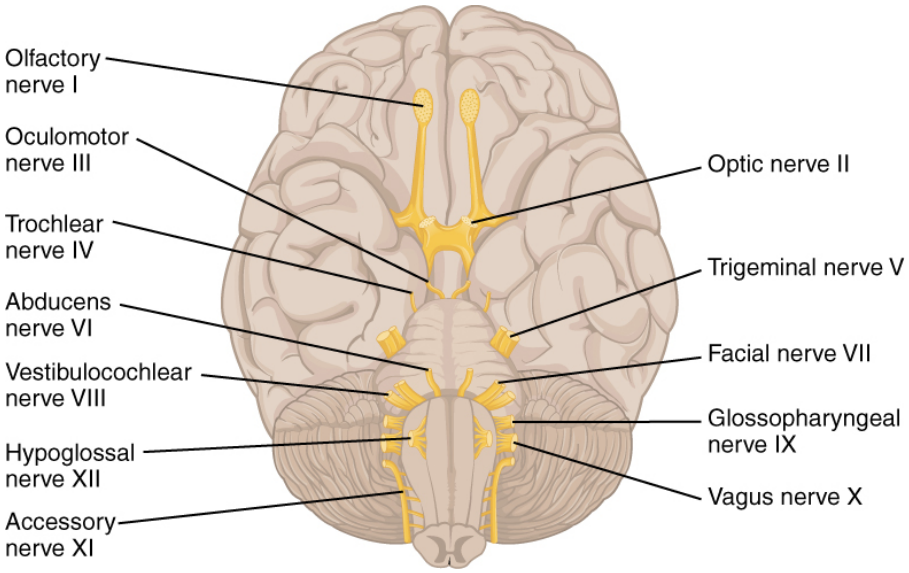


Figure 5. *The Cranial Nerves The anatomical arrangement of the roots of the cranial nerves observed from an inferior view of the brain.*

Table 1. Cranial Nerves

Mnemonic	#	Name	Function (S/M/B)	Central connection (nuclei)	Peripheral connection (ganglion or muscle)
On	I	Olfactory	Smell (S)	Olfactory bulb	Olfactory epithelium
Old	II	Optic	Vision (S)	Hypothalamus/ thalamus/ midbrain	Retina (retinal ganglion cells)
Olympus	III	Oculomotor	Eye movements (M)	Oculomotor nucleus	Extraocular muscles (other 4), levator palpebrae superioris, ciliary ganglion (autonomic)
Towering	IV	Trochlear	Eye movements (M)	Trochlear nucleus	Superior oblique muscle
Tops	V	Trigeminal	Sensory/ motor—face (B)	Trigeminal nuclei in the midbrain, pons, and medulla	Trigemal
A	VI	Abducens	Eye movements (M)	Abducens nucleus	Lateral rectus muscle

Table 1. Cranial Nerves					
Mnemonic	#	Name	Function (S/M/B)	Central connection (nuclei)	Peripheral connection (ganglion or muscle)
Finn	VII	Facial	Motor—face, Taste (B)	Facial nucleus, solitary nucleus, superior salivatory nucleus	Facial muscles, Geniculate ganglion, Pterygopalatine ganglion (autonomic)
And	VIII	Auditory (Vestibulocochlear)	Hearing/balance (S)	Cochlearn nucleus, Vestibular nucleus/ cerebellum	Spiral ganglion (hearing), Vestibular ganglion (balance)
German	IX	Glossopharyngeal	Motor—throat Taste (B)	Solitary nucleus, inferior salivatory nucleus, nucleus ambiguus	Pharyngeal muscles, Geniculate ganglion, Otic ganglion (autonomic)
Viewed	X	Vagus	Motor/ sensory—viscera (autonomic)	Medulla	Terminal ganglia serving thoracic and upper abdominal organs (heart and small intestines)
Some	XI	Spinal Accessory	Motor—head and neck (M)	Spinal accessory nucleus	Neck muscles
Hops	XII	Hypoglossal	Motor—lower throat (M)	Hypoglossal nucleus	Muscles of the larynx and lower pharynx

Three of the cranial nerves also contain autonomic fibers, and a fourth is almost purely a component of the autonomic system. The oculomotor, facial, and glossopharyngeal nerves contain fibers that contact autonomic ganglia. The oculomotor fibers initiate pupillary constriction, whereas the facial and glossopharyngeal fibers both initiate salivation. The vagus nerve primarily targets autonomic ganglia in the thoracic and upper abdominal cavities.

Visit this site to read about a man who wakes with a headache and a loss of vision. His regular doctor sent him to an ophthalmologist to the vision loss. The ophthalmologist recognizes a greater problem and immediately sends him to the emergency room. Once there, the patient undergoes a large battery of tests, but a definite cause cannot be found. A specialist recognizes the problem as meningitis, but the question is what caused it originally. How can that be cured? The loss of vision comes from swelling around the optic nerve, which probably presented as a bulge on the inside of the eye. Why is swelling related to meningitis going to push on the optic nerve?

Another important aspect of the cranial nerves that lends itself to a mnemonic is the functional role each nerve plays. The nerves fall into one of three basic groups. They are sensory, motor, or both (see Table 1). The sentence, “Some Say Marry Money But My Brother Says Brains Beauty Matter More,” corresponds to the basic function of each nerve.

The first, second, and eighth nerves are purely sensory: the olfactory (CNI), optic (CNII), and vestibulocochlear (CNVIII) nerves. The three eye-movement nerves are all motor: the oculomotor (CNIII), trochlear (CNIV), and abducens (CNVI). The spinal accessory (CNXI) and hypoglossal (CNXII) nerves are also strictly motor. The remainder of the nerves contain both sensory and motor fibers. They are the trigeminal (CNV), facial (CNVII), glossopharyngeal (CNIX), and vagus (CNX) nerves.

The nerves that convey both are often related to each other. The trigeminal and facial nerves both concern the face; one concerns the sensations and the other concerns the muscle movements. The facial and glossopharyngeal nerves are both responsible for conveying gustatory, or taste, sensations as well as controlling salivary glands. The vagus nerve is involved in visceral responses to taste, namely the gag reflex. This is not an exhaustive list of what these combination nerves do, but there is a thread of relation between them.

Spinal Nerves

The nerves connected to the spinal cord are the spinal nerves. The arrangement of these nerves is much more regular than that of the cranial nerves. All of the spinal nerves are combined sensory and motor axons that separate into two nerve roots. The sensory axons enter the spinal cord as the dorsal nerve root. The motor fibers, both somatic and autonomic, emerge as the ventral nerve root. The dorsal root ganglion for each nerve is an enlargement of the spinal nerve.

There are 31 spinal nerves, named for the level of the spinal cord at which each one emerges. There are eight pairs of cervical nerves designated C1 to C8, twelve thoracic nerves designated T1 to T12, five pairs of lumbar nerves designated L1 to L5, five pairs of sacral nerves designated S1 to S5, and one pair of coccygeal nerves. The nerves are numbered from the superior to inferior positions, and each emerges from the vertebral column through the intervertebral foramen at its level. The first nerve, C1, emerges between the first cervical vertebra and the occipital bone. The second nerve, C2, emerges between the first and second cervical vertebrae. The same occurs for C3 to C7, but C8 emerges between the seventh cervical vertebra and the first thoracic vertebra. For the thoracic and lumbar nerves, each one emerges between the vertebra that has the same designation and the next vertebra in the column. The sacral nerves emerge from the sacral foramina along the length of that unique vertebra.

Spinal nerves extend outward from the vertebral column to enervate the periphery. The nerves in the periphery are not straight continuations of the spinal nerves, but rather the reorganization of the axons in those nerves to follow different courses. Axons from different spinal nerves will come together into a **systemic nerve**. This occurs at four places along the length of the vertebral column, each identified as a **nerve plexus**, whereas the other spinal nerves directly correspond to nerves at their respective levels. In this instance, the word plexus is used to describe networks of nerve fibers with no associated cell bodies. Of the four nerve plexuses, two are found at the cervical level, one at the lumbar level, and one at the sacral level (Figure 6).

The **cervical plexus** is composed of axons from spinal nerves C1 through C5 and branches into nerves in the posterior neck and head, as well as the **phrenic nerve**, which connects to the diaphragm at the base of the thoracic cavity. The other plexus from the cervical level is the **brachial plexus**.

Spinal nerves C4 through T1 reorganize through this plexus to give rise to the nerves of the arms, as the name brachial suggests. A large nerve from this plexus is the **radial nerve** from which the **axillary nerve** branches to go to the armpit region. The radial nerve continues through the arm and is paralleled by the **ulnar nerve** and the **median nerve**. The **lumbar plexus** arises from all the lumbar spinal nerves and gives rise to nerves enervating the pelvic region and the anterior leg. The **femoral nerve** is one of the major nerves from this plexus, which gives rise to the **saphenous nerve** as a branch that extends through the anterior lower leg.

The **sacral plexus** comes from the lower lumbar nerves L4 and L5 and the sacral nerves S1 to S4. The most significant systemic nerve to come from this plexus is the **sciatic nerve**, which is a combination of the **tibial nerve** and the **fibular nerve**. The sciatic nerve extends across the hip joint and is most commonly associated with the condition **sciatica**, which is the result of compression or irritation of the nerve or any of the spinal nerves giving rise to it.

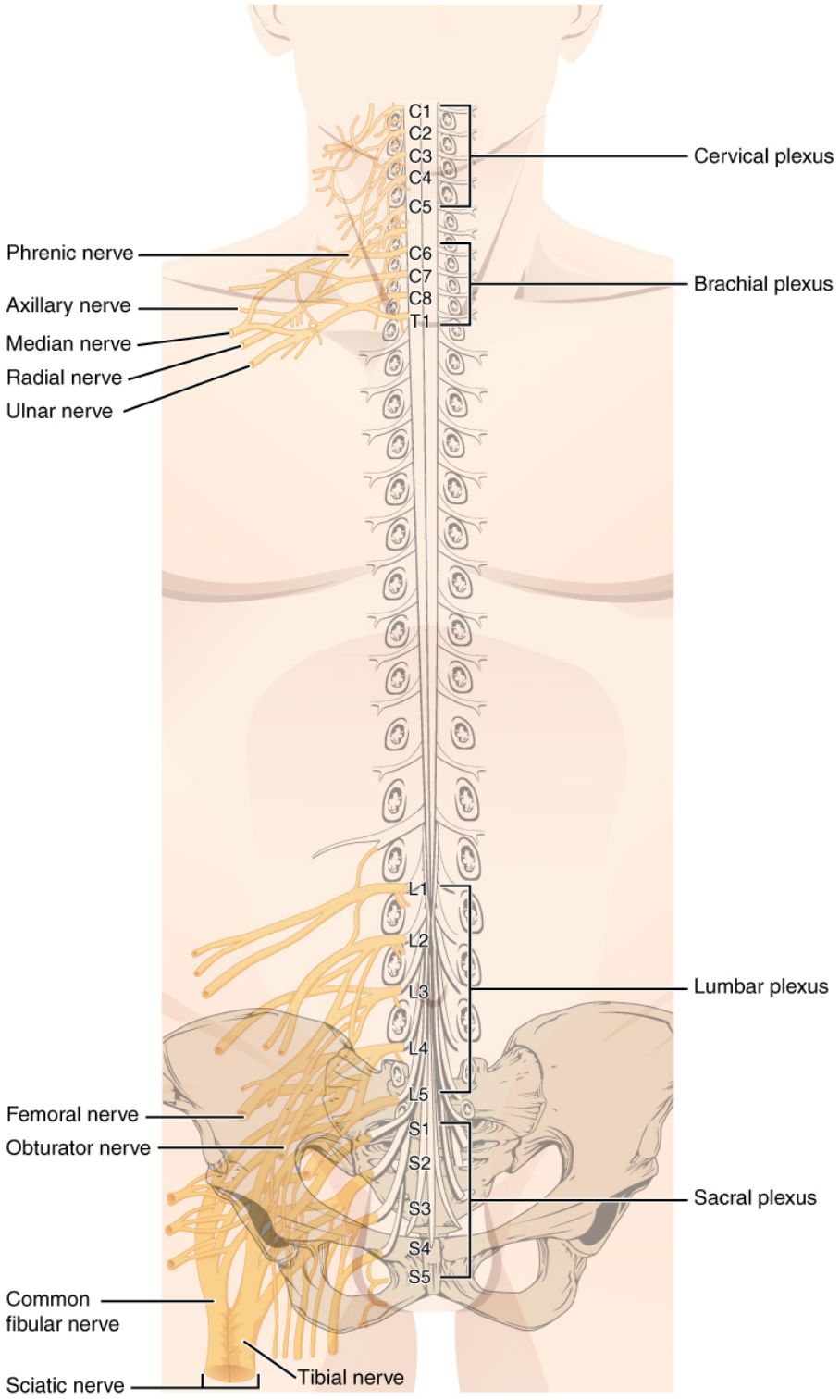


Figure 6. *Nerve Plexuses of the Body There are four main nerve plexuses in the human body. The cervical plexus supplies nerves to the posterior head and neck, as well as to the diaphragm. The brachial plexus supplies nerves to the arm. The lumbar plexus supplies nerves to the anterior leg. The sacral plexus supplies nerves to the posterior leg.*

These plexuses are described as arising from spinal nerves and giving rise to certain systemic nerves, but they contain fibers that serve sensory functions or fibers that serve motor functions. This means that some fibers extend from cutaneous or other peripheral sensory surfaces and send action potentials into the CNS. Those are

axons of sensory neurons in the dorsal root ganglia that enter the spinal cord through the dorsal nerve root. Other fibers are the axons of motor neurons of the anterior horn of the spinal cord, which emerge in the ventral nerve root and send action potentials to cause skeletal muscles to contract in their target regions. For example, the radial nerve contains fibers of cutaneous sensation in the arm, as well as motor fibers that move muscles in the arm. Spinal nerves of the thoracic region, T2 through T11, are not part of the plexuses but rather emerge and give rise to the **intercostal nerves** found between the ribs, which articulate with the vertebrae surrounding the spinal nerve.

Aging and the Nervous System

Anosmia is the loss of the sense of smell. It is often the result of the olfactory nerve being severed, usually because of blunt force trauma to the head. The sensory neurons of the olfactory epithelium have a limited lifespan of approximately one to four months, and new ones are made on a regular basis. The new neurons extend their axons into the CNS by growing along the existing fibers of the olfactory nerve. The ability of these neurons to be replaced is lost with age. Age-related anosmia is not the result of impact trauma to the head, but rather a slow loss of the sensory neurons with no new neurons born to replace them.

Smell is an important sense, especially for the enjoyment of food. There are only five tastes sensed by the tongue, and two of them are generally thought of as unpleasant tastes (sour and bitter). The rich sensory experience of food is the result of odor molecules associated with the food, both as food is moved into the mouth, and therefore passes under the nose, and when it is chewed and molecules are released to move up the pharynx into the posterior nasal cavity.

Anosmia results in a loss of the enjoyment of food. As the replacement of olfactory neurons declines with age, anosmia can set in. Without the sense of smell, many sufferers complain of food tasting bland. Often, the only way to enjoy food is to add seasoning that can be sensed on the tongue, which usually means adding table salt. The problem with this solution, however, is that this increases sodium intake, which can lead to cardiovascular problems through water retention and the associated increase in blood pressure.

VIDEO: THE UNFIXED BRAIN

In this teaching video, Suzanne Stensaas, Ph.D., Professor of Neurobiology and Anatomy at the University of Utah School of Medicine, demonstrates the properties and anatomy of an unfixed brain. WARNING: The video contains graphic images, a human brain from a recent autopsy. Background noise is unrelated to this brain or the deceased. There are two purposes for this video: 1) to stress the vulnerability of the brain to highlight the importance of wearing helmets, seat belts, and taking care of this very precious tissue, and 2) to use as a teaching aid for students who only have access to fixed tissue, models, and pictures.

Watch this video online: https://youtu.be/jHxyP-nUhUY

VIDEO: THE UNFIXED SPINAL CORD

In this teaching video, Suzanne Stensaas, Ph.D., demonstrates the properties and anatomy of an unfixed spinal cord. WARNING: The video contains graphic images, a spinal cord from a recent autopsy.

Watch this video online: https://youtu.be/RiGgNarlvK4

CASE STUDY: THE BRAIN

Interactive Link

Click on the link below to access the case study created by Tangi Mitchell and Cheryl L. Watson of Central Connecticut State University

Biological Sciences Central Connecticut State University

ADDITIONAL LINKS

Interactive Link

Consider downloading the Netter's Anatomy Atlas below:

https://itunes.apple.com/us/app/netters-anatomy-atlas-free/id457575880?mt=8

GLOSSARY: THE NERVOUS SYSTEM

abducens nerve: sixth cranial nerve; responsible for contraction of one of the extraocular muscles

alar plate: developmental region of the spinal cord that gives rise to the posterior horn of the gray matter

amygdala: nucleus deep in the temporal lobe of the cerebrum that is related to memory and emotional behavior

anterior column: white matter between the anterior horns of the spinal cord composed of many different groups of axons of both ascending and descending tracts

anterior horn: gray matter of the spinal cord containing multipolar motor neurons, sometimes referred to as the ventral horn

anterior median fissure: deep midline feature of the anterior spinal cord, marking the separation between the right and left sides of the cord

anterior spinal artery: blood vessel from the merged branches of the vertebral arteries that runs along the anterior surface of the spinal cord

arachnoid granulation: outpocket of the arachnoid membrane into the dural sinuses that allows for reabsorption of CSF into the blood

arachnoid mater: middle layer of the meninges named for the spider-web–like trabeculae that extend between it and the pia mater

arachnoid trabeculae: filaments between the arachnoid and pia mater within the subarachnoid space

ascending tract: central nervous system fibers carrying sensory information from the spinal cord or periphery to the brain

axillary nerve: systemic nerve of the arm that arises from the brachial plexus

Broca's area: region of the frontal lobe associated with the motor commands necessary for speech production and located only in the cerebral hemisphere responsible for language production, which is the left side in approximately 95 percent of the population

Brodmann's areas: mapping of regions of the cerebral cortex based on microscopic anatomy that relates specific areas to functional differences, as described by Brodmann in the early 1900s

basal forebrain: nuclei of the cerebrum related to modulation of sensory stimuli and attention through broad projections to the cerebral cortex, loss of which is related to Alzheimer's disease

basal nuclei: nuclei of the cerebrum (with a few components in the upper brain stem and diencephalon) that are responsible for assessing cortical movement commands and comparing them with the general state of the individual through broad modulatory activity of dopamine neurons; largely related to motor functions, as evidenced through the symptoms of Parkinson's and Huntington's diseases

basal plate: developmental region of the spinal cord that gives rise to the lateral and anterior horns of gray matter

basilar artery: blood vessel from the merged vertebral arteries that runs along the dorsal surface of the brain stem

brachial plexus: nerve plexus associated with the lower cervical spinal nerves and first thoracic spinal nerve

brain stem: region of the adult brain that includes the midbrain, pons, and medulla oblongata and develops from the mesencephalon, metencephalon, and myelencephalon of the embryonic brain

carotid canal: opening in the temporal bone through which the internal carotid artery enters the cranium

cauda equina: bundle of spinal nerve roots that descend from the lower spinal cord below the first lumbar vertebra and lie within the vertebral cavity; has the appearance of a horse's tail

caudate: nucleus deep in the cerebrum that is part of the basal nuclei; along with the putamen, it is part of the striatum

central canal: hollow space within the spinal cord that is the remnant of the center of the neural tube

central sulcus: surface landmark of the cerebral cortex that marks the boundary between the frontal and parietal lobes

cephalic flexure: curve in midbrain of the embryo that positions the forebrain ventrally

cerebellum: region of the adult brain connected primarily to the pons that developed from the metencephalon (along with the pons) and is largely responsible for comparing information from the cerebrum with sensory feedback from the periphery through the spinal cord

cerebral aqueduct: connection of the ventricular system between the third and fourth ventricles located in the midbrain

cerebral cortex: outer gray matter covering the forebrain, marked by wrinkles and folds known as gyri and sulci

cerebral hemisphere: one half of the bilaterally symmetrical cerebrum

cerebrum: region of the adult brain that develops from the telencephalon and is responsible for higher neurological functions such as memory, emotion, and consciousness

cervical plexus: nerve plexus associated with the upper cervical spinal nerves

choroid plexus: specialized structures containing ependymal cells lining blood capillaries that filter blood to produce CSF in the four ventricles of the brain

circle of Willis: unique anatomical arrangement of blood vessels around the base of the brain that maintains perfusion of blood into the brain even if one component of the structure is blocked or narrowed

common carotid artery: blood vessel that branches off the aorta (or the brachiocephalic artery on the right) and supplies blood to the head and neck

corpus callosum: large white matter structure that connects the right and left cerebral hemispheres

cranial nerve ganglion: sensory ganglion of cranial nerves

cranial nerve: one of twelve nerves connected to the brain that are responsible for sensory or motor functions of the head and neck

descending tract: central nervous system fibers carrying motor commands from the brain to the spinal cord or periphery

diencephalon: region of the adult brain that retains its name from embryonic development and includes the thalamus and hypothalamus

direct pathway: connections within the basal nuclei from the striatum to the globus pallidus internal segment and substantia nigra pars reticulata that disinhibit the thalamus to increase cortical control of movement

disinhibition: disynaptic connection in which the first synapse inhibits the second cell, which then stops inhibiting the final target

dorsal (posterior) nerve root: axons entering the posterior horn of the spinal cord

dorsal (posterior) root ganglion: sensory ganglion attached to the posterior nerve root of a spinal nerve

dura mater: tough, fibrous, outer layer of the meninges that is attached to the inner surface of the cranium and vertebral column and surrounds the entire CNS

dural sinus: any of the venous structures surrounding the brain, enclosed within the dura mater, which drain blood from the CNS to the common venous return of the jugular veins

endoneurium: innermost layer of connective tissue that surrounds individual axons within a nerve

enteric nervous system: peripheral structures, namely ganglia and nerves, that are incorporated into the digestive system organs

enteric plexus: neuronal plexus in the wall of the intestines, which is part of the enteric nervous system

epineurium: outermost layer of connective tissue that surrounds an entire nerve

epithalamus: region of the diecephalon containing the pineal gland

esophageal plexus: neuronal plexus in the wall of the esophagus that is part of the enteric nervous system

extraocular muscles: six skeletal muscles that control eye movement within the orbit

facial nerve: seventh cranial nerve; responsible for contraction of the facial muscles and for part of the sense of taste, as well as causing saliva production

fascicle: small bundles of nerve or muscle fibers enclosed by connective tissue

femoral nerve: systemic nerve of the anterior leg that arises from the lumbar plexus

fibular nerve: systemic nerve of the posterior leg that begins as part of the sciatic nerve

foramen magnum: large opening in the occipital bone of the skull through which the spinal cord emerges and the vertebral arteries enter the cranium

forebrain: anterior region of the adult brain that develops from the prosencephalon and includes the cerebrum and diencephalon

fourth ventricle: the portion of the ventricular system that is in the region of the brain stem and opens into the subarachnoid space through the median and lateral apertures

frontal eye field: region of the frontal lobe associated with motor commands to orient the eyes toward an object of visual attention

frontal lobe: region of the cerebral cortex directly beneath the frontal bone of the cranium

gastric plexuses: neuronal networks in the wall of the stomach that are part of the enteric nervous system

globus pallidus: nuclei deep in the cerebrum that are part of the basal nuclei and can be divided into the internal and external segments

glossopharyngeal nerve: ninth cranial nerve; responsible for contraction of muscles in the tongue and throat and for part of the sense of taste, as well as causing saliva production

gyrus: ridge formed by convolutions on the surface of the cerebrum or cerebellum

hindbrain: posterior region of the adult brain that develops from the rhombencephalon and includes the pons, medulla oblongata, and cerebellum

hippocampus: gray matter deep in the temporal lobe that is very important for long-term memory formation

hypoglossal nerve: twelfth cranial nerve; responsible for contraction of muscles of the tongue

hypothalamus: major region of the diencephalon that is responsible for coordinating autonomic and endocrine control of homeostasis

indirect pathway: connections within the basal nuclei from the striatum through the globus pallidus external segment and subthalamic nucleus to the globus pallidus internal segment/substantia nigra pars compacta that result in inhibition of the thalamus to decrease cortical control of movement

inferior colliculus: half of the midbrain tectum that is part of the brain stem auditory pathway

inferior olive: nucleus in the medulla that is involved in processing information related to motor control

intercostal nerve: systemic nerve in the thoracic cavity that is found between two ribs

internal carotid artery: branch from the common carotid artery that enters the cranium and supplies blood to the brain

interventricular foramina: openings between the lateral ventricles and third ventricle allowing for the passage of CSF

jugular veins: blood vessels that return “used” blood from the head and neck

kinesthesia: general sensory perception of movement of the body

lateral apertures: pair of openings from the fourth ventricle to the subarachnoid space on either side and between the medulla and cerebellum

lateral column: white matter of the spinal cord between the posterior horn on one side and the axons from the anterior horn on the same side; composed of many different groups of axons, of both ascending and descending tracts, carrying motor commands to and from the brain

lateral horn: region of the spinal cord gray matter in the thoracic, upper lumbar, and sacral regions that is the central component of the sympathetic division of the autonomic nervous system

lateral sulcus: surface landmark of the cerebral cortex that marks the boundary between the temporal lobe and the frontal and parietal lobes

lateral ventricles: portions of the ventricular system that are in the region of the cerebrum

limbic cortex: collection of structures of the cerebral cortex that are involved in emotion, memory, and behavior and are part of the larger limbic system

limbic system: structures at the edge (limit) of the boundary between the forebrain and hindbrain that are most associated with emotional behavior and memory formation

longitudinal fissure: large separation along the midline between the two cerebral hemispheres

lumbar plexus: nerve plexus associated with the lumbar spinal nerves

lumbar puncture: procedure used to withdraw CSF from the lower lumbar region of the vertebral column that avoids the risk of damaging CNS tissue because the spinal cord ends at the upper lumbar vertebrae

median aperture: singular opening from the fourth ventricle into the subarachnoid space at the midline between the medulla and cerebellum

median nerve: systemic nerve of the arm, located between the ulnar and radial nerves

meninges: protective outer coverings of the CNS composed of connective tissue

mesencephalon: primary vesicle of the embryonic brain that does not significantly change through the rest of embryonic development and becomes the midbrain

metencephalon: secondary vesicle of the embryonic brain that develops into the pons and the cerebellum

midbrain: middle region of the adult brain that develops from the mesencephalon

myelencephalon: secondary vesicle of the embryonic brain that develops into the medulla

nerve plexus: network of nerves without neuronal cell bodies included

neural crest: tissue that detaches from the edges of the neural groove and migrates through the embryo to develop into peripheral structures of both nervous and non-nervous tissues

neural fold: elevated edge of the neural groove

neural groove: region of the neural plate that folds into the dorsal surface of the embryo and closes off to become the neural tube

neural plate: thickened layer of neuroepithelium that runs longitudinally along the dorsal surface of an embryo and gives rise to nervous system tissue

neural tube: precursor to structures of the central nervous system, formed by the invagination and separation of neuroepithelium

neuraxis: central axis to the nervous system, from the posterior to anterior ends of the neural tube; the inferior tip of the spinal cord to the anterior surface of the cerebrum

occipital lobe: region of the cerebral cortex directly beneath the occipital bone of the cranium

occipital sinuses: dural sinuses along the edge of the occipital lobes of the cerebrum

oculomotor nerve: third cranial nerve; responsible for contraction of four of the extraocular muscles, the muscle in the upper eyelid, and pupillary constriction

olfaction: special sense responsible for smell, which has a unique, direct connection to the cerebrum

olfactory nerve: first cranial nerve; responsible for the sense of smell

optic nerve: second cranial nerve; responsible for visual sensation

orthostatic reflex: sympathetic function that maintains blood pressure when standing to offset the increased effect of gravity

paravertebral ganglia: autonomic ganglia superior to the sympathetic chain ganglia

parietal lobe: region of the cerebral cortex directly beneath the parietal bone of the cranium

parieto-occipital sulcus: groove in the cerebral cortex representing the border between the parietal and occipital cortices

perineurium: layer of connective tissue surrounding fascicles within a nerve

phrenic nerve: systemic nerve from the cervical plexus that enervates the diaphragm

pia mater: thin, innermost membrane of the meninges that directly covers the surface of the CNS

plexus: network of nerves or nervous tissue

postcentral gyrus: ridge just posterior to the central sulcus, in the parietal lobe, where somatosensory processing initially takes place in the cerebrum

posterior columns: white matter of the spinal cord that lies between the posterior horns of the gray matter, sometimes referred to as the dorsal column; composed of axons of ascending tracts that carry sensory information up to the brain

posterior horn: gray matter region of the spinal cord in which sensory input arrives, sometimes referred to as the dorsal horn

posterior median sulcus: midline feature of the posterior spinal cord, marking the separation between right and left sides of the cord

posterolateral sulcus: feature of the posterior spinal cord marking the entry of posterior nerve roots and the separation between the posterior and lateral columns of the white matter

precentral gyrus: primary motor cortex located in the frontal lobe of the cerebral cortex

prefrontal lobe: specific region of the frontal lobe anterior to the more specific motor function areas, which can be related to the early planning of movements and intentions to the point of being personality-type functions

premotor area: region of the frontal lobe responsible for planning movements that will be executed through the primary motor cortex

prevertebral ganglia: autonomic ganglia that are anterior to the vertebral column and functionally related to the sympathetic chain ganglia

primary vesicle: initial enlargements of the anterior neural tube during embryonic development that develop into the forebrain, midbrain, and hindbrain

proprioception: general sensory perceptions providing information about location and movement of body parts; the “sense of the self”

prosencephalon: primary vesicle of the embryonic brain that develops into the forebrain, which includes the cerebrum and diencephalon

putamen: nucleus deep in the cerebrum that is part of the basal nuclei; along with the caudate, it is part of the striatum

radial nerve: systemic nerve of the arm, the distal component of which is located near the radial bone

reticular formation: diffuse region of gray matter throughout the brain stem that regulates sleep, wakefulness, and states of consciousness

rhombencephalon: primary vesicle of the embryonic brain that develops into the hindbrain, which includes the pons, cerebellum, and medulla

sacral plexus: nerve plexus associated with the lower lumbar and sacral spinal nerves

saphenous nerve: systemic nerve of the lower anterior leg that is a branch from the femoral nerve

sciatic nerve: systemic nerve from the sacral plexus that is a combination of the tibial and fibular nerves and extends across the hip joint and gluteal region into the upper posterior leg

sciatica: painful condition resulting from inflammation or compression of the sciatic nerve or any of the spinal nerves that contribute to it

secondary vesicle: five vesicles that develop from primary vesicles, continuing the process of differentiation of the embryonic brain

sigmoid sinuses: dural sinuses that drain directly into the jugular veins

somatosensation: general senses related to the body, usually thought of as the senses of touch, which would include pain, temperature, and proprioception

spinal accessory nerve: eleventh cranial nerve; responsible for contraction of neck muscles

spinal nerve: one of 31 nerves connected to the spinal cord

straight sinus: dural sinus that drains blood from the deep center of the brain to collect with the other sinuses

striatum: the caudate and putamen collectively, as part of the basal nuclei, which receive input from the cerebral cortex

subarachnoid space: space between the arachnoid mater and pia mater that contains CSF and the fibrous connections of the arachnoid trabeculae

subcortical nucleus: all the nuclei beneath the cerebral cortex, including the basal nuclei and the basal forebrain

substantia nigra pars compacta: nuclei within the basal nuclei that release dopamine to modulate the function of the striatum; part of the motor pathway

substantia nigra pars reticulata: nuclei within the basal nuclei that serve as an output center of the nuclei; part of the motor pathway

subthalamus: nucleus within the basal nuclei that is part of the indirect pathway

sulcus: groove formed by convolutions in the surface of the cerebral cortex

superior colliculus: half of the midbrain tectum that is responsible for aligning visual, auditory, and somatosensory spatial perceptions

superior sagittal sinus: dural sinus that runs along the top of the longitudinal fissure and drains blood from the majority of the outer cerebrum

sympathetic chain ganglia: autonomic ganglia in a chain along the anterolateral aspect of the vertebral column that are responsible for contributing to homeostatic mechanisms of the autonomic nervous system

systemic nerve: nerve in the periphery distal to a nerve plexus or spinal nerve

tectum: region of the midbrain, thought of as the roof of the cerebral aqueduct, which is subdivided into the inferior and superior colliculi

tegmentum: region of the midbrain, thought of as the floor of the cerebral aqueduct, which continues into the pons and medulla as the floor of the fourth ventricle

telencephalon: secondary vesicle of the embryonic brain that develops into the cerebrum

temporal lobe: region of the cerebral cortex directly beneath the temporal bone of the cranium

terminal ganglion: autonomic ganglia that are near or within the walls of organs that are responsible for contributing to homeostatic mechanisms of the autonomic nervous system

thalamus: major region of the diencephalon that is responsible for relaying information between the cerebrum and the hindbrain, spinal cord, and periphery

third ventricle: portion of the ventricular system that is in the region of the diencephalon

tibial nerve: systemic nerve of the posterior leg that begins as part of the sciatic nerve

transverse sinuses: dural sinuses that drain along either side of the occipital–cerebellar space

trigeminal ganglion: sensory ganglion that contributes sensory fibers to the trigeminal nerve

trigeminal nerve: fifth cranial nerve; responsible for cutaneous sensation of the face and contraction of the muscles of mastication

trochlear nerve: fourth cranial nerve; responsible for contraction of one of the extraocular muscles

ulnar nerve: systemic nerve of the arm located close to the ulna, a bone of the forearm

vagus nerve: tenth cranial nerve; responsible for the autonomic control of organs in the thoracic and upper abdominal cavities

ventral (anterior) nerve root: axons emerging from the anterior or lateral horns of the spinal cord

ventricles: remnants of the hollow center of the neural tube that are spaces for cerebrospinal fluid to circulate through the brain

vertebral arteries: arteries that ascend along either side of the vertebral column through the transverse foramina of the cervical vertebrae and enter the cranium through the foramen magnum

vestibulocochlear nerve: eighth cranial nerve; responsible for the sensations of hearing and balance

PRACTICE TEST: ANATOMY OF THE NERVOUS SYSTEM

Review the material from this module by completing the practice in course online.

MODULE 14: THE NERVOUS SYSTEM AND NERVOUS TISSUE

INTRODUCTION TO THE NERVOUS SYSTEM AND NERVOUS TISSUE

Learning Objectives

- Name the major divisions of the nervous system, both anatomical and functional
- Describe the functional and structural differences between gray matter and white matter structures
- Name the parts of the multipolar neuron in order of polarity
- List the types of glial cells and assign each to the proper division of the nervous system, along with their function(s)
- Distinguish the major functions of the nervous system: sensation, integration, and response
- Describe the components of the membrane that establish the resting membrane potential
- Describe the changes that occur to the membrane that result in the action potential
- Explain the differences between types of graded potentials
- Categorize the major neurotransmitters by chemical type and effect

The nervous system is a very complex organ system. In Peter D. Kramer's book *Listening to Prozac*, a pharmaceutical researcher is quoted as saying, "If the human brain were simple enough for us to understand, we would be too simple to understand it" (1994). That quote is from the early 1990s; in the two decades since, progress has continued at an amazing rate within the scientific disciplines of neuroscience. It is an interesting conundrum to consider that the complexity of the nervous system may be too complex for it (that is, for us) to completely unravel. But our current level of understanding is probably nowhere close to that limit.

One easy way to begin to understand the structure of the nervous system is to start with the large divisions and work through to a more in-depth understanding. In other chapters, the finer details of the

Figure 1. Robotic Arms Playing Foosball *As the neural circuitry of the nervous system has become more fully understood and robotics more*

nervous system will be explained, but first looking at an overview of the system will allow you to begin to understand how its parts work together. The focus of this chapter is on nervous (neural) tissue, both its structure and its function. But before you learn about that, you will see a big picture of the system—actually, a few big pictures.

sophisticated, it is now possible to integrate technology with the body and restore abilities following traumatic events. At some point in the future, will this type of technology lead to the ability to augment our nervous systems? (credit: U.S. Army/Wikimedia Commons)

BASIC STRUCTURE AND FUNCTION OF THE NERVOUS SYSTEM

Learning Objectives

- Identify the anatomical and functional divisions of the nervous system
- Relate the functional and structural differences between gray matter and white matter structures of the nervous system to the structure of neurons
- List the basic functions of the nervous system

The picture you have in your mind of 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. In comparison, it is easy to see that the stomach is different than the esophagus or the liver, so you can imagine the digestive system as a collection of specific organs.

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)** is everything else (Figure 1). 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. It is a bit of an oversimplification to say that the CNS is what is inside these two cavities and the peripheral nervous system is outside of them, but that is one way to start to think about it. In actuality, there are some elements of the peripheral nervous system that are within the cranial or vertebral cavities. The peripheral nervous system is so named because it is on the periphery—meaning beyond the brain and spinal cord. Depending on different aspects of the nervous system, the dividing line between central and peripheral is not necessarily universal.

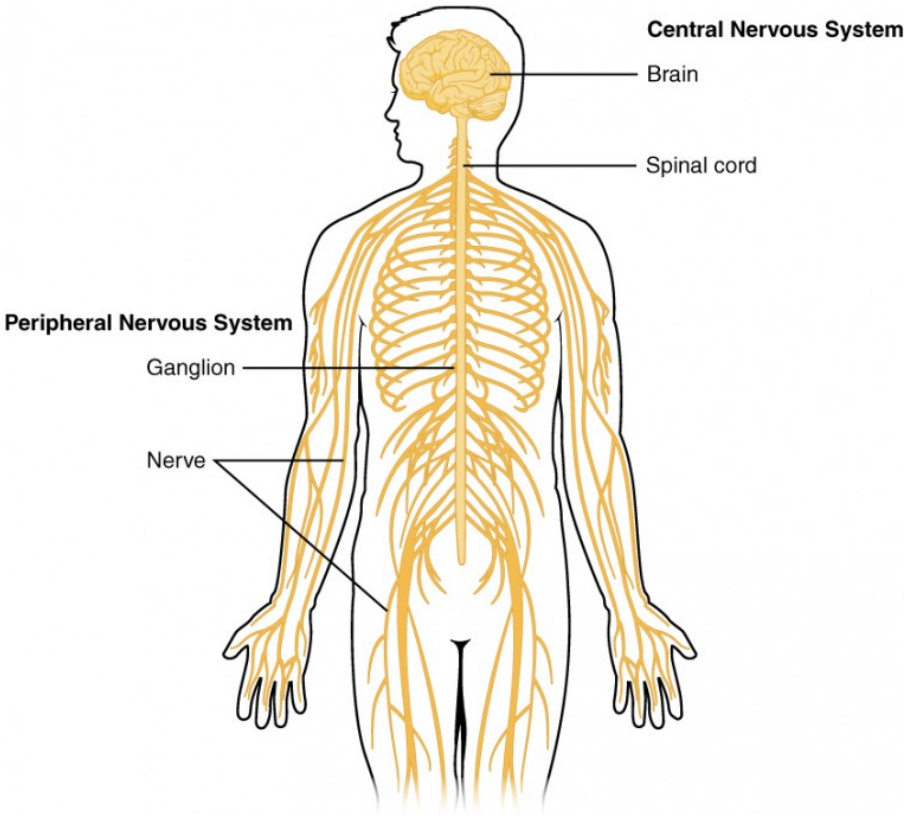


Figure 1. Central and Peripheral Nervous System *The structures of the PNS are referred to as ganglia and nerves, which can be seen as distinct structures. The equivalent structures in the CNS are not obvious from this overall perspective and are best examined in prepared tissue under the microscope.*

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.

In order 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). Figure 2 demonstrates the appearance of these regions in the brain and spinal cord. The colors ascribed to these regions are what would be seen in "fresh," or unstained, nervous tissue. Gray matter is not necessarily gray. It can be pinkish because of blood content, or even slightly tan, depending on how long the tissue has been preserved. But white matter is white because axons are insulated by a lipid-rich substance called **myelin**. Lipids can appear as white ("fatty") material, much like the fat on a raw piece of chicken or beef. Actually, gray matter may have that color ascribed to it because next to the white matter, it is just darker—hence, gray.

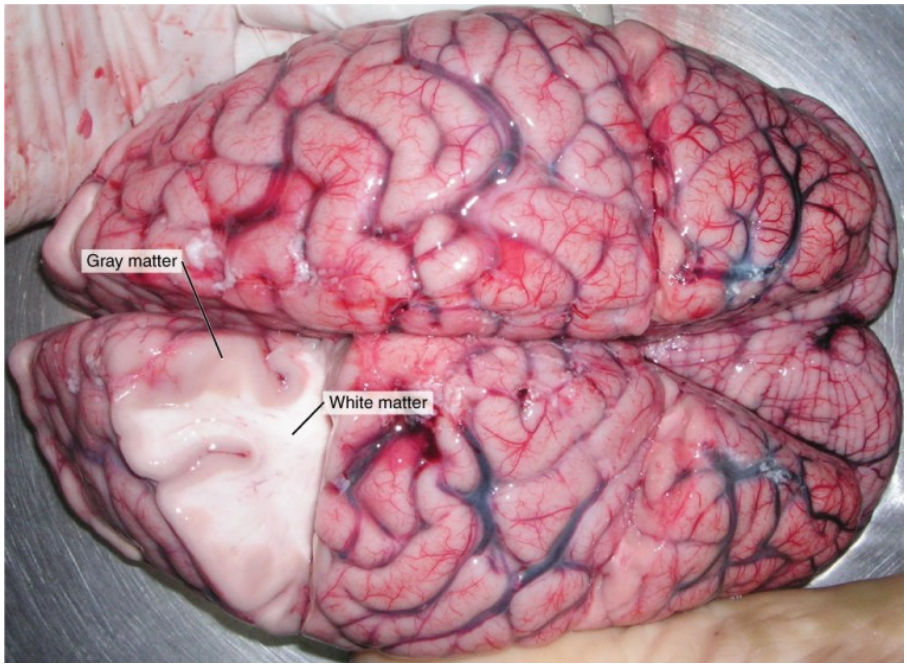


Figure 2. Gray Matter and White Matter *A brain removed during an autopsy, with a partial section removed, shows white matter surrounded by gray matter. Gray matter makes up the outer cortex of the brain. (credit: modification of work by "Suseno"/Wikimedia Commons)*

The distinction between gray matter and white matter is most often applied to central nervous tissue, which has large regions that can be seen with the unaided eye. When looking at peripheral structures, often a microscope is used and the tissue is stained with artificial colors. That is not to say that central nervous tissue cannot be stained and viewed under a microscope, but unstained tissue is most likely from the CNS—for example, a frontal section of the brain or cross section of the spinal cord.

Regardless of the appearance of stained or unstained tissue, the cell bodies of neurons or axons can be located in discrete anatomical structures that need to be named. Those names are specific to whether the structure is central or peripheral. A localized collection of neuron cell bodies in the CNS is referred to as a **nucleus**. In the PNS, a cluster of neuron cell bodies is referred to as a **ganglion**. Figure 3 indicates how the term nucleus has a few different meanings within anatomy and physiology. It is the center of an atom, where protons and neutrons are found; it is the center of a cell, where the DNA is found; and it is a center of some function in the CNS. There is also a potentially confusing use of the word ganglion (plural = ganglia) that has a historical explanation. In the central nervous system, there is a group of nuclei that are connected together and were once called the basal ganglia before "ganglion" became accepted as a description for a peripheral structure. Some sources refer to this group of nuclei as the "basal nuclei" to avoid confusion.

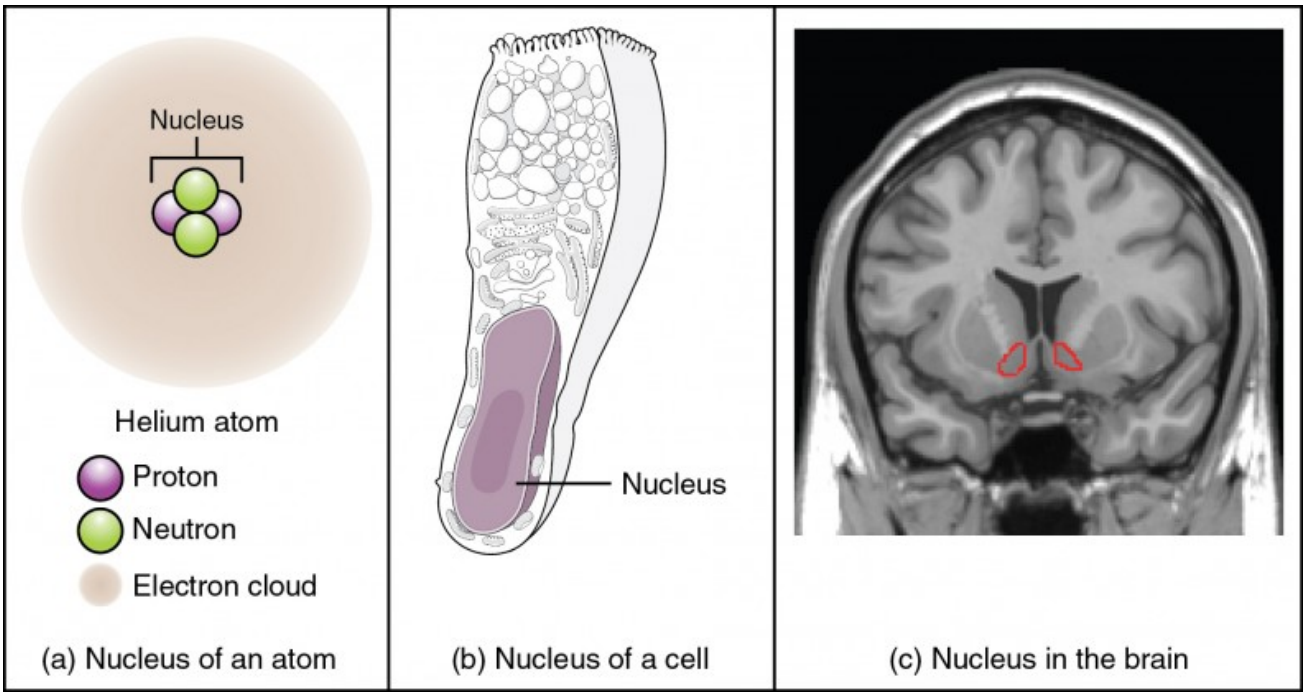


Figure 3. What Is a Nucleus? *(a) The nucleus of an atom contains its protons and neutrons. (b) The nucleus of a cell is the organelle that contains DNA. (c) A nucleus in the CNS is a localized center of function with the cell bodies of several neurons, shown here circled in red. (credit c: "Was a bee"/Wikimedia Commons)*

Terminology applied to bundles of axons also differs depending on location. A bundle of axons, or fibers, found in the CNS is called a **tract** whereas the same thing in the PNS would be called a **nerve**. There is an important point to make about these terms, which is that they can both be used to refer to the same bundle of axons. When those axons are in the PNS, the term is nerve, but if they are CNS, the term is tract. The most obvious example of this is the axons that project from the retina into the brain. Those axons are called the optic nerve as they leave the eye, but when they are inside the cranium, they are referred to as the optic tract. There is a specific place where the name changes, which is the optic chiasm, but they are still the same axons (Figure 4).

A similar situation outside of science can be described for some roads. Imagine a road called "Broad Street" in a town called "Anyville." The road leaves Anyville and goes to the next town over, called "Hometown." When the road crosses the line between the two towns and is in Hometown, its name changes to "Main Street." That is the idea behind the naming of the retinal axons. In the PNS, they are called the optic nerve, and in the CNS, they are the optic tract. Table 1 helps to clarify which of these terms apply to the central or peripheral nervous systems.

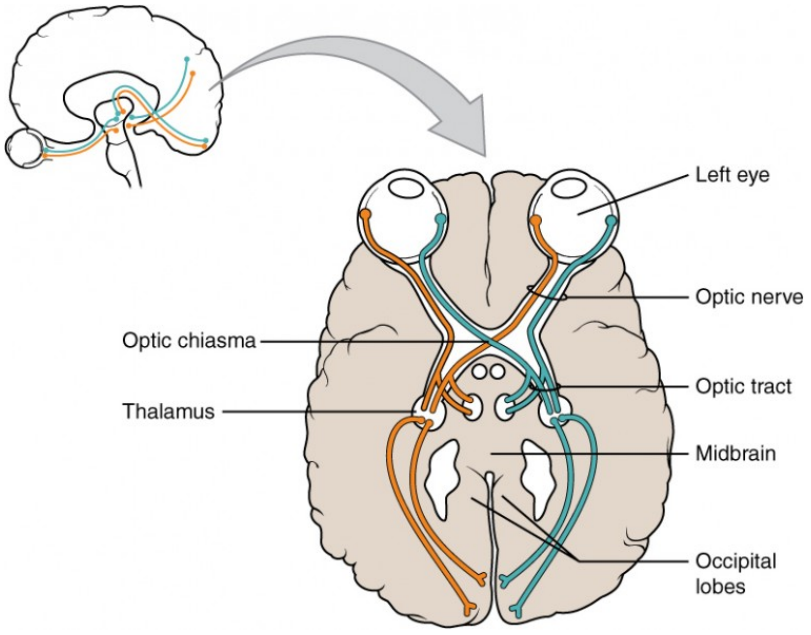


Figure 4. Optic Nerve Versus Optic Tract *This drawing of the connections of the eye to the brain shows the optic nerve extending from the eye to the chiasm, where the structure continues as the optic tract. The same axons*

In 2003, the Nobel Prize in Physiology or Medicine was awarded to Paul C. Lauterbur and Sir Peter Mansfield for discoveries related to magnetic resonance imaging (MRI). This is a tool to see the structures of the body (not just the nervous system) that depends on magnetic fields associated with certain atomic nuclei. The utility of this technique

in the nervous system is that fat tissue and water appear as different shades between black and white. Because white matter is fatty (from myelin) and gray matter is not, they can be easily distinguished in MRI images.

extend from the eye to the brain through these two bundles of fibers, but the chiasm represents the border between peripheral and central.

Table 1. Structures of the CNS and PNS

	CNS	PNS
Group of Neuron Cell Bodies (i.e., gray matter)	Nucleus	Ganglion
Bundle of Axons (i.e., white matter)	Tract	Nerve

Visit the Nobel Prize web site to play an interactive game that demonstrates the use of this technology and compares it with other types of imaging technologies. Also, the results from an MRI session are compared with images obtained from X-ray or computed tomography. How do the imaging techniques shown in this game indicate the separation of white and gray matter compared with the freshly dissected tissue shown earlier?

Functional Divisions of the Nervous System

The nervous system can also be divided on the basis of its functions, but anatomical divisions and functional divisions are different. The CNS and the PNS both contribute to the same functions, but those functions can be attributed to different regions of the brain (such as the cerebral cortex or the hypothalamus) or to different ganglia in the periphery. The problem with trying to fit functional differences into anatomical divisions is that sometimes the same structure can be part of several functions. For example, the optic nerve carries signals from the retina that are either used for the conscious perception of visual stimuli, which takes place in the cerebral cortex, or for the reflexive responses of smooth muscle tissue that are processed through the hypothalamus.

There are two ways to consider how the nervous system is divided functionally. First, the basic functions of the nervous system are sensation, integration, and response. Secondly, control of the body can be somatic or autonomic—divisions that are largely defined by the structures that are involved in the response. There is also a region of the peripheral nervous system that is called the enteric nervous system that is responsible for a specific set of the functions within the realm of autonomic control related to gastrointestinal functions.

Basic Functions

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. The stimuli for taste and smell are both chemical substances (molecules, compounds, ions, etc.), touch is physical or mechanical stimuli

that interact with the skin, sight is light stimuli, and hearing is the perception of sound, which is a physical stimulus similar to some aspects of touch. There are actually more senses than just those, but that list represents the major senses. Those five are all senses that receive stimuli from the outside world, and of which there is conscious perception. Additional sensory stimuli might be from the internal environment (inside the body), such as the stretch of an organ wall or the concentration of certain ions in the blood.

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.

Responses can be divided into those that are voluntary or conscious (contraction of skeletal muscle) and those that are involuntary (contraction of smooth muscles, regulation of cardiac muscle, activation of glands). Voluntary responses are governed by the somatic nervous system and involuntary responses are governed by the autonomic nervous system, which are discussed in the next section.

Integration

Stimuli that are received by sensory structures are communicated to the nervous system where that information is processed. This is called integration. Stimuli are compared with, or integrated with, other stimuli, memories of previous stimuli, or the state of a person at a particular time. This leads to the specific response that will be generated. Seeing a baseball pitched to a batter will not automatically cause the batter to swing. The trajectory of the ball and its speed will need to be considered. Maybe the count is three balls and one strike, and the batter wants to let this pitch go by in the hope of getting a walk to first base. Or maybe the batter's team is so far ahead, it would be fun to just swing away.

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. The motor output extends to smooth and cardiac muscle as well as glandular tissue. The role of the autonomic system is to regulate the organ systems of the body, which usually means to control homeostasis. Sweat glands, for example, are controlled by the autonomic system. When you are hot, sweating helps cool your body down. That is a homeostatic mechanism. But when you are nervous, you might start sweating also. That is not homeostatic, it is the physiological response to an emotional state.

There is another division of the nervous system that describes functional responses. The **enteric nervous system (ENS)** is responsible for controlling the smooth muscle and glandular tissue in your digestive system. It is a large part of the PNS, and is not dependent on the CNS. It is sometimes valid, however, to consider the enteric system to be a part of the autonomic system because the neural structures that make up the enteric system are a component of the autonomic output that regulates digestion. There are some differences between the two, but for

our purposes here there will be a good bit of overlap. See Figure 5 for examples of where these divisions of the nervous system can be found.

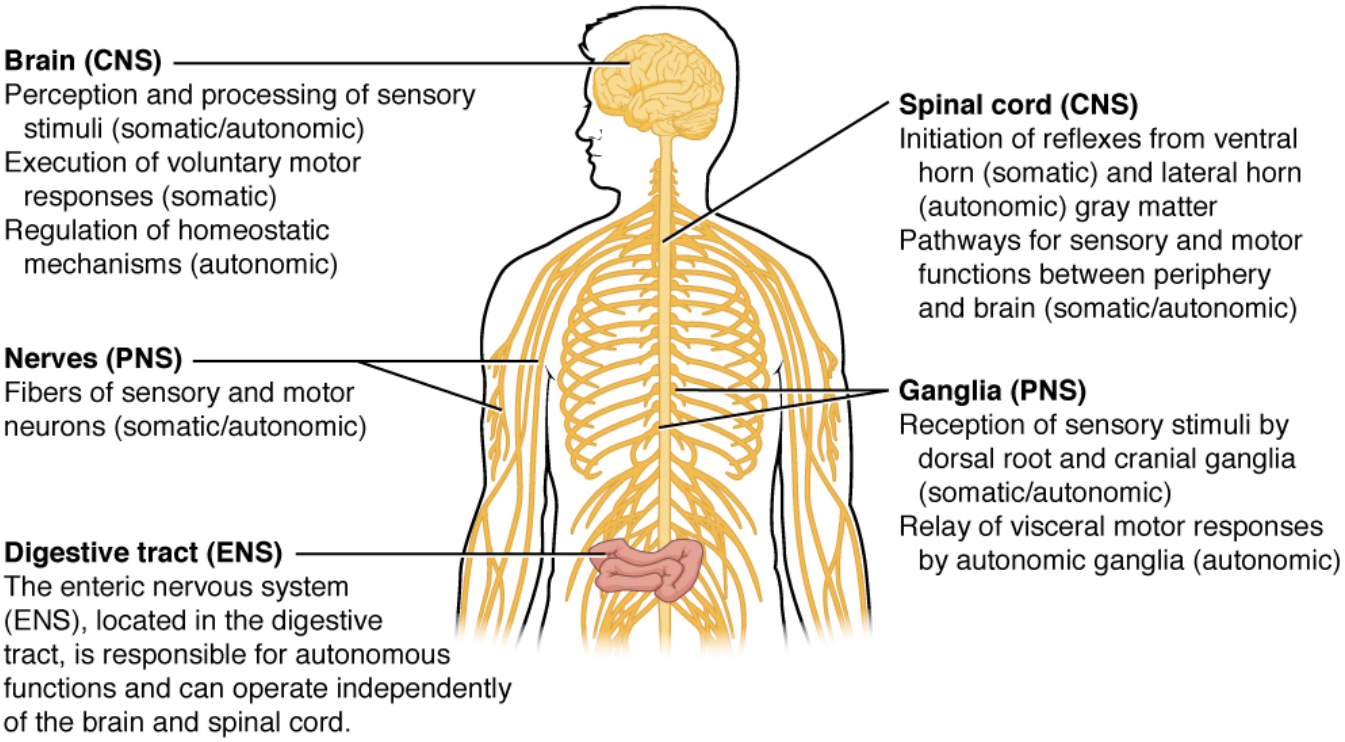


Figure 5. Somatic, Autonomic, and Enteric Structures of the Nervous System *Somatic structures include the spinal nerves, both motor and sensory fibers, as well as the sensory ganglia (posterior root ganglia and cranial nerve ganglia). Autonomic structures are found in the nerves also, but include the sympathetic and parasympathetic ganglia. The enteric nervous system includes the nervous tissue within the organs of the digestive tract.*

Visit this site to read about a woman that notices that her daughter is having trouble walking up the stairs. This leads to the discovery of a hereditary condition that affects the brain and spinal cord. The electromyography and MRI tests indicated deficiencies in the spinal cord and cerebellum, both of which are responsible for controlling coordinated movements. To what functional division of the nervous system would these structures belong?

Everyday Connection: How Much of Your Brain Do You Use?

Have you ever heard the claim that humans only use 10 percent of their brains? Maybe you have seen an advertisement on a website saying that there is a secret to unlocking the full potential of your mind—as if there were 90 percent of your brain sitting idle, just waiting for you to use it. If you see an ad like that, don't click. It isn't true.

An easy way to see how much of the brain a person uses is to take measurements of brain activity while performing a task. An example of this kind of measurement is functional magnetic resonance imaging (fMRI), which generates a map of the most active areas and can be generated and presented in three dimensions (Figure 6). This procedure is different from the standard MRI technique because it is measuring changes in the tissue in time with an experimental condition or event.

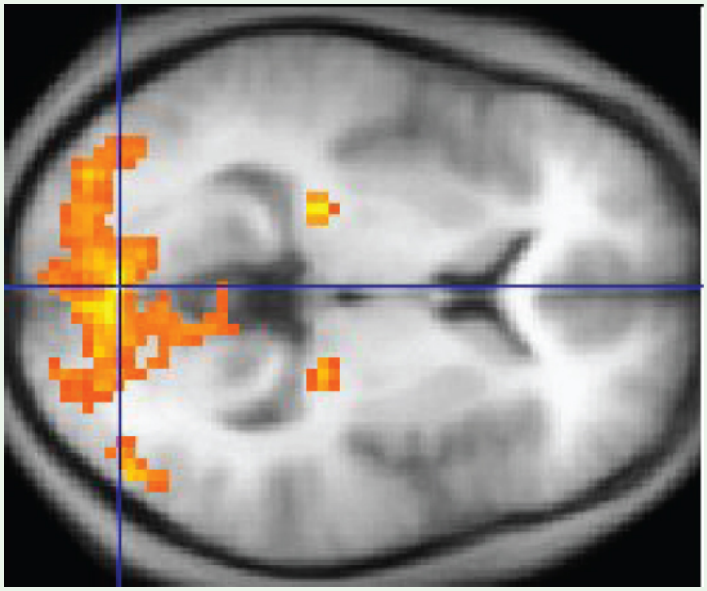


Figure 6. fMRI *This fMRI shows activation of the visual cortex in response to visual stimuli. (credit: "Superborsuk"/Wikimedia Commons)*

The underlying assumption is that active nervous tissue will have greater blood flow. By having the subject perform a visual task, activity all over the brain can be measured. Consider this possible experiment: the subject is told to look at a screen with a black dot in the middle (a fixation point). A photograph of a face is projected on the screen away from the center. The subject has to look at the photograph and decipher what it is. The subject has been instructed to push a button if the photograph is of someone they recognize. The photograph might be of a celebrity, so the subject would press the button, or it might be of a random person unknown to the subject, so the subject would not press the button.

In this task, visual sensory areas would be active, integrating areas would be active, motor areas responsible for moving the eyes would be active, and motor areas for pressing the button with a finger would be active. Those areas are distributed all around the brain and the fMRI images would show activity in more than just 10 percent of the brain (some evidence suggests that about 80 percent of the brain is using energy—based on blood flow to the tissue—during well-defined tasks similar to the one suggested above). This task does not even include all of the functions the brain performs. There is no language response, the body is mostly lying still in the MRI machine, and it does not consider the autonomic functions that would be ongoing in the background.

Self-Check Questions

Visit your course online to take a quiz to check your understanding of the Basic Structure and Function of the Nervous System:

NERVOUS TISSUE

Learning Objectives

- Describe the basic structure of a neuron
- Identify the different types of neurons on the basis of polarity
- List the glial cells of the CNS and describe their function
- List the glial cells of the PNS and describe their function

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. They are electrically active and release chemical signals to target cells. Glial cells, or glia, are known to play a supporting role for nervous tissue. Ongoing research pursues an expanded role that glial cells might play in signaling, but neurons are still considered the basis of this function. Neurons are important, but without glial support they would not be able to perform their function.

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 three-dimensional 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 1 shows the relationship of these parts to one another.

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**.

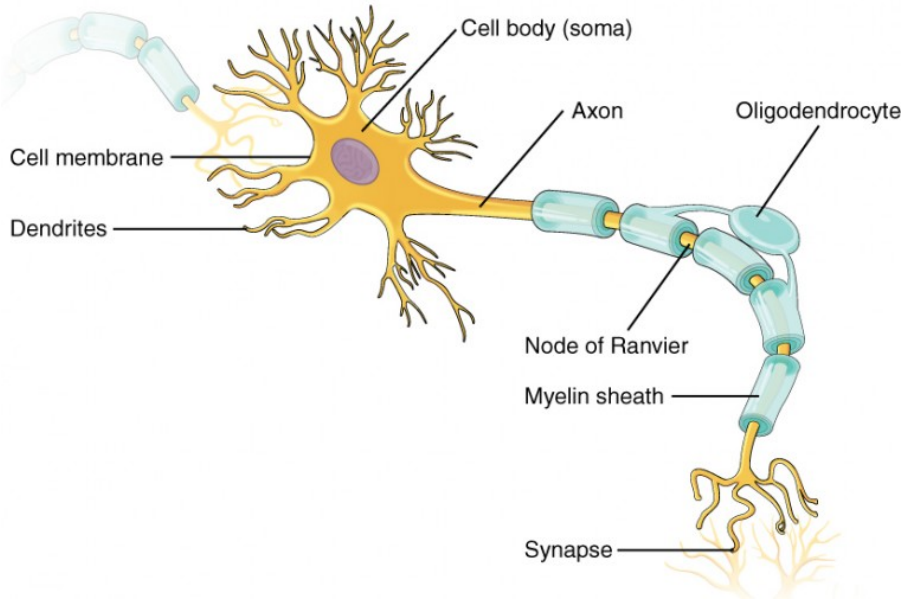


Figure 1. Parts of a Neuron *The major parts of the neuron are labeled on a multipolar neuron from the CNS.*

Many axons are wrapped by an insulating substance called myelin, which is actually made from glial cells. Myelin acts as insulation much like the plastic or rubber that is used to insulate electrical wires. A key difference between myelin and the insulation on a wire is that there are gaps in the myelin covering of an axon. Each gap is called a **node of Ranvier** and is important to the way that electrical signals travel down the axon. The length of the axon between each gap, which is wrapped in myelin, is referred to as an **axon segment**. At the end of the axon is the **axon terminal**, where there are usually several branches extending toward the target cell, each of which ends in an enlargement called a **synaptic end bulb**. These bulbs are what make the connection with the target cell at the synapse.

Visit this site to learn about how nervous tissue is composed of neurons and glial cells. Neurons are dynamic cells with the ability to make a vast number of connections, to respond incredibly quickly to stimuli, and to initiate movements on the basis of those stimuli. They are the focus of intense research because failures in physiology can lead to devastating illnesses. Why are neurons only found in animals? Based on what this article says about neuron function, why wouldn't they be helpful for plants or microorganisms?

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 (Figure 2).

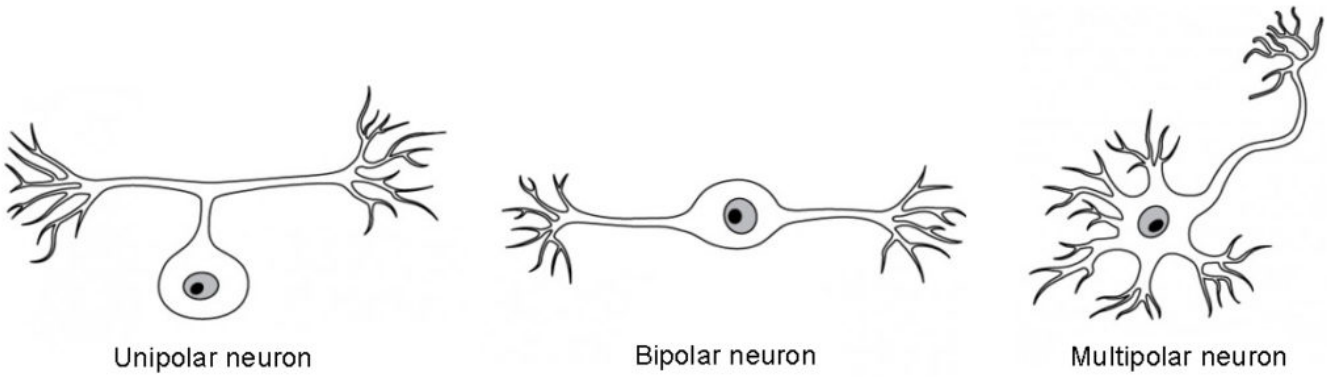


Figure 2. Neuron Classification by Shape. *Unipolar cells have one process that includes both the axon and dendrite. Bipolar cells have two processes, the axon and a dendrite. Multipolar cells have more than two processes, the axon and two or more dendrites.*

Unipolar

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

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

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.

Other Neuron Classifications

Neurons can also be classified on the basis of where they are found, who found them, what they do, or even what chemicals they use to communicate with each other. Some neurons referred to in this section on the nervous system are named on the basis of those sorts of classifications (Figure 3). For example, a multipolar neuron that has a very important role to play in a part of the brain called the cerebellum is known as a Purkinje (commonly pronounced per-KIN-gee) cell. It is named after the anatomist who discovered it (Jan Evangilista Purkinje, 1787–1869).

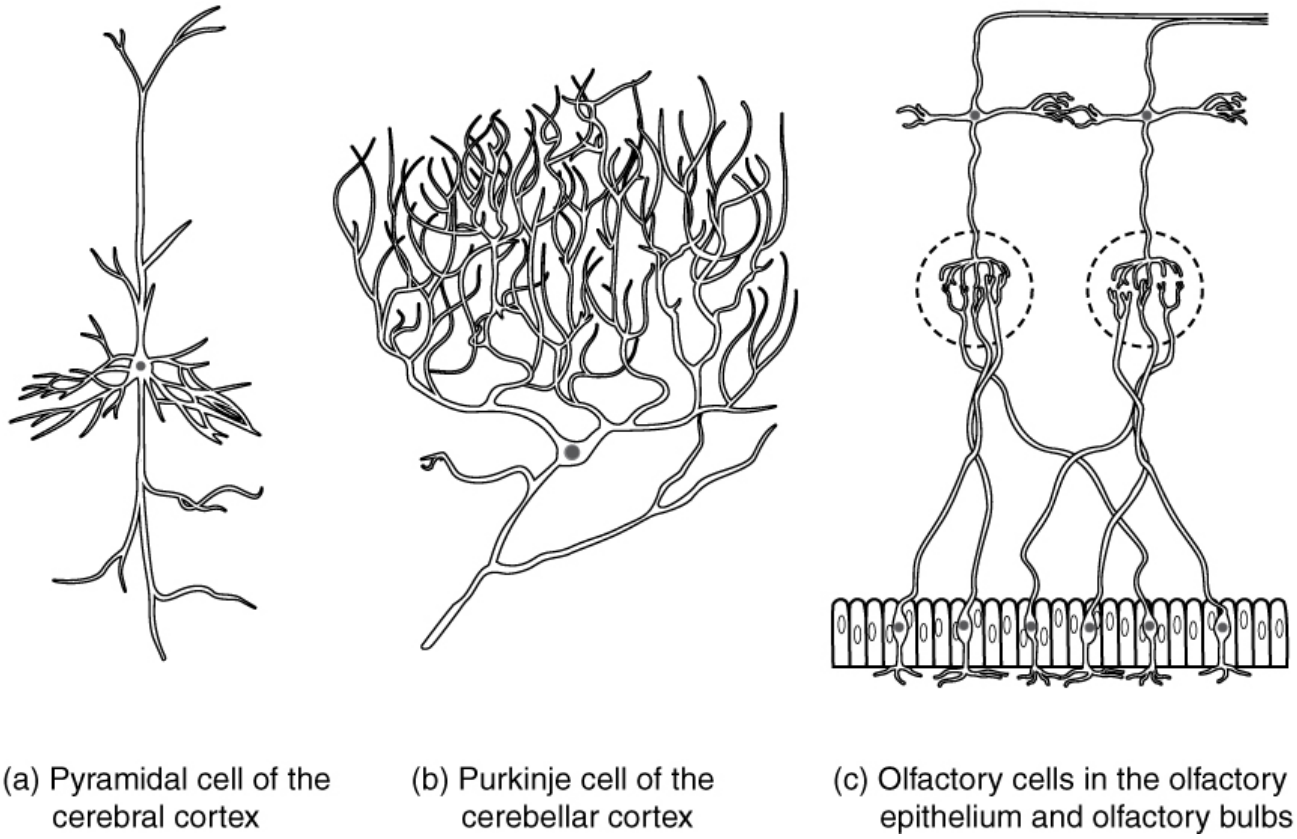


Figure 3. Other Neuron Classifications *Three examples of neurons that are classified on the basis of other criteria. (a) The pyramidal cell is a multipolar cell with a cell body that is shaped something like a pyramid. (b) The Purkinje cell in the cerebellum was named after the scientist who originally described it. (c) Olfactory neurons are named for the functional group with which they belong.*

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.” Today, research into nervous tissue has shown that there are many deeper roles that these cells play. And research may find much more about them in the future.

There are six types of glial cells. Four of them are found in the CNS and two are found in the PNS. Table 1 outlines some common characteristics and functions.

Table 1. Glial Cell Types by Location and Basic Function

CNS glia	PNS glia	Basic function
Astrocyte	Satellite cell	Support
Oligodendrocyte	Schwann cell	Insulation, myelination
Microglia	–	Immune surveillance and phagocytosis
Ependymal cell	–	Creating CSF

Glial Cells of the CNS

One cell providing support to neurons of the CNS is the **astrocyte**, so named because it appears to be star-shaped under the microscope (*astro–* = "star"). Astrocytes have many processes extending from their main cell body (not axons or dendrites like neurons, just cell extensions). Those processes extend to interact with neurons, blood vessels, or the connective tissue covering the CNS that is called the pia mater (Figure 4).

Generally, they are supporting cells for the neurons in the central nervous system. Some ways in which they support neurons in the central nervous system are by maintaining the concentration of chemicals in the extracellular space, removing excess signaling molecules, reacting to tissue damage, and contributing to the **blood-brain barrier (BBB)**. The blood-brain barrier is a physiological barrier that keeps many substances that circulate in the rest of the body from getting into the central nervous system, restricting what can cross from circulating blood into the CNS. Nutrient molecules, such as glucose or amino acids, can pass through the BBB, but other molecules cannot. This actually causes problems with drug delivery to the CNS. Pharmaceutical companies are challenged to design drugs that can cross the BBB as well as have an effect on the nervous system.

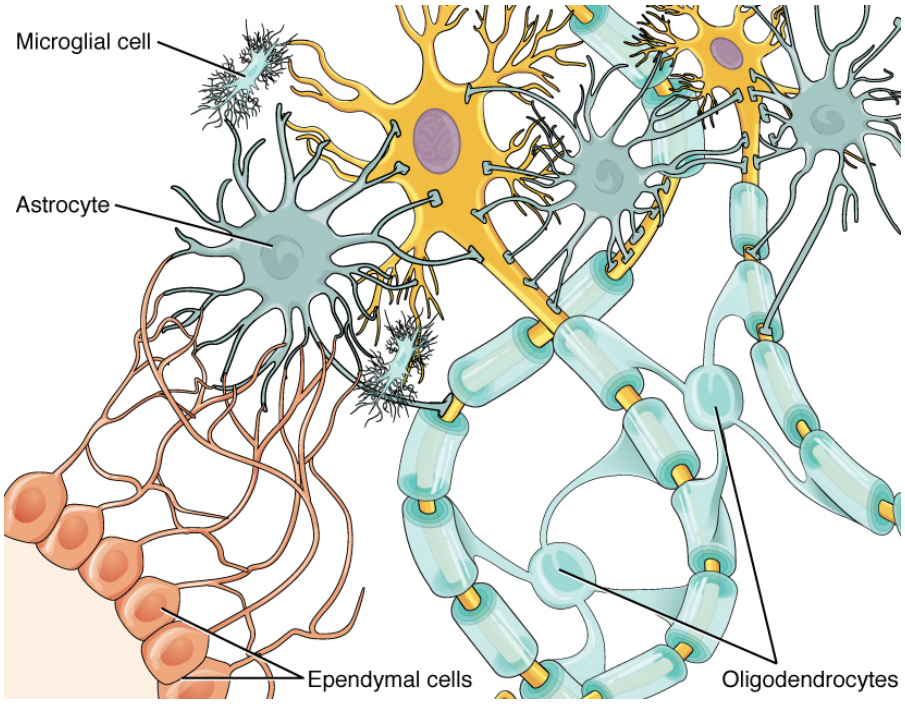


Figure 4. Glial Cells of the CNS *The CNS has astrocytes, oligodendrocytes, microglia, and ependymal cells that support the neurons of the CNS in several ways.*

Like a few other parts of the body, the brain has a privileged blood supply. Very little can pass through by diffusion. Most substances that cross the wall of a blood vessel into the CNS must do so through an active transport process. Because of this, only specific types of molecules can enter the CNS. Glucose—the primary energy source—is allowed, as are amino acids. Water and some other small particles, like gases and ions, can enter. But most everything else cannot, including white blood cells, which are one of the body's main lines of defense. While this barrier protects the CNS from exposure to toxic or pathogenic substances, it also keeps out the cells that could protect the brain and spinal cord from disease and damage. The BBB also makes it harder for pharmaceuticals to be developed that can affect the nervous system. Aside from finding efficacious substances, the means of delivery is also crucial.

Also found in CNS tissue is the **oligodendrocyte**, sometimes called just "oligo," which is the glial cell type that insulates axons in the CNS. The name means "cell of a few branches" (*oligo–* = "few"; *dendro–* = "branches"; *–cyte* = "cell"). There are a few processes that extend from the cell body. Each one reaches out and surrounds an axon to insulate it in myelin. One oligodendrocyte will provide the myelin for multiple axon segments, either for the same axon or for separate axons. The function of myelin will be discussed below.

Microglia are, as the name implies, smaller than most of the other glial cells. Ongoing research into these cells, although not entirely conclusive, suggests that they may originate as white blood cells, called macrophages, that become part of the CNS during early development. While their origin is not conclusively determined, their function is related to what macrophages do in the rest of the body. When macrophages encounter diseased or damaged cells in the rest of the body, they ingest and digest those cells or the pathogens that cause disease. Microglia are the cells in the CNS that can do this in normal, healthy tissue, and they are therefore also referred to as CNS-resident macrophages.

The **ependymal cell** is a glial cell that filters blood to make **cerebrospinal fluid (CSF)**, the fluid that circulates through the CNS. Because of the privileged blood supply inherent in the BBB, the extracellular space in nervous tissue does not easily exchange components with the blood. Ependymal cells line each **ventricle**, one of four central cavities that are remnants of the hollow center of the neural tube formed during the embryonic development of the brain. The **choroid plexus** is a specialized structure in the ventricles where ependymal cells come in contact with blood vessels and filter and absorb components of the blood to produce cerebrospinal fluid. Because of this, ependymal cells can be considered a component of the BBB, or a place where the BBB breaks down. These glial cells appear similar to epithelial cells, making a single layer of cells with little intracellular space and tight connections between adjacent cells. They also have cilia on their apical surface to help move the CSF through the ventricular space. The relationship of these glial cells to the structure of the CNS is seen in Figure 4.

Glial Cells of the PNS

One of the two types of glial cells found in the PNS is the **satellite cell**. Satellite cells are found in sensory and autonomic ganglia, where they surround the cell bodies of neurons. This accounts for the name, based on their appearance under the microscope. They provide support, performing similar functions in the periphery as astrocytes do in the CNS—except, of course, for establishing the BBB.

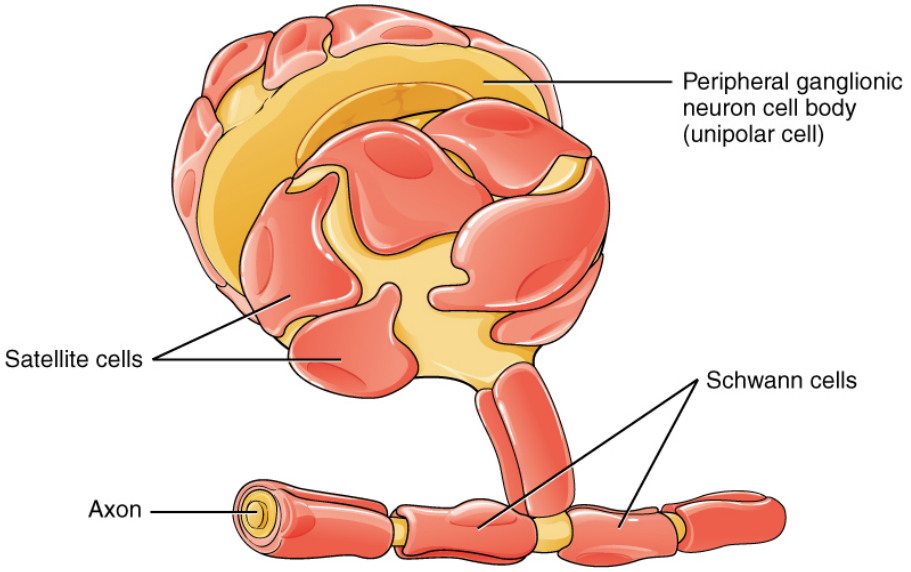


Figure 5. Glial Cells of the PNS *The PNS has satellite cells and Schwann cells.*

The second type of glial cell is the **Schwann cell**, which insulate axons with myelin in the periphery. Schwann cells are different than oligodendrocytes, in that a Schwann cell wraps around a portion of only one axon segment and no others. Oligodendrocytes have processes that reach out to multiple axon segments, whereas the entire Schwann cell surrounds just one axon segment. The nucleus and cytoplasm of the Schwann cell are on the edge of the myelin sheath. The relationship of these two types of glial cells to ganglia and nerves in the PNS is seen in Figure 5.

Myelin

The insulation for axons in the nervous system is provided by glial cells, oligodendrocytes in the CNS, and Schwann cells in the PNS. Whereas the manner in which either cell is associated with the axon segment, or segments, that it insulates is different, the means of myelinating an axon segment is mostly the same in the two situations. Myelin is a lipid-rich sheath that surrounds the axon and by doing so creates a **myelin sheath** that facilitates the transmission of electrical signals along the axon. The lipids are essentially the phospholipids of the glial cell membrane. Myelin, however, is more than just the membrane of the glial cell. It also includes important proteins that are integral to that membrane. Some of the proteins help to hold the layers of the glial cell membrane closely together.

The appearance of the myelin sheath can be thought of as similar to the pastry wrapped around a hot dog for “pigs in a blanket” or a similar food. The glial cell is wrapped around the axon several times with little to no cytoplasm between the glial cell layers. For oligodendrocytes, the rest of the cell is separate from the myelin sheath as a cell process extends back toward the cell body. A few other processes provide the same insulation for other axon segments in the area. For Schwann cells, the outermost layer of the cell membrane contains cytoplasm and the nucleus of the cell as a bulge on one side of the myelin sheath. During development, the glial cell is loosely or incompletely wrapped around the axon (Figure 6a). The edges of this loose enclosure extend

toward each other, and one end tucks under the other. The inner edge wraps around the axon, creating several layers, and the other edge closes around the outside so that the axon is completely enclosed.

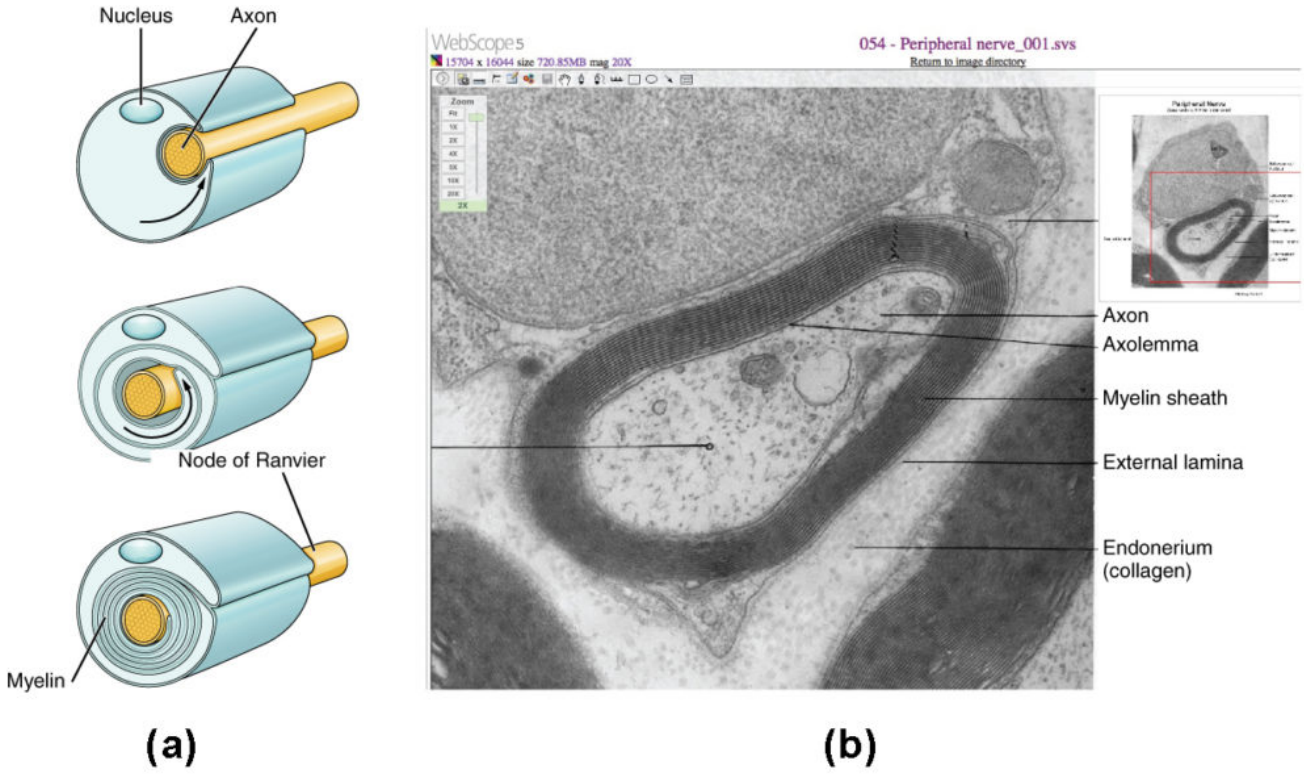


Figure 6. The Process of Myelination. *Myelinating glia wrap several layers of cell membrane around the cell membrane of an axon segment. A single Schwann cell insulates a segment of a peripheral nerve, whereas in the CNS, an oligodendrocyte may provide insulation for a few separate axon segments. EM × 1,460,000. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

View the University of Michigan WebScope at to see an electron micrograph of a cross-section of a myelinated nerve fiber. The axon contains microtubules and neurofilaments that are bounded by a plasma membrane known as the axolemma. Outside the plasma membrane of the axon is the myelin sheath, which is composed of the tightly wrapped plasma membrane of a Schwann cell. What aspects of the cells in this image react with the stain to make them a deep, dark, black color, such as the multiple layers that are the myelin sheath?

Myelin sheaths can extend for one or two millimeters, depending on the diameter of the axon. Axon diameters can be as small as 1 to 20 micrometers. Because a micrometer is 1/1000 of a millimeter, this means that the length of a myelin sheath can be 100–1000 times the diameter of the axon. Figure 1, Figure 4, and Figure 5 show the myelin sheath surrounding an axon segment, but are not to scale. If the myelin sheath were drawn to scale, the neuron would have to be immense—possibly covering an entire wall of the room in which you are sitting.

Disorders of the Nervous Tissue

Several diseases can result from the demyelination of axons. The causes of these diseases are not the same; some have genetic causes, some are caused by pathogens, and others are the result of autoimmune disorders. Though the causes are varied, the results are largely similar. The myelin insulation of axons is compromised, making electrical signaling slower.

Multiple sclerosis (MS) is one such disease. It is an example of an autoimmune disease. The antibodies produced by lymphocytes (a type of white blood cell) mark myelin as something that should not be in the body. This causes inflammation and the destruction of the myelin in the central nervous system. As the

insulation around the axons is destroyed by the disease, scarring becomes obvious. This is where the name of the disease comes from; sclerosis means hardening of tissue, which is what a scar is. Multiple scars are found in the white matter of the brain and spinal cord. The symptoms of MS include both somatic and autonomic deficits. Control of the musculature is compromised, as is control of organs such as the bladder.

Guillain-Barré (Note: pronounced gee-YAN bah-RAY) syndrome is an example of a demyelinating disease of the peripheral nervous system. It is also the result of an autoimmune reaction, but the inflammation is in peripheral nerves. Sensory symptoms or motor deficits are common, and autonomic failures can lead to changes in the heart rhythm or a drop in blood pressure, especially when standing, which causes dizziness.

THE FUNCTION OF NERVOUS TISSUE

Learning Objectives

- Distinguish the major functions of the nervous system: sensation, integration, and response
- List the sequence of events in a simple sensory receptor–motor response pathway

Having looked at the components of nervous tissue, and the basic anatomy of the nervous system, next comes an understanding of how nervous tissue is capable of communicating within the nervous system. Before getting to the nuts and bolts of how this works, an illustration of how the components come together will be helpful.

Imagine you are about to take a shower in the morning before going to school. You have turned on the faucet to start the water as you prepare to get in the shower. After a few minutes, you expect the water to be a temperature that will be comfortable to enter. So you put your hand out into the spray of water. What happens next depends on how your nervous system interacts with the stimulus of the water temperature and what you do in response to that stimulus. Figure 1 shows one possible path you may follow.

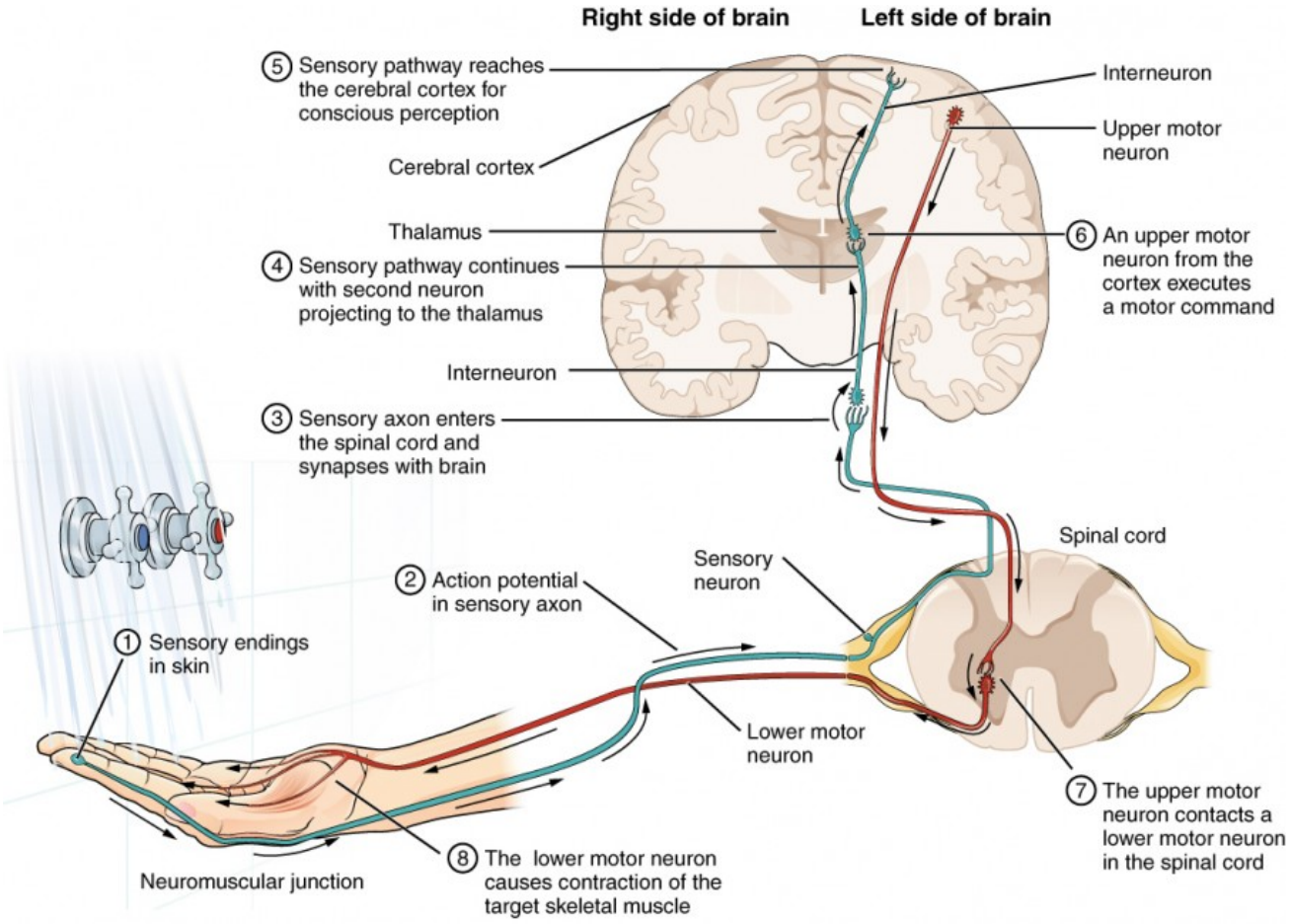


Figure 1. Testing the Water

Here's a more detailed breakdown of the processes found in Figure 1:

1. The sensory neuron has endings in the skin that sense a stimulus such as water temperature. The strength of the signal that starts here is dependent on the strength of the stimulus.
2. The graded potential from the sensory endings, if strong enough, will initiate an action potential at the initial segment of the axon (which is immediately adjacent to the sensory endings in the skin).
3. The axon of the peripheral sensory neuron enters the spinal cord and contacts another neuron in the gray matter. The contact is a synapse where another graded potential is caused by the release of a chemical signal from the axon terminals.
4. An action potential is initiated at the initial segment of this neuron and travels up the sensory pathway to a region of the brain called the thalamus. Another synapse passes the information along to the next neuron.
5. The sensory pathway ends when the signal reaches the cerebral cortex.
6. After integration with neurons in other parts of the cerebral cortex, a motor command is sent from the precentral gyrus of the frontal cortex.
7. The upper motor neuron sends an action potential down to the spinal cord. The target of the upper motor neuron is the dendrites of the lower motor neuron in the gray matter of the spinal cord.
8. The axon of the lower motor neuron emerges from the spinal cord in a nerve and connects to a muscle through a neuromuscular junction to cause contraction of the target muscle.

Found in the skin of your fingers or toes is a type of sensory receptor that is sensitive to temperature, called a thermoreceptor. When you place your hand under the shower (Figure 2), the cell membrane of the thermoreceptors changes its electrical state (voltage).

The amount of change is dependent on the strength of the stimulus (how hot the water is). This is called a **graded potential**. If the stimulus is strong, the voltage of the cell membrane will change enough to generate an electrical signal that will travel down the axon. You have learned about this type of signaling before, with respect to the interaction of nerves and muscles at the neuromuscular junction. The voltage at which such a signal is generated is called the **threshold**, and the resulting electrical signal is called an **action potential**. In this example, the action potential travels—a process known as **propagation**—along the axon from the axon hillock to the axon terminals and into the synaptic end bulbs. When this signal reaches the end bulbs, it causes the release of a signaling molecule called a **neurotransmitter**.

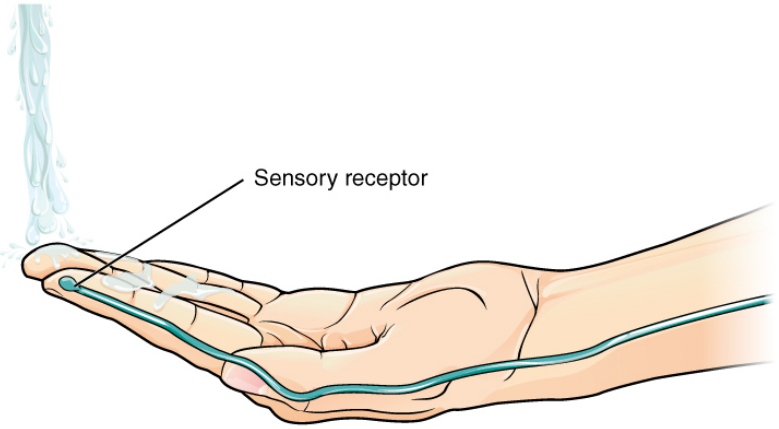


Figure 2. The Sensory Input *Receptors in the skin sense the temperature of the water.*

The neurotransmitter diffuses across the short distance of the synapse and binds to a receptor protein of the target neuron. When the molecular signal binds to the receptor, the cell membrane of the target neuron changes its electrical state and a new graded potential begins. If that graded potential is strong enough to reach threshold, the second neuron generates an action potential at its axon hillock. The target of this neuron is another neuron in the **thalamus** of the brain, the part of the CNS that acts as a relay for sensory information. At another synapse, neurotransmitter is released and binds to its receptor. The thalamus then sends the sensory information to the **cerebral cortex**, the outermost layer of gray matter in the brain, where conscious perception of that water temperature begins.

Within the cerebral cortex, information is processed among many neurons, integrating the stimulus of the water temperature with other sensory stimuli, with your emotional state (you just aren't ready to wake up; the bed is calling to you), memories (perhaps of the lab notes you have to study before a quiz). Finally, a plan is developed about what to do, whether that is to turn the temperature up, turn the whole shower off and go back to bed, or step into the shower. To do any of these things, the cerebral cortex has to send a command out to your body to move muscles (Figure 3).

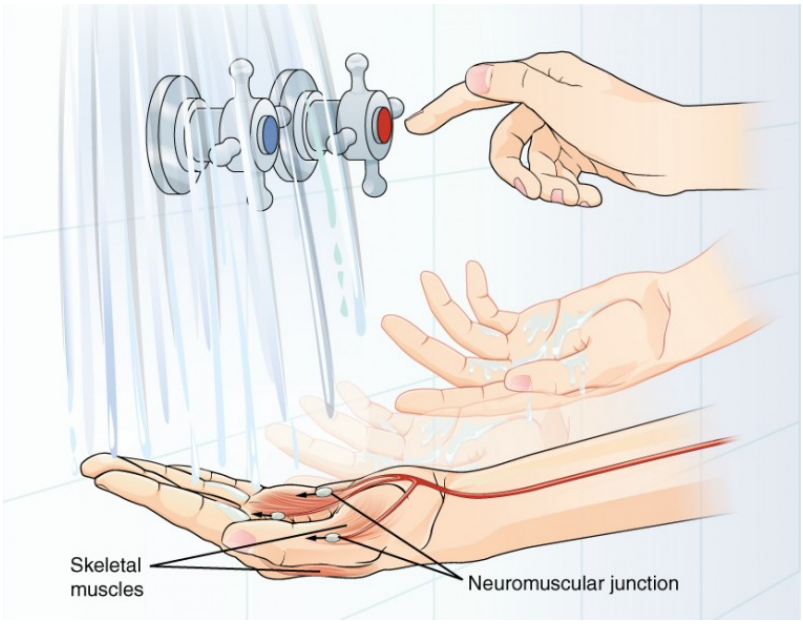


Figure 3. The Motor Response *On the basis of the sensory input and the integration in the CNS, a motor response is formulated and executed.*

A region of the cortex is specialized for sending signals down to the spinal cord for movement. The **upper motor neuron** is in this region, called the **precentral gyrus of the frontal cortex**, which has an axon that extends all the way down the spinal cord. At the level of the spinal cord at which this axon makes a synapse, a graded potential occurs in the cell membrane of a **lower motor neuron**. This second motor neuron is responsible for causing muscle fibers to contract. In the manner described in the chapter on muscle tissue, an action potential travels along the motor neuron axon into the periphery. The axon terminates on muscle fibers at the neuromuscular junction. Acetylcholine is released at this specialized synapse, which causes the muscle action potential to begin, following a large potential known as an end plate potential. When the lower motor neuron excites the muscle fiber, it contracts. All of this occurs in a fraction of a second, but this story is the basis of how the nervous system functions.

Career Connections: Neurophysiologist

Understanding how the nervous system works could be a driving force in your career. Studying neurophysiology is a very rewarding path to follow. It means that there is a lot of work to do, but the rewards are worth the effort.

The career path of a research scientist can be straightforward: college, graduate school, postdoctoral research, academic research position at a university. A Bachelor's degree in science will get you started, and for neurophysiology that might be in biology, psychology, computer science, engineering, or neuroscience. But the real specialization comes in graduate school. There are many different programs out there to study the nervous system, not just neuroscience itself. Most graduate programs are doctoral, meaning that a Master's degree is not part of the work. These are usually considered five-year programs, with the first two years dedicated to course work and finding a research mentor, and the last three years dedicated to finding a research topic and pursuing that with a near single-mindedness. The research will usually result in a few publications in scientific journals, which will make up the bulk of a doctoral dissertation. After graduating with a Ph.D., researchers will go on to find specialized work called a postdoctoral fellowship within established labs. In this position, a researcher starts to establish their own research career with the hopes of finding an academic position at a research university.

Other options are available if you are interested in how the nervous system works. Especially for neurophysiology, a medical degree might be more suitable so you can learn about the clinical applications of neurophysiology and possibly work with human subjects. An academic career is not a necessity. Biotechnology firms are eager to find motivated scientists ready to tackle the tough questions about how the nervous system works so that therapeutic chemicals can be tested on some of the most challenging disorders such as Alzheimer's disease or Parkinson's disease, or spinal cord injury.

Others with a medical degree and a specialization in neuroscience go on to work directly with patients, diagnosing and treating mental disorders. You can do this as a psychiatrist, a neuropsychologist, a neuroscience nurse, or a neurodiagnostic technician, among other possible career paths.

THE ACTION POTENTIAL

Learning Objectives

- Describe the components of the membrane that establish the resting membrane potential
- Describe the changes that occur to the membrane that result in the action potential

The functions of the nervous system—sensation, integration, and response—depend on the functions of the neurons underlying these pathways. To understand how neurons are able to communicate, it is necessary to describe the role of an **excitable membrane** in generating these signals. The basis of this communication is the action potential, which demonstrates how changes in the membrane can constitute a signal. Looking at the way these signals work in more variable circumstances involves a look at graded potentials, which will be covered in the next section.

Electrically Active Cell Membranes

Most cells in the body make use of charged particles, ions, to build up a charge across the cell membrane. Previously, this was shown to be a part of how muscle cells work. For skeletal muscles to contract, based on excitation–contraction coupling, requires input from a neuron. Both of the cells make use of the cell membrane to regulate ion movement between the extracellular fluid and cytosol.

As you learned in the chapter on cells, the cell membrane is primarily responsible for regulating what can cross the membrane and what stays on only one side. The cell membrane is a phospholipid bilayer, so only substances that can pass directly through the hydrophobic core can diffuse through unaided. Charged particles, which are hydrophilic by definition, cannot pass through the cell membrane without assistance (Figure 1). Transmembrane proteins, specifically channel proteins, make this possible. Several channels, as well as specialized energy dependent "ion-pumps," are necessary to generate a transmembrane potential and to generate an action potential. Of special interest is the carrier protein referred to as the sodium/potassium pump that moves sodium ions (Na^+) out of a cell and potassium ions (K^+) into a cell, thus regulating ion concentration on both sides of the cell membrane.

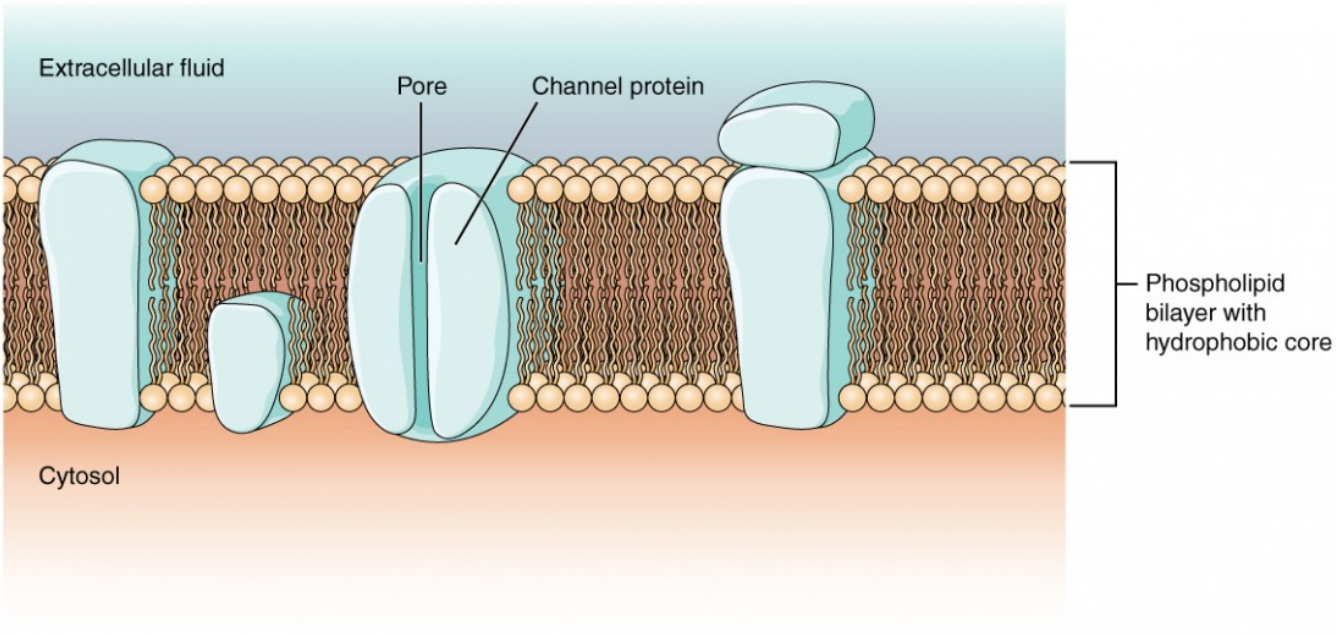


Figure 1. Cell Membrane and Transmembrane Proteins *The cell membrane is composed of a phospholipid bilayer and has many transmembrane proteins, including different types of channel proteins that serve as ion channels.*

The sodium/potassium pump requires energy in the form of adenosine triphosphate (ATP), so it is also referred to as an ATPase. As was explained in the cell chapter, the concentration of Na^+ is higher outside the cell than inside, and the concentration of K^+ is higher inside the cell is higher than outside. That means that this pump is moving the ions against the concentration gradients for sodium and potassium, which is why it requires energy. In fact, the pump basically maintains those concentration gradients.

Ion channels are pores that allow specific charged particles to cross the membrane in response to an existing concentration gradient. Proteins are capable of spanning the cell membrane, including its hydrophobic core, and can interact with the charge of ions because of the varied properties of amino acids found within specific domains or regions of the protein channel. Hydrophobic amino acids are found in the domains that are apposed to the hydrocarbon tails of the phospholipids. Hydrophilic amino acids are exposed to the fluid environments of the extracellular fluid and cytosol. Additionally, the ions will interact with the hydrophilic amino acids, which will be selective for the charge of the ion. Channels for cations (positive ions) will have negatively charged side chains in the pore. Channels for anions (negative ions) will have positively charged side chains in the pore. This is called **electrochemical exclusion**, meaning that the channel pore is charge-specific.

Ions can also be specified by the diameter of the pore. The distance between the amino acids will be specific for the diameter of the ion when it dissociates from the water molecules surrounding it. Because of the surrounding water molecules, larger pores are not ideal for smaller ions because the water molecules will interact, by hydrogen bonds, more readily than the amino acid side chains. This is called **size exclusion**. Some ion channels are selective for charge but not necessarily for size, and thus are called a **nonspecific channel**. These nonspecific channels allow cations—particularly Na^+, K^+, and Ca^{2+}—to cross the membrane, but exclude anions.

Ion channels do not always freely allow ions to diffuse across the membrane. They are opened by certain events, meaning the channels are **gated**. So another way that channels can be categorized is on the basis of how they are gated. Although these classes of ion channels are found primarily in cells of nervous or muscular tissue, they also can be found in cells of epithelial and connective tissues.

A **ligand-gated channel** opens because a signaling molecule, a ligand, binds to the extracellular region of the channel. This type of channel is also known as an **ionotropic receptor** because when the ligand, known as a neurotransmitter in the nervous system, binds to the protein, ions cross the membrane changing its charge (Figure 2).

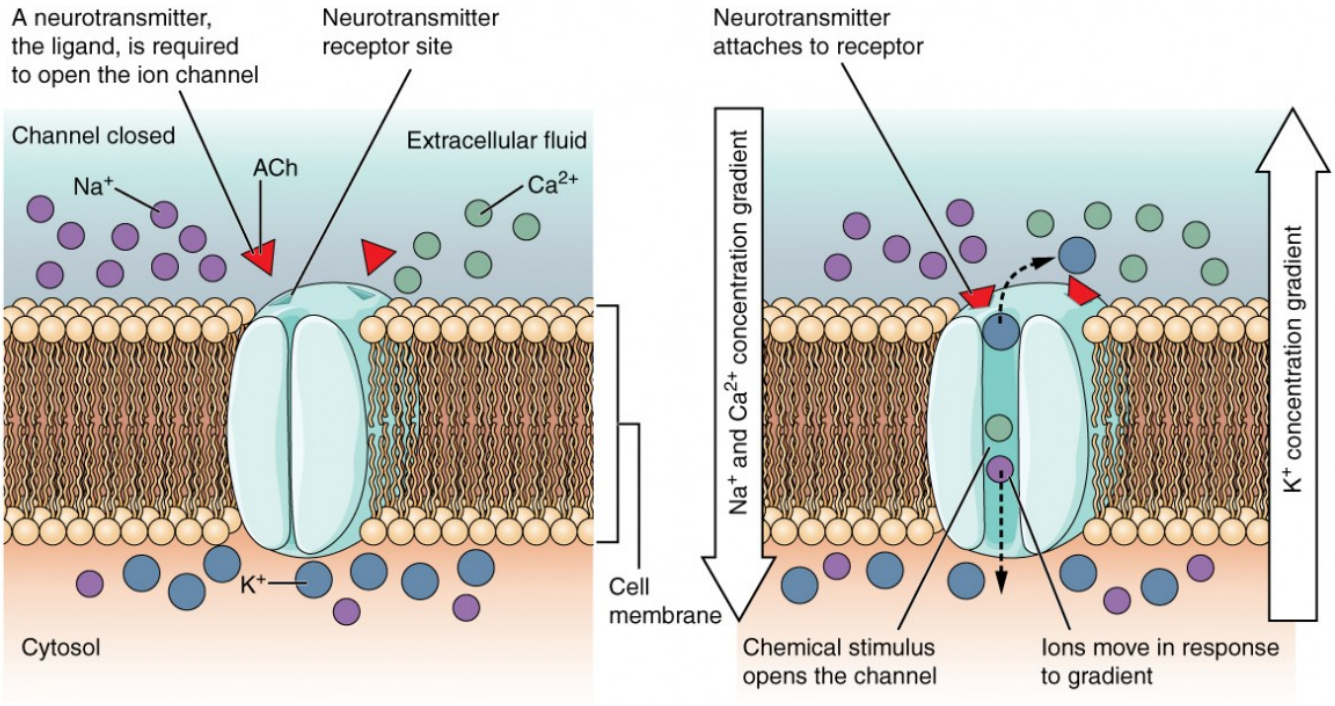


Figure 2. Ligand-Gated Channels *When the ligand, in this case the neurotransmitter acetylcholine, binds to a specific location on the extracellular surface of the channel protein, the pore opens to allow select ions through. The ions, in this case, are cations of sodium, calcium, and potassium.*

A **mechanically gated channel** opens because of a physical distortion of the cell membrane. Many channels associated with the sense of touch (somatosensation) are mechanically gated. For example, as pressure is applied to the skin, these channels open and allow ions to enter the cell. Similar to this type of channel would be the channel that opens on the basis of temperature changes, as in testing the water in the shower (Figure 3).

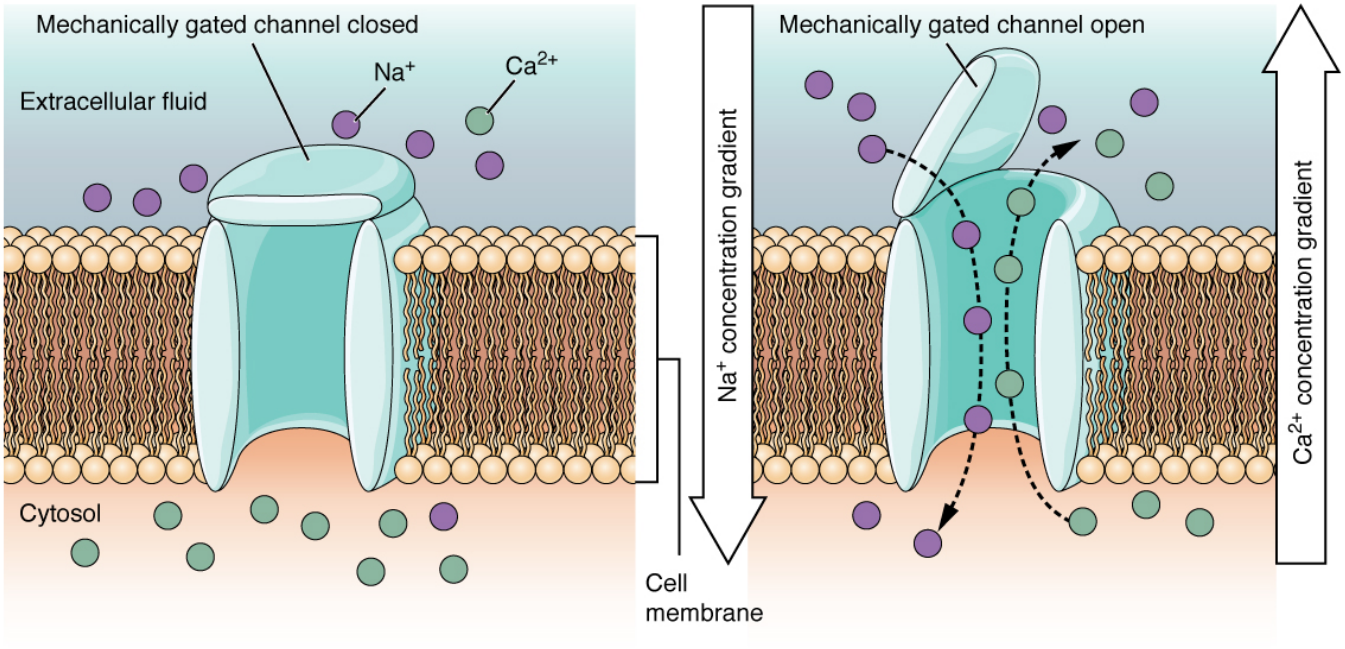


Figure 3. Mechanically Gated Channels *When a mechanical change occurs in the surrounding tissue, such as pressure or touch, the channel is physically opened. Thermoreceptors work on a similar principle. When the local tissue temperature changes, the protein reacts by physically opening the channel.*

A voltage-gated channel is a channel that responds to changes in the electrical properties of the membrane in which it is embedded. Normally, the inner portion of the membrane is at a negative voltage. When that voltage becomes less negative, the channel begins to allow ions to cross the membrane (Figure 4).

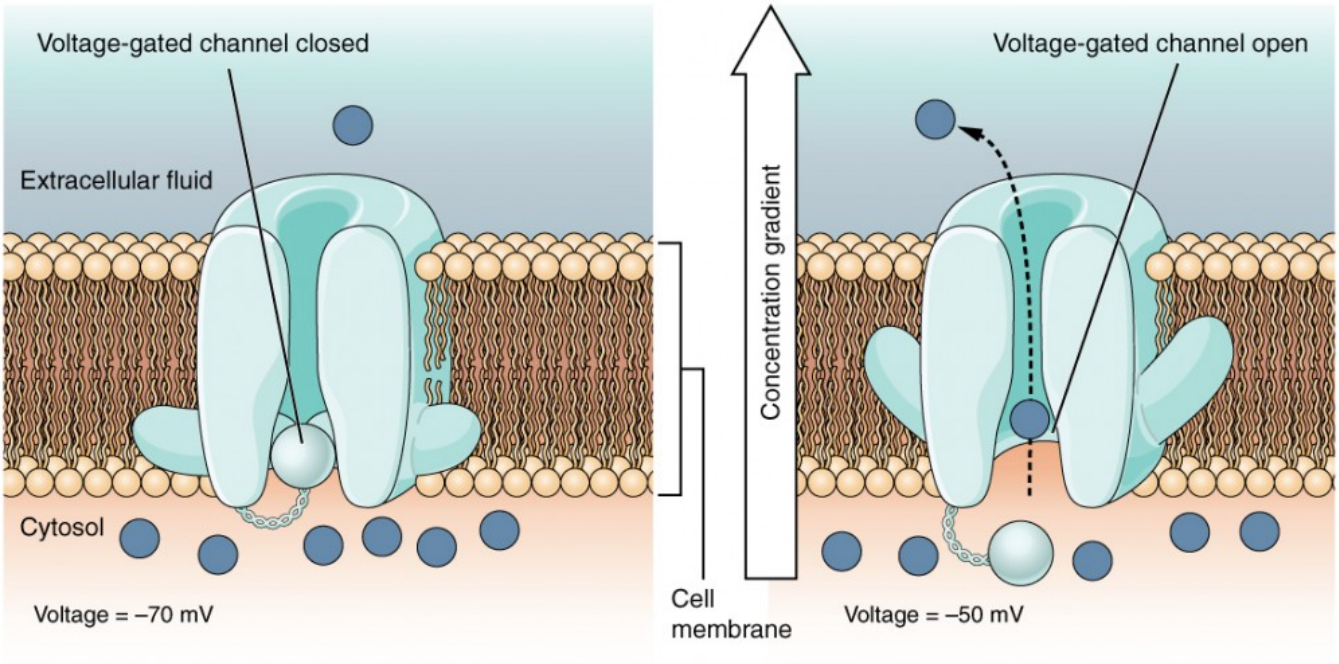


Figure 4. Voltage-Gated Channels *Voltage-gated channels open when the transmembrane voltage changes around them. Amino acids in the structure of the protein are sensitive to charge and cause the pore to open to the selected ion.*

A leakage channel is randomly gated, meaning that it opens and closes at random, hence the reference to leaking. There is no actual event that opens the channel; instead, it has an intrinsic rate of switching between the

open and closed states. Leakage channels contribute to the resting transmembrane voltage of the excitable membrane (Figure 5).

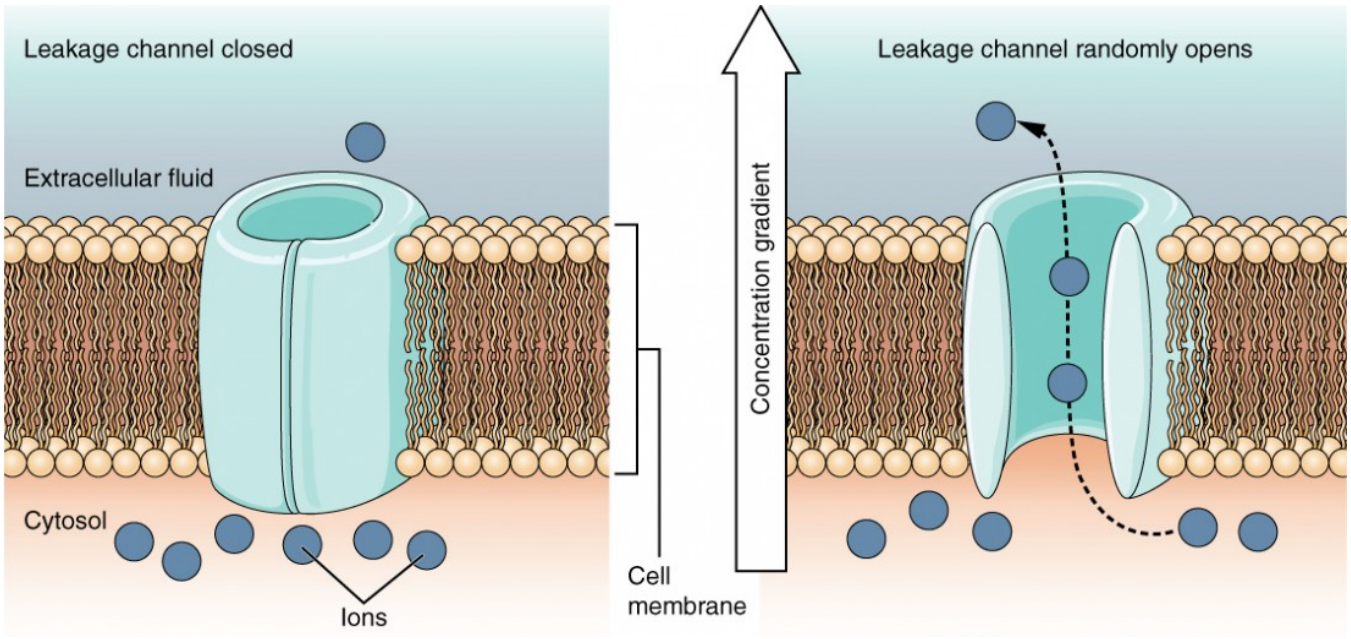


Figure 5. Leakage Channels *In certain situations, ions need to move across the membrane randomly. The particular electrical properties of certain cells are modified by the presence of this type of channel.*

The Membrane Potential

The electrical state of the cell membrane can have several variations. These are all variations in the **membrane potential**. A potential is a distribution of charge across the cell membrane, measured in millivolts (mV). The standard is to compare the inside of the cell relative to the outside, so the membrane potential is a value representing the charge on the intracellular side of the membrane based on the outside being zero, relatively speaking (Figure 6).

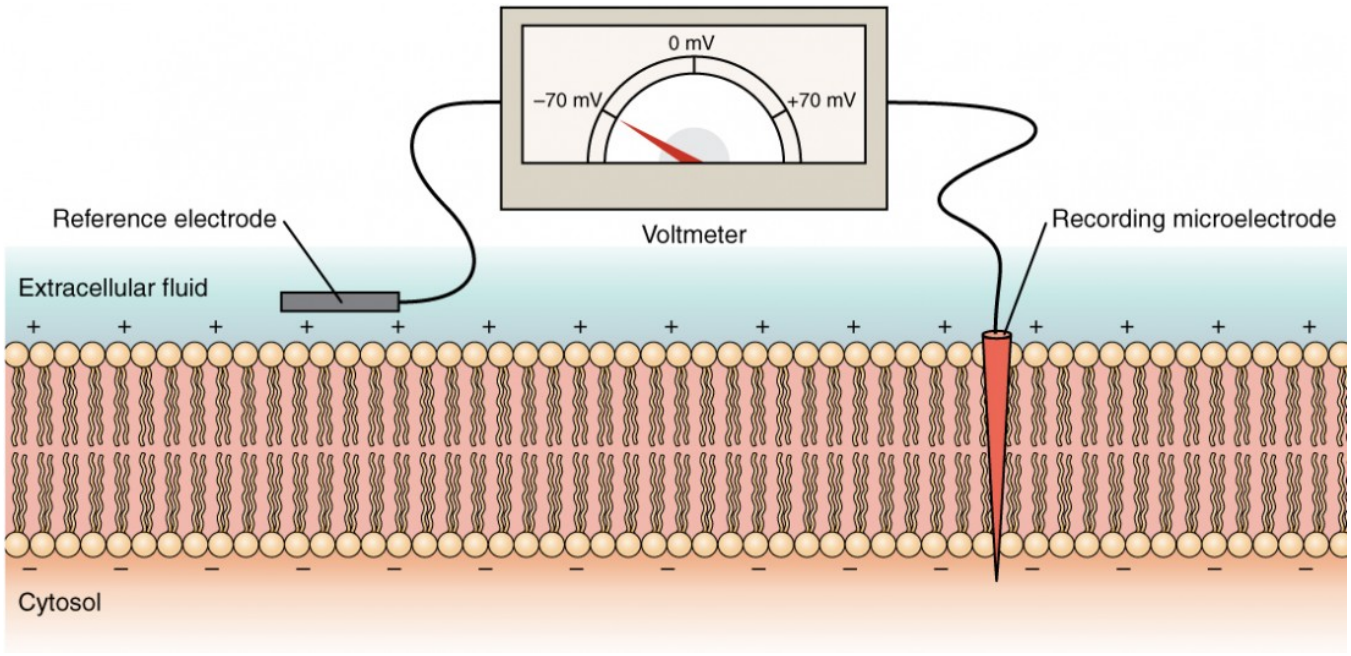


Figure 6. Measuring Charge across a Membrane with a Voltmeter *A recording electrode is inserted into the cell and a reference electrode is outside the cell. By comparing the charge measured by these two electrodes, the transmembrane voltage is determined. It is conventional to express that value for the cytosol relative to the outside.*

The concentration of ions in extracellular and intracellular fluids is largely balanced, with a net neutral charge. However, a slight difference in charge occurs right at the membrane surface, both internally and externally. It is the difference in this very limited region that has all the power in neurons (and muscle cells) to generate electrical signals, including action potentials.

Before these electrical signals can be described, the resting state of the membrane must be explained. When the cell is at rest, and the ion channels are closed (except for leakage channels which randomly open), ions are distributed across the membrane in a very predictable way. The concentration of Na^+ outside the cell is 10 times greater than the concentration inside. Also, the concentration of K^+ inside the cell is greater than outside. The cytosol contains a high concentration of anions, in the form of phosphate ions and negatively charged proteins. Large anions are a component of the inner cell membrane, including specialized phospholipids and proteins associated with the inner leaflet of the membrane (leaflet is a term used for one side of the lipid bilayer membrane). The negative charge is localized in the large anions.

With the ions distributed across the membrane at these concentrations, the difference in charge is measured at –70 mV, the value described as the **resting membrane potential**. The exact value measured for the resting membrane potential varies between cells, but –70 mV is most commonly used as this value. This voltage would actually be much lower except for the contributions of some important proteins in the membrane. Leakage channels allow Na^+ to slowly move into the cell or K^+ to slowly move out, and the Na^+/K^+ pump restores them. This may appear to be a waste of energy, but each has a role in maintaining the membrane potential.

The Action Potential

Resting membrane potential describes the steady state of the cell, which is a dynamic process that is balanced by ion leakage and ion pumping. Without any outside influence, it will not change. To get an electrical signal started, the membrane potential has to change.

This starts with a channel opening for Na^+ in the membrane. Because the concentration of Na^+ is higher outside the cell than inside the cell by a factor of 10, ions will rush into the cell that are driven largely by the concentration gradient. Because sodium is a positively charged ion, it will change the relative voltage immediately inside the cell relative to immediately outside. The resting potential is the state of the membrane at a voltage of –70 mV, so the sodium cation entering the cell will cause it to become less negative. This is known as **depolarization**, meaning the membrane potential moves toward zero.

The concentration gradient for Na^+ is so strong that it will continue to enter the cell even after the membrane potential has become zero, so that the voltage immediately around the pore begins to become positive. The electrical gradient also plays a role, as negative proteins below the membrane attract the sodium ion. The membrane potential will reach +30 mV by the time sodium has entered the cell.

As the membrane potential reaches +30 mV, other voltage-gated channels are opening in the membrane. These channels are specific for the potassium ion. A concentration gradient acts on K^+, as well. As K^+ starts to leave the cell, taking a positive charge with it, the membrane potential begins to move back toward its resting voltage. This is called **repolarization**, meaning that the membrane voltage moves back toward the –70 mV value of the resting membrane potential.

Repolarization returns the membrane potential to the –70 mV value that indicates the resting potential, but it actually overshoots that value. Potassium ions reach equilibrium when the membrane voltage is below –70 mV, so a period of hyperpolarization occurs while the K^+ channels are open. Those K^+ channels are slightly delayed in closing, accounting for this short overshoot.

What has been described here is the action potential, which is presented as a graph of voltage over time in Figure 7. It is the electrical signal that nervous tissue generates for communication. The change in the membrane voltage from –70 mV at rest to +30 mV at the end of depolarization is a 100-mV change. That can also be written as a 0.1-V change.

To put that value in perspective, think about a battery. An AA battery that you might find in a television remote has a voltage of 1.5 V, or a 9-V battery (the rectangular battery with two posts on one end) is, obviously, 9 V. The change seen in the action potential is one or two orders of magnitude less than the charge in these batteries. In fact, the membrane potential can be described as a battery. A charge is stored across the membrane that can be released under the correct conditions. A battery in your remote has stored a charge that is "released" when you push a button.

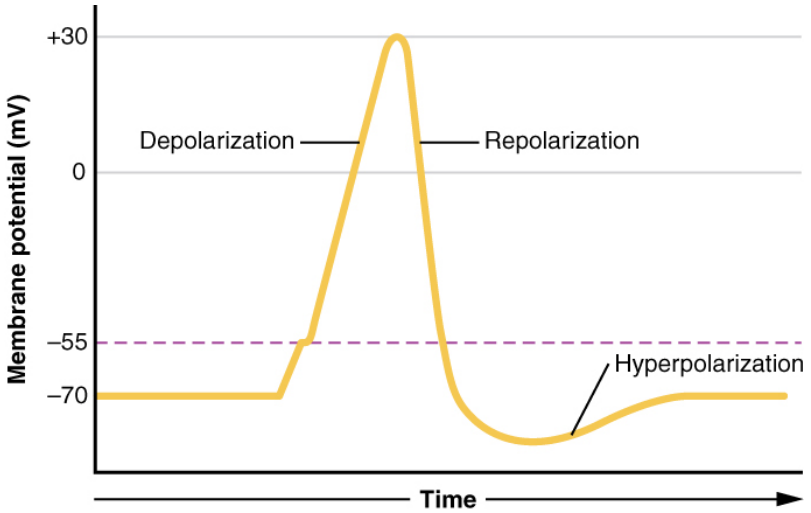


Figure 7. Graph of Action Potential *Plotting voltage measured across the cell membrane against time, the action potential begins with depolarization, followed by repolarization, which goes past the resting potential into hyperpolarization, and finally the membrane returns to rest.*

What happens across the membrane of an electrically active cell is a dynamic process that is hard to visualize with static images or through text descriptions. View this animation to learn more about this process.

Watch this video online: https://youtu.be/HnKMB11ih2o

What is the difference between the driving force for Na^+ and K^+? And what is similar about the movement of these two ions?

The question is, now, what initiates the action potential? The description above conveniently glosses over that point. But it is vital to understanding what is happening. The membrane potential will stay at the resting voltage until something changes. The description above just says that a Na^+ channel opens. Now, to say "a channel opens" does not mean that one individual transmembrane protein changes. Instead, it means that one kind of channel opens. There are a few different types of channels that allow Na^+ to cross the membrane. A ligand-gated Na^+ channel will open when a neurotransmitter binds to it and a mechanically gated Na^+ channel will open when a physical stimulus affects a sensory receptor (like pressure applied to the skin compresses a touch receptor). Whether it is a neurotransmitter binding to its receptor protein or a sensory stimulus activating a sensory receptor cell, some stimulus gets the process started. Sodium starts to enter the cell and the membrane becomes less negative.

A third type of channel that is an important part of depolarization in the action potential is the voltage-gated Na^+ channel. The channels that start depolarizing the membrane because of a stimulus help the cell to depolarize from –70 mV to –55 mV. Once the membrane reaches that voltage, the voltage-gated Na^+ channels open. This is what is known as the threshold. Any depolarization that does not change the membrane potential to –55 mV or higher will not reach threshold and thus will not result in an action potential. Also, any stimulus that depolarizes the membrane to –55 mV or beyond will cause a large number of channels to open and an action potential will be initiated.

Because of the threshold, the action potential can be likened to a digital event—it either happens or it does not. If the threshold is not reached, then no action potential occurs. If depolarization reaches –55 mV, then the action potential continues and runs all the way to +30 mV, at which K^+ causes repolarization, including the hyperpolarizing overshoot. Also, those changes are the same for every action potential, which means that once the threshold is reached, the exact same thing happens. A stronger stimulus, which might depolarize the membrane well past threshold, will not make a "bigger" action potential. Action potentials are "all or none." Either

the membrane reaches the threshold and everything occurs as described above, or the membrane does not reach the threshold and nothing else happens. All action potentials peak at the same voltage (+30 mV), so one action potential is not bigger than another. Stronger stimuli will initiate multiple action potentials more quickly, but the individual signals are not bigger. Thus, for example, you will not feel a greater sensation of pain, or have a stronger muscle contraction, because of the size of the action potential because they are not different sizes.

As we have seen, the depolarization and repolarization of an action potential are dependent on two types of channels (the voltage-gated Na^+ channel and the voltage-gated K^+ channel). The voltage-gated Na^+ channel actually has two gates. One is the **activation gate**, which opens when the membrane potential crosses –55 mV. The other gate is the **inactivation gate**, which closes after a specific period of time—on the order of a fraction of a millisecond. When a cell is at rest, the activation gate is closed and the inactivation gate is open. However, when the threshold is reached, the activation gate opens, allowing Na^+ to rush into the cell. Timed with the peak of depolarization, the inactivation gate closes. During repolarization, no more sodium can enter the cell. When the membrane potential passes –55 mV again, the activation gate closes. After that, the inactivation gate re-opens, making the channel ready to start the whole process over again.

The voltage-gated K^+ channel has only one gate, which is sensitive to a membrane voltage of –50 mV. However, it does not open as quickly as the voltage-gated Na^+ channel does. It might take a fraction of a millisecond for the channel to open once that voltage has been reached. The timing of this coincides exactly with when the Na^+ flow peaks, so voltage-gated K^+ channels open just as the voltage-gated Na^+ channels are being inactivated. As the membrane potential repolarizes and the voltage passes –50 mV again, the channel closes—again, with a little delay. Potassium continues to leave the cell for a short while and the membrane potential becomes more negative, resulting in the hyperpolarizing overshoot. Then the channel closes again and the membrane can return to the resting potential because of the ongoing activity of the non-gated channels and the Na^+/K^+ pump.

All of this takes place within approximately 2 milliseconds (Figure 8). While an action potential is in progress, another one cannot be initiated. That effect is referred to as the **refractory period**. There are two phases of the refractory period: the **absolute refractory period** and the **relative refractory period**. During the absolute phase, another action potential will not start. This is because of the inactivation gate of the voltage-gated Na^+ channel. Once that channel is back to its resting conformation (less than –55 mV), a new action potential could be started, but only by a stronger stimulus than the one that initiated the current action potential. This is because of the flow of K^+ out of the cell. Because that ion is rushing out, any Na^+ that tries to enter will not depolarize the cell, but will only keep the cell from hyperpolarizing.

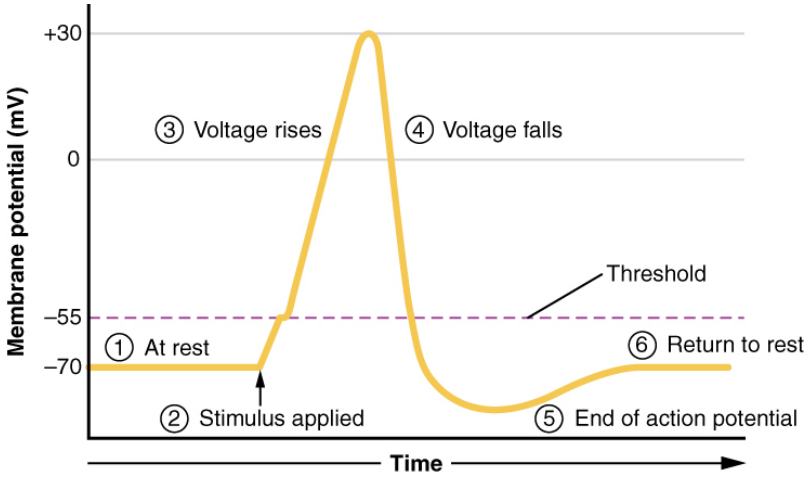


Figure 8. Stages of an Action Potential

Plotting voltage measured across the cell membrane against time (as shown in Figure 8), the events of the action potential can be related to specific changes in the membrane voltage.

1. At rest, the membrane voltage is –70 mV.
2. The membrane begins to depolarize when an external stimulus is applied.
3. The membrane voltage begins a rapid rise toward +30 mV.
4. The membrane voltage starts to return to a negative value.
5. Repolarization continues past the resting membrane voltage, resulting in hyperpolarization.
6. The membrane voltage returns to the resting value shortly after hyperpolarization.

Propagation of the Action Potential

The action potential is initiated at the beginning of the axon, at what is called the initial segment. There is a high density of voltage-gated Na^+ channels so that rapid depolarization can take place here. Going down the length of the axon, the action potential is propagated because more voltage-gated Na^+ channels are opened as the depolarization spreads. This spreading occurs because Na^+ enters through the channel and moves along the inside of the cell membrane. As the Na^+ moves, or flows, a short distance along the cell membrane, its positive charge depolarizes a little more of the cell membrane. As that depolarization spreads, new voltage-gated Na^+ channels open and more ions rush into the cell, spreading the depolarization a little farther.

Because voltage-gated Na^+ channels are inactivated at the peak of the depolarization, they cannot be opened again for a brief time—the absolute refractory period. Because of this, depolarization spreading back toward previously opened channels has no effect. The action potential must propagate toward the axon terminals; as a result, the polarity of the neuron is maintained, as mentioned above.

Propagation, as described above, applies to unmyelinated axons. When myelination is present, the action potential propagates differently. Sodium ions that enter the cell at the initial segment start to spread along the length of the axon segment, but there are no voltage-gated Na^+ channels until the first node of Ranvier. Because there is not constant opening of these channels along the axon segment, the depolarization spreads at an optimal speed. The distance between nodes is the optimal distance to keep the membrane still depolarized above threshold at the next node. As Na^+ spreads along the inside of the membrane of the axon segment, the charge starts to dissipate. If the node were any farther down the axon, that depolarization would have fallen off too much for voltage-gated Na^+ channels to be activated at the next node of Ranvier. If the nodes were any closer together, the speed of propagation would be slower.

Propagation along an unmyelinated axon is referred to as **continuous conduction**; along the length of a myelinated axon, it is **saltatory conduction**. Continuous conduction is slow because there are always voltage-gated Na^+ channels opening, and more and more Na^+ is rushing into the cell. Saltatory conduction is faster because the action potential basically jumps from one node to the next (*saltare* = "to leap"), and the new influx of Na^+ renews the depolarized membrane. Along with the myelination of the axon, the diameter of the axon can influence the speed of conduction. Much as water runs faster in a wide river than in a narrow creek, Na^+-based depolarization spreads faster down a wide axon than down a narrow one. This concept is known as **resistance** and is generally true for electrical wires or plumbing, just as it is true for axons, although the specific conditions are different at the scales of electrons or ions versus water in a river.

Homeostatic Imbalances: Potassium Concentration

Glial cells, especially astrocytes, are responsible for maintaining the chemical environment of the CNS tissue. The concentrations of ions in the extracellular fluid are the basis for how the membrane potential is established and changes in electrochemical signaling. If the balance of ions is upset, drastic outcomes are possible.

Normally the concentration of K^+ is higher inside the neuron than outside. After the repolarizing phase of the action potential, K^+ leakage channels and the Na^+/K^+ pump ensure that the ions return to their original locations. Following a stroke or other ischemic event, extracellular K^+ levels are elevated. The astrocytes in the area are equipped to clear excess K^+ to aid the pump. But when the level is far out of balance, the effects can be irreversible.

Astrocytes can become reactive in cases such as these, which impairs their ability to maintain the local chemical environment. The glial cells enlarge and their processes swell. They lose their K^+ buffering ability and the function of the pump is affected, or even reversed. If a Na^+ gradient breaks down, this has a more important effect than interrupting the action potential. Glucose transport into cells is coupled with Na^+ co-transport. When that is lost, the cell cannot get the energy it needs. In the central nervous system,

carbohydrate metabolism is the only means of producing ATP. Elsewhere in the body, cells rely on carbohydrates, lipids, or amino acids to power mitochondrial ATP production. But the CNS does not store lipids in adipocytes (fat cells) as an energy reserve. The lipids in the CNS are in the cell membranes of neurons and glial cells, notably as an integral component of myelin. Proteins in the CNS are crucial to neuronal function, in roles such as channels for electrical signaling or as part of the cytoskeleton. Those macromolecules are not used to power mitochondrial ATP production in neurons.

Visit this site to see a virtual neurophysiology lab, and to observe electrophysiological processes in the nervous system, where scientists directly measure the electrical signals produced by neurons. Often, the action potentials occur so rapidly that watching a screen to see them occur is not helpful. A speaker is powered by the signals recorded from a neuron and it "pops" each time the neuron fires an action potential. These action potentials are firing so fast that it sounds like static on the radio. Electrophysiologists can recognize the patterns within that static to understand what is happening. Why is the leech model used for measuring the electrical activity of neurons instead of using humans?

COMMUNICATION BETWEEN NEURONS

Learning Objectives

- Explain the differences between the types of graded potentials
- Categorize the major neurotransmitters by chemical type and effect

The electrical changes taking place within a neuron, as described in the previous section, are similar to a light switch being turned on. A stimulus starts the depolarization, but the action potential runs on its own once a threshold has been reached. The question is now, "What flips the light switch on?" Temporary changes to the cell membrane voltage can result from neurons receiving information from the environment, or from the action of one neuron on another. These special types of potentials influence a neuron and determine whether an action potential will occur or not. Many of these transient signals originate at the synapse.

Graded Potentials

Local changes in the membrane potential are called graded potentials and are usually associated with the dendrites of a neuron. The amount of change in the membrane potential is determined by the size of the stimulus that causes it. In the example of testing the temperature of the shower, slightly warm water would only initiate a small change in a thermoreceptor, whereas hot water would cause a large amount of change in the membrane potential.

Graded potentials can be of two sorts, either they are depolarizing or hyperpolarizing (Figure 1). For a membrane at the resting potential, a graded potential represents a change in that voltage either above –70 mV or below –70 mV. Depolarizing graded potentials are often the result of Na^+ or Ca^{2+} entering the cell. Both of these ions have higher concentrations outside the cell than inside; because they have a positive charge, they will move into the cell causing it to become less negative relative to the outside. Hyperpolarizing graded potentials can be caused

by K^+ leaving the cell or Cl^- entering the cell. If a positive charge moves out of a cell, the cell becomes more negative; if a negative charge enters the cell, the same thing happens.

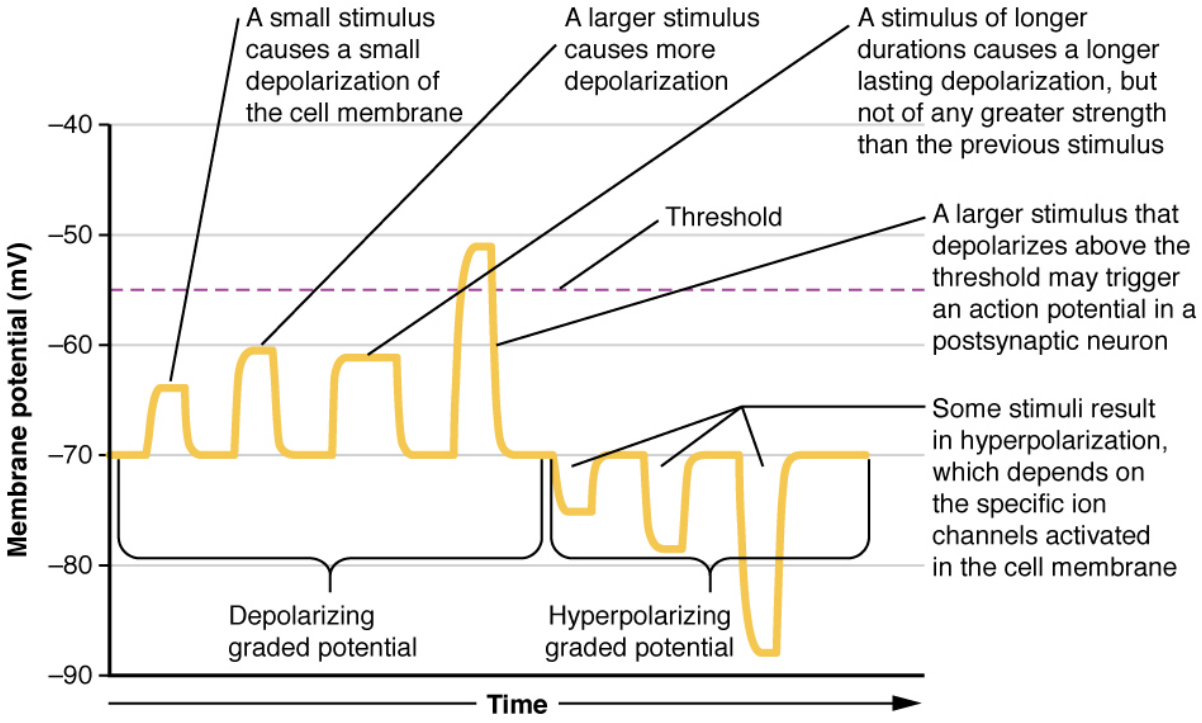


Figure 1. Graded Potentials. *Graded potentials are temporary changes in the membrane voltage, the characteristics of which depend on the size of the stimulus. Some types of stimuli cause depolarization of the membrane, whereas others cause hyperpolarization. It depends on the specific ion channels that are activated in the cell membrane.*

Types of Graded Potentials

For the unipolar cells of sensory neurons—both those with free nerve endings and those within encapsulations—graded potentials develop in the dendrites that influence the generation of an action potential in the axon of the same cell. This is called a **generator potential**. For other sensory receptor cells, such as taste cells or photoreceptors of the retina, graded potentials in their membranes result in the release of neurotransmitters at synapses with sensory neurons. This is called a **receptor potential**.

A **postsynaptic potential (PSP)** is the graded potential in the dendrites of a neuron that is receiving synapses from other cells. Postsynaptic potentials can be depolarizing or hyperpolarizing. Depolarization in a postsynaptic potential is called an **excitatory postsynaptic potential (EPSP)** because it causes the membrane potential to move toward threshold. Hyperpolarization in a postsynaptic potential is an **inhibitory postsynaptic potential (IPSP)** because it causes the membrane potential to move away from threshold.

Summation

All types of graded potentials will result in small changes of either depolarization or hyperpolarization in the voltage of a membrane. These changes can lead to the neuron reaching threshold if the changes add together, or **summate**. The combined effects of different types of graded potentials are illustrated in Figure 2. If the total change in voltage in the membrane is a positive 15 mV, meaning that the membrane depolarizes from –70 mV to –55 mV, then the graded potentials will result in the membrane reaching threshold.

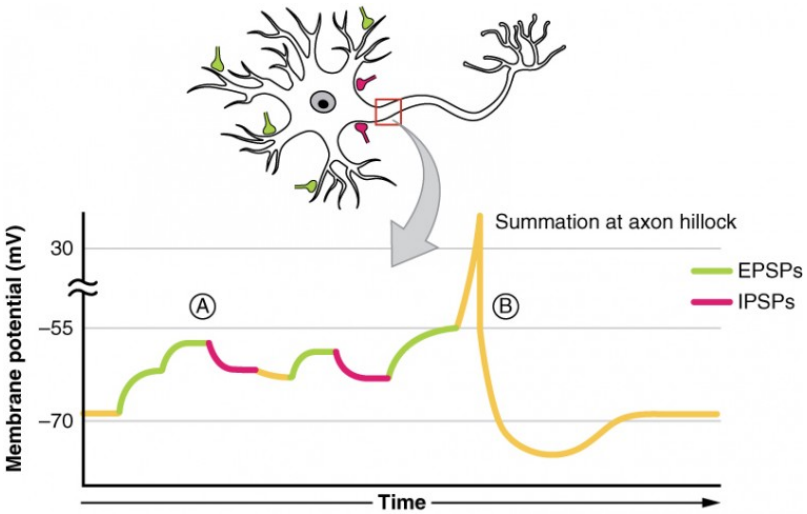


Figure 2. Postsynaptic Potential Summation *The result of summation of postsynaptic potentials is the overall change in the membrane potential. At point A, several different excitatory postsynaptic potentials add up to a large depolarization. At point B, a mix of excitatory and inhibitory postsynaptic potentials result in a different end result for the membrane potential.*

For receptor potentials, threshold is not a factor because the change in membrane potential for receptor cells directly causes neurotransmitter release. However, generator potentials can initiate action potentials in the sensory neuron axon, and postsynaptic potentials can initiate an action potential in the axon of other neurons. Graded potentials summate at a specific location at the beginning of the axon to initiate the action potential, namely the initial segment. For sensory neurons, which do not have a cell body between the dendrites and the axon, the initial segment is directly adjacent to the dendritic endings. For all other neurons, the axon hillock is essentially the initial segment of the axon, and it is where summation takes place. These locations have a high density of voltage-gated Na^+ channels that initiate the depolarizing phase of the action potential.

Summation can be spatial or temporal, meaning it can be the result of multiple graded potentials at different locations on the neuron, or all at the same place but separated in time. **Spatial summation** is related to associating the activity of multiple inputs to a neuron with each other. **Temporal summation** is the relationship of multiple action potentials from a single cell resulting in a significant change in the membrane potential. Spatial and temporal summation can act together, as well.

Watch this video to learn about summation.

Watch this video online: https://youtu.be/Pd0IQ-Nx8dM

The process of converting electrical signals to chemical signals and back requires subtle changes that can result in transient increases or decreases in membrane voltage. To cause a lasting change in the target cell, multiple signals are usually added together, or summated. Does spatial summation have to happen all at once, or can the separate signals arrive on the postsynaptic neuron at slightly different times? Explain your answer.

Synapses

There are two types of connections between electrically active cells, chemical synapses and electrical synapses. In a **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.

An example of a chemical synapse is the neuromuscular junction (NMJ) described in the chapter on muscle tissue. In the nervous system, there are many more synapses that are essentially the same as the NMJ. All synapses have common characteristics, which can be summarized in this list:

- presynaptic element
- neurotransmitter (packaged in vesicles)
- synaptic cleft
- receptor proteins
- postsynaptic element
- neurotransmitter elimination or re-uptake

For the NMJ, these characteristics are as follows: the presynaptic element is the motor neuron's axon terminals, the neurotransmitter is acetylcholine, the synaptic cleft is the space between the cells where the neurotransmitter diffuses, the receptor protein is the nicotinic acetylcholine receptor, the postsynaptic element is the sarcolemma of the muscle cell, and the neurotransmitter is eliminated by acetylcholinesterase. Other synapses are similar to this, and the specifics are different, but they all contain the same characteristics.

Neurotransmitter Release

When an action potential reaches the axon terminals, voltage-gated Ca^{2+} channels in the membrane of the synaptic end bulb open. The concentration of Ca^{2+} increases inside the end bulb, and the Ca^{2+} ion associates with proteins in the outer surface of neurotransmitter vesicles. The Ca^{2+} facilitates the merging of the vesicle with the presynaptic membrane so that the neurotransmitter is released through exocytosis into the small gap between the cells, known as the **synaptic cleft**.

Once in the synaptic cleft, the neurotransmitter diffuses the short distance to the postsynaptic membrane and can interact with neurotransmitter receptors. Receptors are specific for the neurotransmitter, and the two fit together like a key and lock. One neurotransmitter binds to its receptor and will not bind to receptors for other neurotransmitters, making the binding a specific chemical event (Figure 3).

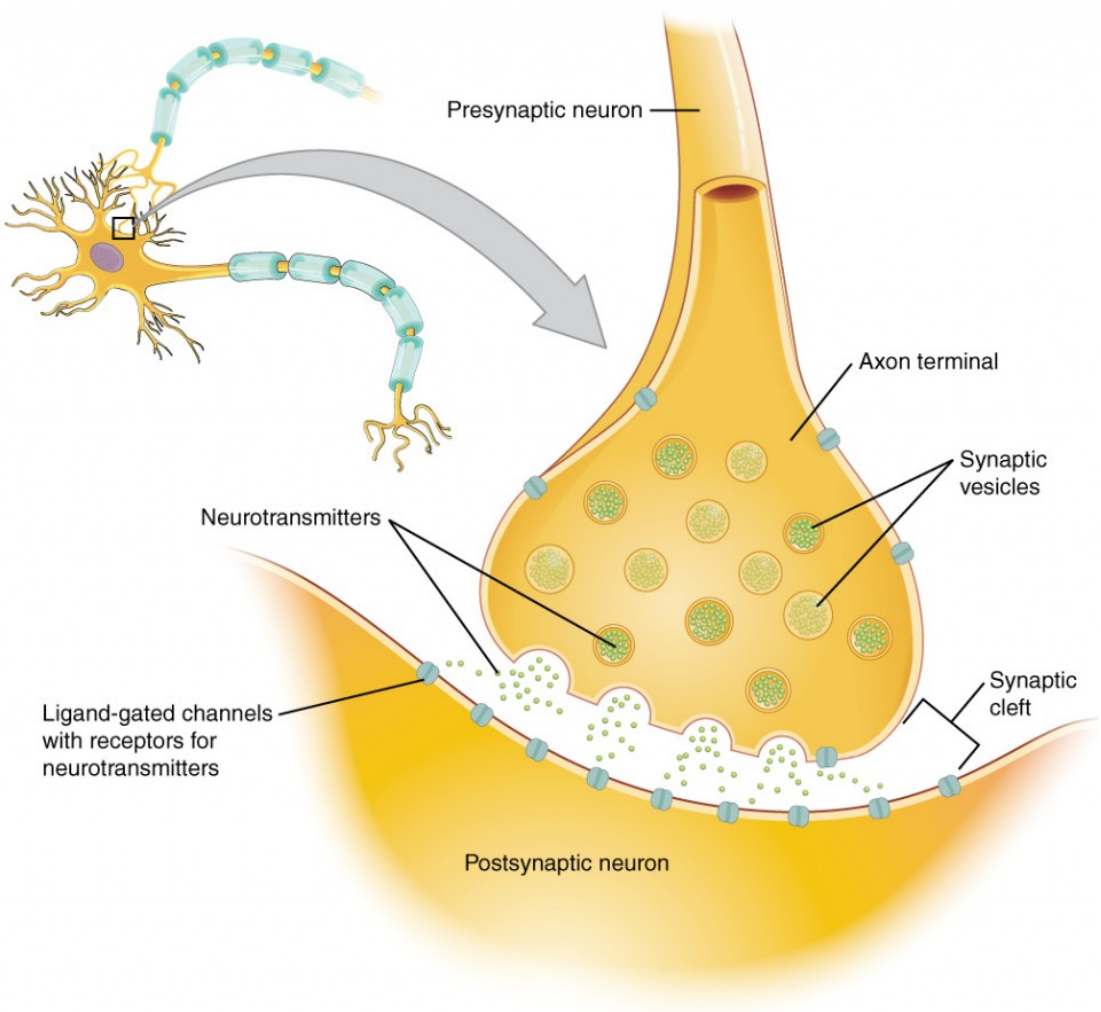


Figure 3. The Synapse. *The synapse is a connection between a neuron and its target cell (which is not necessarily a neuron). The presynaptic element is the synaptic end bulb of the axon where Ca^{2+} enters the bulb to cause vesicle fusion and neurotransmitter release. The neurotransmitter diffuses 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.*

Neurotransmitter Systems

There are several systems of neurotransmitters that are found at various synapses in the nervous system. These groups refer to the chemicals that are the neurotransmitters, and within the groups are specific systems.

The first group, which is a neurotransmitter system of its own, is the **cholinergic system**. It is the system based on acetylcholine. This includes the NMJ as an example of a cholinergic synapse, but cholinergic synapses are found in other parts of the nervous system. They are in the autonomic nervous system, as well as distributed throughout the brain.

The cholinergic system has two types of receptors, the **nicotinic receptor** is found in the NMJ as well as other synapses. There is also an acetylcholine receptor known as the **muscarinic receptor**. Both of these receptors are named for drugs that interact with the receptor in addition to acetylcholine. Nicotine will bind to the nicotinic receptor and activate it similar to acetylcholine. Muscarine, a product of certain mushrooms, will bind to the muscarinic receptor. However, nicotine will not bind to the muscarinic receptor and muscarine will not bind to the nicotinic receptor.

Another group of neurotransmitters are amino acids. This includes glutamate (Glu), GABA (gamma-aminobutyric acid, a derivative of glutamate), and glycine (Gly). These amino acids have an amino group and a carboxyl group

in their chemical structures. Glutamate is one of the 20 amino acids that are used to make proteins. Each amino acid neurotransmitter would be part of its own system, namely the glutamatergic, GABAergic, and glycinergic systems. They each have their own receptors and do not interact with each other. Amino acid neurotransmitters are eliminated from the synapse by reuptake. A pump in the cell membrane of the presynaptic element, or sometimes a neighboring glial cell, will clear the amino acid from the synaptic cleft so that it can be recycled, repackaged in vesicles, and released again.

Another class of neurotransmitter is the **biogenic amine**, a group of neurotransmitters that are enzymatically made from amino acids. They have amino groups in them, but no longer have carboxyl groups and are therefore no longer classified as amino acids. Serotonin is made from tryptophan. It is the basis of the serotonergic system, which has its own specific receptors. Serotonin is transported back into the presynaptic cell for repackaging.

Other biogenic amines are made from tyrosine, and include dopamine, norepinephrine, and epinephrine. Dopamine is part of its own system, the dopaminergic system, which has dopamine receptors. Dopamine is removed from the synapse by transport proteins in the presynaptic cell membrane. Norepinephrine and epinephrine belong to the adrenergic neurotransmitter system. The two molecules are very similar and bind to the same receptors, which are referred to as alpha and beta receptors. Norepinephrine and epinephrine are also transported back into the presynaptic cell. The chemical epinephrine (*epi–* = “on”; “*-nephrine*” = kidney) is also known as adrenaline (*renal* = “kidney”), and norepinephrine is sometimes referred to as noradrenaline. The adrenal gland produces epinephrine and norepinephrine to be released into the blood stream as hormones.

A **neuropeptide** is a neurotransmitter molecule made up of chains of amino acids connected by peptide bonds. This is what a protein is, but the term protein implies a certain length to the molecule. Some neuropeptides are quite short, such as met-enkephalin, which is five amino acids long. Others are long, such as beta-endorphin, which is 31 amino acids long. Neuropeptides are often released at synapses in combination with another neurotransmitter, and they often act as hormones in other systems of the body, such as vasoactive intestinal peptide (VIP) or substance P.

The effect of a neurotransmitter on the postsynaptic element is entirely dependent on the receptor protein. First, if there is no receptor protein in the membrane of the postsynaptic element, then the neurotransmitter has no effect. The depolarizing or hyperpolarizing effect is also dependent on the receptor. When acetylcholine binds to the nicotinic receptor, the postsynaptic cell is depolarized. This is because the receptor is a cation channel and positively charged Na^+ will rush into the cell. However, when acetylcholine binds to the muscarinic receptor, of which there are several variants, it might cause depolarization or hyperpolarization of the target cell.

The amino acid neurotransmitters, glutamate, glycine, and GABA, are almost exclusively associated with just one effect. Glutamate is considered an excitatory amino acid, but only because Glu receptors in the adult cause depolarization of the postsynaptic cell. Glycine and GABA are considered inhibitory amino acids, again because their receptors cause hyperpolarization.

The biogenic amines have mixed effects. For example, the dopamine receptors that are classified as D1 receptors are excitatory whereas D2-type receptors are inhibitory. Biogenic amine receptors and neuropeptide receptors can have even more complex effects because some may not directly affect the membrane potential, but rather have an effect on gene transcription or other metabolic processes in the neuron. The characteristics of the various neurotransmitter systems presented in this section are organized in Table 1.

Table 1. Characteristics of Neurotransmitter Systems

System	Chlolinergic	Amino acids	Biogenic amines	Neuropeptides
Neurotransmitters	Acetylchlonie	Glutamate, glycine, GABA	Serotonin (5-HT)	met-enkaphalin, beta-endorphin, VIP, Substance P, etc.
Receptors	Nicotonic and muscarinic receptors	Glu receptors, gly receptors, GABA receptors	5-HT receptors, D1 and D2 receptors, a-adrenergic and B-adrenergetic receptors	Receptors are too numerous to list, but are

Table 1. Characteristics of Neurotransmitter Systems				
System	Chlolinergic	Amino acids	Biogenic amines	Neuropeptides
				specific to the peptides
Elimination	Degredation by acetylcholinesterase	Reuptake by neurons of glia	Reuptake by neurons	Degredation by enzymes called peptidases
Postsynaptic effect	Nicotonic receptor causes depolarization. Muscarinic receptors can cause both depolarization of hyperpolarization depending on the subtype	Glu receptors cause depolarization. Gly and GABA receptors cause hyperpolarization	Depolarization or hyperpolarization depends on the specific receptor. For example, D1 receptors cause depolarization and D2 receptors cause hyperpolarization	Depolarization or hyperpolarization depends on the specific receptor

The important thing to remember about neurotransmitters, and signaling chemicals in general, is that the effect is entirely dependent on the receptor. Neurotransmitters bind to one of two classes of receptors at the cell surface, ionotropic or metabotropic (Figure 4). Ionotropic receptors are ligand-gated ion channels, such as the nicotinic receptor for acetylcholine or the glycine receptor. A **metabotropic receptor** involves a complex of proteins that result in metabolic changes within the cell. The receptor complex includes the transmembrane receptor protein, a G protein, and an effector protein. The neurotransmitter, referred to as the first messenger, binds to the receptor protein on the extracellular surface of the cell, and the intracellular side of the protein initiates activity of the G protein. The **G protein** is a guanosine triphosphate (GTP) hydrolase that physically moves from the receptor protein to the effector protein to activate the latter. An **effector protein** is an enzyme that catalyzes the generation of a new molecule, which acts as the intracellular mediator of the signal that binds to the receptor. This intracellular mediator is called the second messenger.

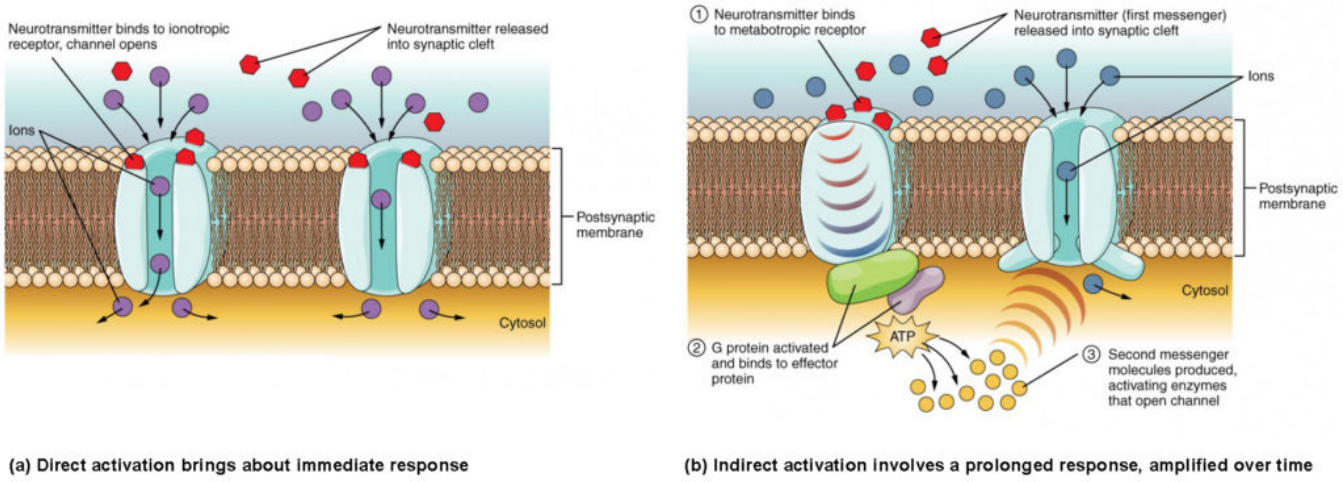


Figure 4. Receptor Types. *(a) An ionotropic receptor is a channel that opens when the neurotransmitter binds to it. (b) A metabotropic receptor is a complex that causes metabolic changes in the cell when the neurotransmitter binds to it (1). After binding, the G protein hydrolyzes GTP and moves to the effector protein (2). When the G protein contacts the effector protein, a second messenger is generated, such as cAMP (3). The second messenger can then go on to cause changes in the neuron, such as opening or closing ion channels, metabolic changes, and changes in gene transcription.*

Different receptors use different second messengers. Two common examples of second messengers are cyclic adenosine monophosphate (cAMP) and inositol triphosphate (IP_3). The enzyme adenylate cyclase (an example of

an effector protein) makes cAMP, and phospholipase C is the enzyme that makes IP_3. Second messengers, after they are produced by the effector protein, cause metabolic changes within the cell. These changes are most likely the activation of other enzymes in the cell. In neurons, they often modify ion channels, either opening or closing them. These enzymes can also cause changes in the cell, such as the activation of genes in the nucleus, and therefore the increased synthesis of proteins. In neurons, these kinds of changes are often the basis of stronger connections between cells at the synapse and may be the basis of learning and memory.

Watch this video to learn about the release of a neurotransmitter.

Watch this video online: https://youtu.be/XGINQ7xhPkM

The action potential reaches the end of the axon, called the axon terminal, and a chemical signal is released to tell the target cell to do something—either to initiate a new action potential, or to suppress that activity. In a very short space, the electrical signal of the action potential is changed into the chemical signal of a neurotransmitter and then back to electrical changes in the target cell membrane. What is the importance of voltage-gated calcium channels in the release of neurotransmitters?

Disorders of the Nervous System

The underlying cause of some neurodegenerative diseases, such as Alzheimer's and Parkinson's, appears to be related to proteins—specifically, to proteins behaving badly. One of the strongest theories of what causes Alzheimer's disease is based on the accumulation of beta-amyloid plaques, dense conglomerations of a protein that is not functioning correctly. Parkinson's disease is linked to an increase in a protein known as alpha-synuclein that is toxic to the cells of the substantia nigra nucleus in the midbrain.

For proteins to function correctly, they are dependent on their three-dimensional shape. The linear sequence of amino acids folds into a three-dimensional shape that is based on the interactions between and among those amino acids. When the folding is disturbed, and proteins take on a different shape, they stop functioning correctly. But the disease is not necessarily the result of functional loss of these proteins; rather, these altered proteins start to accumulate and may become toxic. For example, in Alzheimer's, the hallmark of the disease is the accumulation of these amyloid plaques in the cerebral cortex. The term coined to describe this sort of disease is "proteopathy" and it includes other diseases. Creutzfeld-Jacob disease, the human variant of the prion disease known as mad cow disease in the bovine, also involves the accumulation of amyloid plaques, similar to Alzheimer's. Diseases of other organ systems can fall into this group as well, such as cystic fibrosis or type 2 diabetes. Recognizing the relationship between these diseases has suggested new therapeutic possibilities. Interfering with the accumulation of the proteins, and possibly as early as their original production within the cell, may unlock new ways to alleviate these devastating diseases.

Self-Check Questions

Visit your course online to take a quiz to check your understanding of Communication Between Neurons:

VIDEO: NEURON STRUCTURE

Watch this video online: https://youtu.be/03GUyBNKBPc

GLOSSARY: THE NERVOUS SYSTEM

absolute refractory period: time during an action period when another action potential cannot be generated because the voltage-gated Na^+ channel is inactivated

action potential: change in voltage of a cell membrane in response to a stimulus that results in transmission of an electrical signal; unique to neurons and muscle fibers

activation gate: part of the voltage-gated Na^+ channel that opens when the membrane voltage reaches threshold

astrocyte: glial cell type of the CNS that provides support for neurons and maintains the blood-brain barrier

autonomic nervous system (ANS): functional division of the nervous system that is responsible for homeostatic reflexes that coordinate control of cardiac and smooth muscle, as well as glandular tissue

axon hillock: tapering of the neuron cell body that gives rise to the axon

axon segment: single stretch of the axon insulated by myelin and bounded by nodes of Ranvier at either end (except for the first, which is after the initial segment, and the last, which is followed by the axon terminal)

axon terminal: end of the axon, where there are usually several branches extending toward the target cell

axon: single process of the neuron that carries an electrical signal (action potential) away from the cell body toward a target cell

axoplasm: cytoplasm of an axon, which is different in composition than the cytoplasm of the neuronal cell body

biogenic amine: class of neurotransmitters that are enzymatically derived from amino acids but no longer contain a carboxyl group

bipolar: shape of a neuron with two processes extending from the neuron cell body—the axon and one dendrite

blood-brain barrier (BBB): physiological barrier between the circulatory system and the central nervous system that establishes a privileged blood supply, restricting the flow of substances into the CNS

brain: the large organ of the central nervous system composed of white and gray matter, contained within the cranium and continuous with the spinal cord

central nervous system (CNS): anatomical division of the nervous system located within the cranial and vertebral cavities, namely the brain and spinal cord

cerebral cortex: outermost layer of gray matter in the brain, where conscious perception takes place

cerebrospinal fluid (CSF): circulatory medium within the CNS that is produced by ependymal cells in the choroid plexus filtering the blood

chemical synapse: connection between two neurons, or between a neuron and its target, where a neurotransmitter diffuses across a very short distance

cholinergic system: neurotransmitter system of acetylcholine, which includes its receptors and the enzyme acetylcholinesterase

choroid plexus: specialized structure containing ependymal cells that line blood capillaries and filter blood to produce CSF in the four ventricles of the brain

continuous conduction: slow propagation of an action potential along an unmyelinated axon owing to voltage-gated Na^+ channels located along the entire length of the cell membrane

dendrite: one of many branchlike processes that extends from the neuron cell body and functions as a contact for incoming signals (synapses) from other neurons or sensory cells

depolarization: change in a cell membrane potential from rest toward zero

effector protein: enzyme that catalyzes the generation of a new molecule, which acts as the intracellular mediator of the signal that binds to the receptor

electrical synapse: connection between two neurons, or any two electrically active cells, where ions flow directly through channels spanning their adjacent cell membranes

electrochemical exclusion: principle of selectively allowing ions through a channel on the basis of their charge

enteric nervous system (ENS): neural tissue associated with the digestive system that is responsible for nervous control through autonomic connections

ependymal cell: glial cell type in the CNS responsible for producing cerebrospinal fluid

excitable membrane: cell membrane that regulates the movement of ions so that an electrical signal can be generated

excitatory postsynaptic potential (EPSP): graded potential in the postsynaptic membrane that is the result of depolarization and makes an action potential more likely to occur

G protein: guanosine triphosphate (GTP) hydrolase that physically moves from the receptor protein to the effector protein to activate the latter

ganglion: localized collection of neuron cell bodies in the peripheral nervous system

gated: property of a channel that determines how it opens under specific conditions, such as voltage change or physical deformation

generator potential: graded potential from dendrites of a unipolar cell which generates the action potential in the initial segment of that cell's axon

glial cell: one of the various types of neural tissue cells responsible for maintenance of the tissue, and largely responsible for supporting neurons

graded potential: change in the membrane potential that varies in size, depending on the size of the stimulus that elicits it

gray matter: regions of the nervous system containing cell bodies of neurons with few or no myelinated axons; actually may be more pink or tan in color, but called gray in contrast to white matter

inactivation gate: part of a voltage-gated Na^+ channel that closes when the membrane potential reaches +30 mV

inhibitory postsynaptic potential (IPSP): graded potential in the postsynaptic membrane that is the result of hyperpolarization and makes an action potential less likely to occur

initial segment: first part of the axon as it emerges from the axon hillock, where the electrical signals known as action potentials are generated

integration: nervous system function that combines sensory perceptions and higher cognitive functions (memories, learning, emotion, etc.) to produce a response

ionotropic receptor: neurotransmitter receptor that acts as an ion channel gate, and opens by the binding of the neurotransmitter

leakage channel: ion channel that opens randomly and is not gated to a specific event, also known as a non-gated channel

ligand-gated channels: another name for an ionotropic receptor for which a neurotransmitter is the ligand

lower motor neuron: second neuron in the motor command pathway that is directly connected to the skeletal muscle

mechanically gated channel: ion channel that opens when a physical event directly affects the structure of the protein

membrane potential: distribution of charge across the cell membrane, based on the charges of ions

metabotropic receptor: neurotransmitter receptor that involves a complex of proteins that cause metabolic changes in a cell

microglia: glial cell type in the CNS that serves as the resident component of the immune system

multipolar: shape of a neuron that has multiple processes—the axon and two or more dendrites

muscarinic receptor: type of acetylcholine receptor protein that is characterized by also binding to muscarine and is a metabotropic receptor

myelin sheath: lipid-rich layer of insulation that surrounds an axon, formed by oligodendrocytes in the CNS and Schwann cells in the PNS; facilitates the transmission of electrical signals

myelin: lipid-rich insulating substance surrounding the axons of many neurons, allowing for faster transmission of electrical signals

nerve: cord-like bundle of axons located in the peripheral nervous system that transmits sensory input and response output to and from the central nervous system

neuron: neural tissue cell that is primarily responsible for generating and propagating electrical signals into, within, and out of the nervous system

neuropeptide: neurotransmitter type that includes protein molecules and shorter chains of amino acids

neurotransmitter: chemical signal that is released from the synaptic end bulb of a neuron to cause a change in the target cell

nicotinic receptor: type of acetylcholine receptor protein that is characterized by also binding to nicotine and is an ionotropic receptor

node of Ranvier: gap between two myelinated regions of an axon, allowing for strengthening of the electrical signal as it propagates down the axon

nonspecific channel: channel that is not specific to one ion over another, such as a nonspecific cation channel that allows any positively charged ion across the membrane

nucleus: in the nervous system, a localized collection of neuron cell bodies that are functionally related; a “center” of neural function

oligodendrocyte: glial cell type in the CNS that provides the myelin insulation for axons in tracts

peripheral nervous system (PNS): anatomical division of the nervous system that is largely outside the cranial and vertebral cavities, namely all parts except the brain and spinal cord

postsynaptic potential (PSP): graded potential in the postsynaptic membrane caused by the binding of neurotransmitter to protein receptors

precentral gyrus of the frontal cortex: region of the cerebral cortex responsible for generating motor commands, where the upper motor neuron cell body is located

process: in cells, an extension of a cell body; in the case of neurons, this includes the axon and dendrites

propagation: movement of an action potential along the length of an axon

receptor potential: graded potential in a specialized sensory cell that directly causes the release of neurotransmitter without an intervening action potential

refractory period: time after the initiation of an action potential when another action potential cannot be generated

relative refractory period: time during the refractory period when a new action potential can only be initiated by a stronger stimulus than the current action potential because voltage-gated K^+ channels are not closed

repolarization: return of the membrane potential to its normally negative voltage at the end of the action potential

resistance: property of an axon that relates to the ability of particles to diffuse through the cytoplasm; this is inversely proportional to the fiber diameter

response: nervous system function that causes a target tissue (muscle or gland) to produce an event as a consequence to stimuli

resting membrane potential: the difference in voltage measured across a cell membrane under steady-state conditions, typically -70 mV

Schwann cell: glial cell type in the PNS that provides the myelin insulation for axons in nerves

saltatory conduction: quick propagation of the action potential along a myelinated axon owing to voltage-gated Na^+ channels being present only at the nodes of Ranvier

satellite cell: glial cell type in the PNS that provides support for neurons in the ganglia

sensation: nervous system function that receives information from the environment and translates it into the electrical signals of nervous tissue

size exclusion: principle of selectively allowing ions through a channel on the basis of their relative size

soma: in neurons, that portion of the cell that contains the nucleus; the cell body, as opposed to the cell processes (axons and dendrites)

somatic nervous system (SNS): functional division of the nervous system that is concerned with conscious perception, voluntary movement, and skeletal muscle reflexes

spatial summation: combination of graded potentials across the neuronal cell membrane caused by signals from separate presynaptic elements that add up to initiate an action potential

spinal cord: organ of the central nervous system found within the vertebral cavity and connected with the periphery through spinal nerves; mediates reflex behaviors

stimulus: an event in the external or internal environment that registers as activity in a sensory neuron

summate: to add together, as in the cumulative change in postsynaptic potentials toward reaching threshold in the membrane, either across a span of the membrane or over a certain amount of time

synapse: narrow junction across which a chemical signal passes from neuron to the next, initiating a new electrical signal in the target cell

synaptic cleft: small gap between cells in a chemical synapse where neurotransmitter diffuses from the presynaptic element to the postsynaptic element

synaptic end bulb: swelling at the end of an axon where neurotransmitter molecules are released onto a target cell across a synapse

temporal summation: combination of graded potentials at the same location on a neuron resulting in a strong signal from one input

thalamus: region of the central nervous system that acts as a relay for sensory pathways

thermoreceptor: type of sensory receptor capable of transducing temperature stimuli into neural action potentials

threshold: membrane voltage at which an action potential is initiated

tract: bundle of axons in the central nervous system having the same function and point of origin

unipolar: shape of a neuron which has only one process that includes both the axon and dendrite

upper motor neuron: first neuron in the motor command pathway with its cell body in the cerebral cortex that synapses on the lower motor neuron in the spinal cord

ventricle: central cavity within the brain where CSF is produced and circulates

voltage-gated channel: ion channel that opens because of a change in the charge distributed across the membrane where it is located

white matter: regions of the nervous system containing mostly myelinated axons, making the tissue appear white because of the high lipid content of myelin

PRACTICE TEST: THE NERVOUS SYSTEM AND NERVOUS TISSUE

Review the material from this module by completing the practice in course online.

LAB AND STUDY PACKET: THE NERVOUS SYSTEM

Instructors, make a copy of this packet to modify this worksheet and lab to fit your classroom needs:

https://docs.google.com/document/d/1-y2E5FTY-TEXy5FCqfiIHe5wO6CN85KUophQmHl9iqc/pub

MODULE 15: THE AUTONOMIC NERVOUS SYSTEM

INTRODUCTION TO THE AUTONOMIC NERVOUS SYSTEM

Learning Objectives

- Describe the components of the autonomic nervous system
- Differentiate between the structures of the sympathetic and parasympathetic divisions in the autonomic nervous system
- Name the components of a visceral reflex specific to the autonomic division to which it belongs
- Predict the response of a target effector to autonomic input on the basis of the released signaling molecule
- Describe how the central nervous system coordinates and contributes to autonomic functions

The autonomic nervous system is often associated with the "fight-or-flight response," which refers to the preparation of the body to either run away from a threat or to stand and fight in the face of that threat. To suggest what this means, consider the (very unlikely) situation of seeing a lioness hunting out on the savannah. Though this is not a common threat that humans deal with in the modern world, it represents the type of environment in which the human species thrived and adapted. The spread of humans around the world to the present state of the modern age occurred much more quickly than any species would adapt to environmental pressures such as predators. However, the reactions modern humans have in the modern world are based on these prehistoric situations. If your boss is walking down the hallway on Friday afternoon looking for "volunteers" to come in on the weekend, your response is the same as the prehistoric human seeing the lioness running across the savannah: fight or flight.

Figure 1. Fight or Flight? *Though the threats that modern humans face are not large predators, the autonomic nervous system is adapted to this type of stimulus. The modern world presents stimuli that trigger the same response. (credit: Vernon Swanepoel)*

Most likely, your response to your boss—not to mention the lioness—would be flight. Run away! The autonomic system is responsible for the physiological response to make that possible, and hopefully successful. Adrenaline

starts to flood your circulatory system. Your heart rate increases. Sweat glands become active. The bronchi of the lungs dilate to allow more air exchange. Pupils dilate to increase visual information. Blood pressure increases in general, and blood vessels dilate in skeletal muscles. Time to run. Similar physiological responses would occur in preparation for fighting off the threat.

This response should sound a bit familiar. The autonomic nervous system is tied into emotional responses as well, and the fight-or-flight response probably sounds like a panic attack. In the modern world, these sorts of reactions are associated with anxiety as much as with response to a threat. It is engrained in the nervous system to respond like this. In fact, the adaptations of the autonomic nervous system probably predate the human species and are likely to be common to all mammals, and perhaps shared by many animals. That lioness might herself be threatened in some other situation.

However, the autonomic nervous system is not just about responding to threats. Besides the fight-or-flight response, there are the responses referred to as “rest and digest.” If that lioness is successful in her hunting, then she is going to rest from the exertion. Her heart rate will slow. Breathing will return to normal. The digestive system has a big job to do. Much of the function of the autonomic system is based on the connections within an autonomic, or visceral, reflex.

DIVISIONS OF THE AUTONOMIC NERVOUS SYSTEM

Learning Objectives

- Name the components that generate the sympathetic and parasympathetic responses of the autonomic nervous system
- Explain the differences in output connections within the two divisions of the autonomic nervous system
- Describe the signaling molecules and receptor proteins involved in communication within the two divisions of the autonomic nervous system

The nervous system can be divided into two functional parts: the somatic nervous system and the autonomic nervous system. The major differences between the two systems are evident in the responses that each produces. The somatic nervous system causes contraction of skeletal muscles. The autonomic nervous system controls cardiac and smooth muscle, as well as glandular tissue. The somatic nervous system is associated with voluntary responses (though many can happen without conscious awareness, like breathing), and the autonomic nervous system is associated with involuntary responses, such as those related to homeostasis.

The autonomic nervous system regulates many of the internal organs through a balance of two aspects, or divisions. In ition to the endocrine system, the autonomic nervous system is instrumental in homeostatic mechanisms in the body. The two divisions of the autonomic nervous system are the **sympathetic division** and the **parasympathetic division**. The sympathetic system is associated with the **fight-or-flight response**, and parasympathetic activity is referred to by the epithet of **rest and digest**. Homeostasis is the balance between the two systems. At each target effector, dual innervation determines activity. For example, the heart receives connections from both the sympathetic and parasympathetic divisions. One causes heart rate to increase, whereas the other causes heart rate to decrease.

Watch this video to learn more about adrenaline and the fight-or-flight response.

Watch this video online: https://youtu.be/m2GywoS77qc

When someone is said to have a rush of adrenaline, the image of bungee jumpers or skydivers usually comes to mind. But adrenaline, also known as epinephrine, is an important chemical in coordinating the body's fight-or-flight response. In this video, you look inside the physiology of the fight-or-flight response, as envisioned for a firefighter. His body's reaction is the result of the sympathetic division of the autonomic nervous system causing system-wide changes as it prepares for extreme responses. What two changes does adrenaline bring about to help the skeletal muscle response?

Sympathetic Division of the Autonomic Nervous System

To respond to a threat—to fight or to run away—the sympathetic system causes divergent effects as many different effector organs are activated together for a common purpose. More oxygen needs to be inhaled and delivered to skeletal muscle. The respiratory, cardiovascular, and musculoskeletal systems are all activated together. itionally, sweating keeps the excess heat that comes from muscle contraction from causing the body to overheat. The digestive system shuts down so that blood is not absorbing nutrients when it should be delivering oxygen to skeletal muscles. To coordinate all these responses, the connections in the sympathetic system diverge from a limited region of the central nervous system (CNS) to a wide array of ganglia that project to the many effector organs simultaneously. The complex set of structures that compose the output of the sympathetic system make it possible for these disparate effectors to come together in a coordinated, systemic change.

The sympathetic division of the autonomic nervous system influences the various organ systems of the body through connections emerging from the thoracic and upper lumbar spinal cord. It is referred to as the **thoracolumbar system** to reflect this anatomical basis. A **central neuron** in the lateral horn of any of these spinal regions projects to ganglia adjacent to the vertebral column through the ventral spinal roots.

The majority of ganglia of the sympathetic system belong to a network of **sympathetic chain ganglia** that runs alongside the vertebral column. The ganglia appear as a series of clusters of neurons linked by axonal bridges. There are typically 23 ganglia in the chain on either side of the spinal column. Three correspond to the cervical region, 12 are in the thoracic region, four are in the lumbar region, and four correspond to the sacral region. The cervical and sacral levels are not connected to the spinal cord directly through the spinal roots, but through ascending or descending connections through the bridges within the chain.

A diagram that shows the connections of the sympathetic system is somewhat like a circuit diagram that shows the electrical connections between different receptacles and devices. In Figure 1, the "circuits" of the sympathetic system are intentionally simplified.

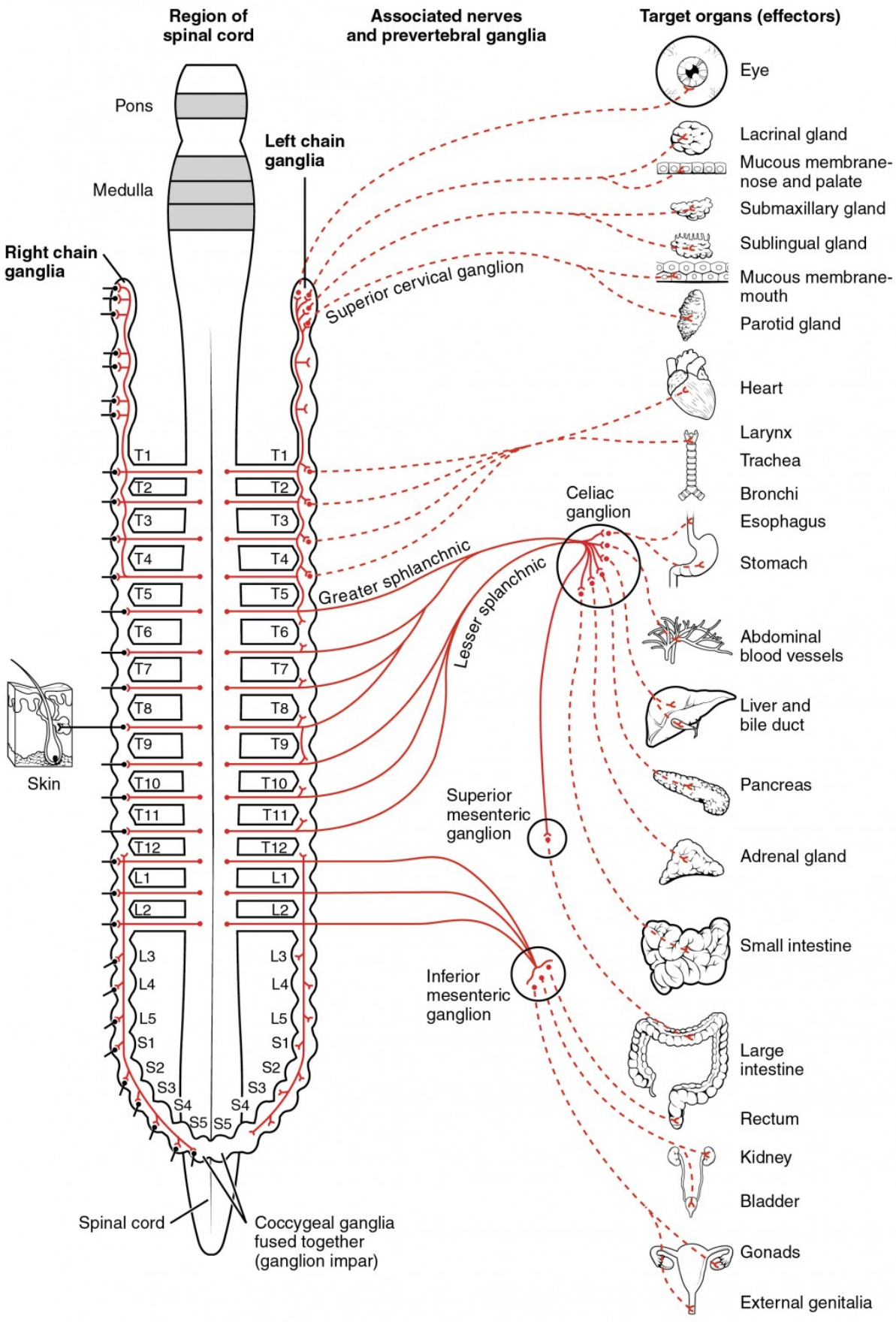

Region of spinal cord
Associated nerves and prevertebral ganglia
Target organs (effectors)
Pons
Medulla
Left chain ganglia
Right chain ganglia
Superior cervical ganglion
Greater sphlanchnic
Lesser splanchnic
Celiac ganglion
Superior mesenteric ganglion
Inferior mesenteric ganglion
T1
T2
T3
T4
T5
T6
T7
T8
T9
T10
T11
T12
L1
L2
L3
L4
L5
S1
S2
S3
S4
S5
Skin
Spinal cord
Coccygeal ganglia fused together (ganglion impar)
Eye
Lacrinal gland
Mucous membrane-nose and palate
Submaxillary gland
Sublingual gland
Mucous membrane-mouth
Parotid gland
Heart
Larynx
Trachea
Bronchi
Esophagus
Stomach
Abdominal blood vessels
Liver and bile duct
Pancreas
Adrenal gland
Small intestine
Large intestine
Rectum
Kidney
Bladder
Gonads
External genitalia

Figure 1. Connections of Sympathetic Division of the Autonomic Nervous System. *Neurons from the lateral horn of the spinal cord (preganglionic neurons) project to the chain ganglia on either side of the vertebral column or to collateral (prevertebral) ganglia that are anterior to the vertebral column in the abdominal cavity. Axons from these ganglionic neurons (postganglionic fibers) then project to target effectors throughout the body.*

To continue with the analogy of the circuit diagram, there are three different types of "junctions" that operate within the sympathetic system (Figure 2). The first type is most direct: the sympathetic nerve projects to the chain ganglion at the same level as the **target effector** (the organ, tissue, or gland to be innervated).

An example of this type is spinal nerve T1 that synapses with the T1 chain ganglion to innervate the trachea. The fibers of this branch are called **white rami communicantes** (singular = *ramus communicans*); they are myelinated and therefore referred to as white (see Figure 2a). The axon from the central neuron (the preganglionic fiber shown as a solid line) synapses with the **ganglionic neuron** (with the postganglionic fiber shown as a dashed line). This neuron then projects to a target effector—in this case, the trachea—via **gray rami communicantes**, which are unmyelinated axons.

In some cases, the target effectors are located superior or inferior to the spinal segment at which the preganglionic fiber emerges. With respect to the "wiring" involved, the synapse with the ganglionic neuron occurs at chain ganglia superior or inferior to the location of the central neuron. An example of this is spinal nerve T1 that innervates the eye. The spinal nerve tracks up through the chain until it reaches the **superior cervical ganglion**, where it synapses with the postganglionic neuron (see Figure 2b). The cervical ganglia are referred to as **paravertebral ganglia**, given their location adjacent to prevertebral ganglia in the sympathetic chain.

Not all axons from the central neurons terminate in the chain ganglia. itional branches from the ventral nerve root continue through the chain and on to one of the collateral ganglia as the **greater splanchnic nerve** or **lesser splanchnic nerve**. For example, the greater splanchnic nerve at the level of T5 synapses with a collateral ganglion outside the chain before making the connection to the postganglionic nerves that innervate the stomach (see Figure 2c).

Collateral ganglia, also called **prevertebral ganglia**, are situated anterior to the vertebral column and receive inputs from splanchnic nerves as well as central sympathetic neurons. They are associated with controlling organs in the abdominal cavity, and are also considered part of the enteric nervous system. The three collateral ganglia are the **celiac ganglion**, the **superior mesenteric ganglion**, and the **inferior mesenteric ganglion** (see Figure 1). The word celiac is derived from the Latin word "coelom," which refers to a body cavity (in this case, the abdominal cavity), and the word mesenteric refers to the digestive system.

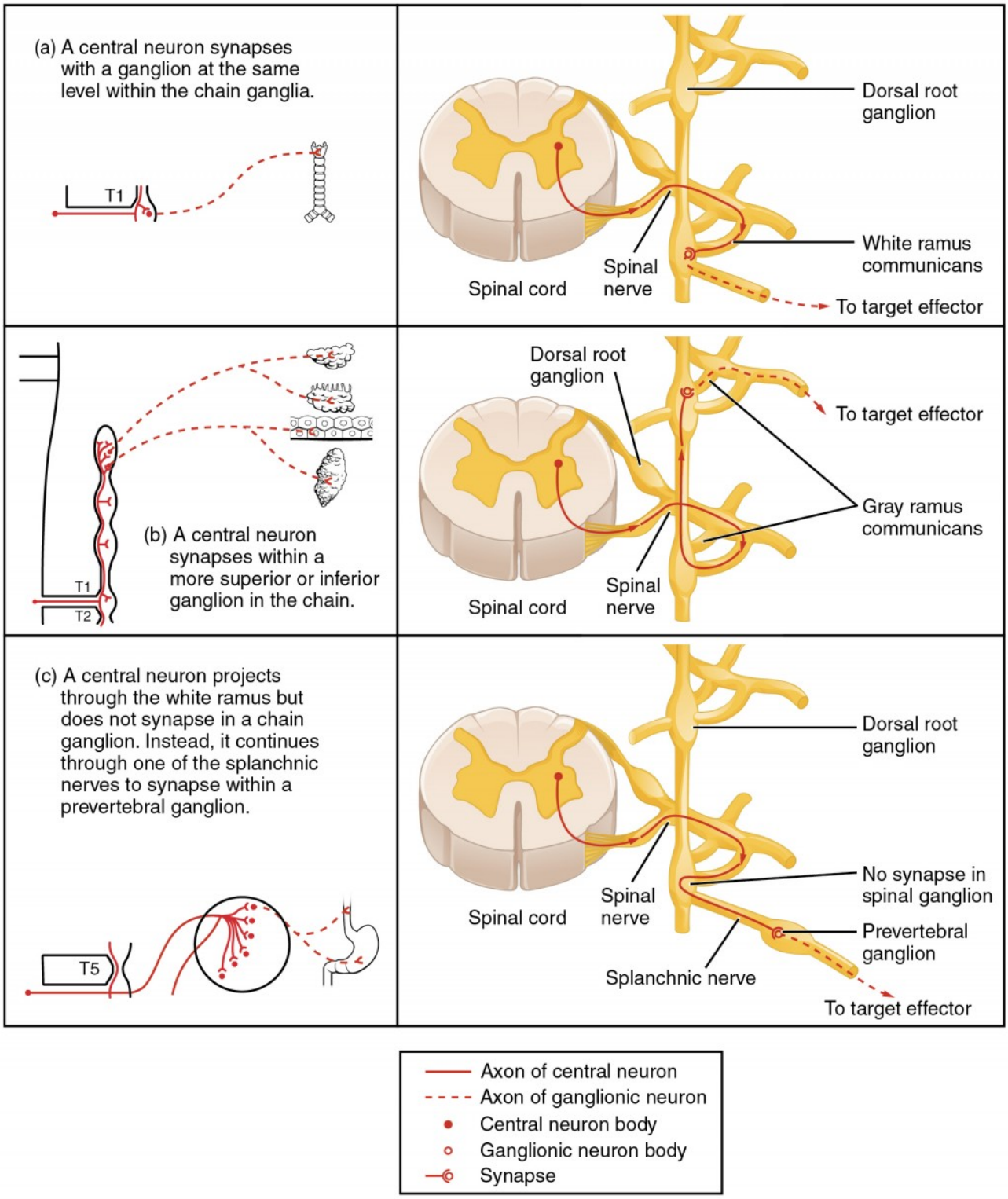


Figure 2. Sympathetic Connections and Chain Ganglia. *The axon from a central sympathetic neuron in the spinal cord can project to the periphery in a number of different ways. (a) The fiber can project out to the ganglion at the same level and synapse on a ganglionic neuron. (b) A branch can project to more superior or inferior ganglion in the chain. (c) A branch can project through the white ramus communicans, but not terminate on a ganglionic neuron in the chain. Instead, it projects through one of the splanchnic nerves to a collateral ganglion or the adrenal medulla (not pictured).*

An axon from the central neuron that projects to a sympathetic ganglion is referred to as a preganglionic fiber or neuron, and represents the output from the CNS to the ganglion. Because the sympathetic ganglia are adjacent to

the vertebral column, preganglionic sympathetic fibers are relatively short, and they are myelinated. A **postganglionic fiber**—the axon from a ganglionic neuron that projects to the target effector—represents the output of a ganglion that directly influences the organ.

Compared with the preganglionic fibers, postganglionic sympathetic fibers are long because of the relatively greater distance from the ganglion to the target effector. These fibers are unmyelinated. (Note that the term "postganglionic neuron" may be used to describe the projection from a ganglion to the target. The problem with that usage is that the cell body is in the ganglion, and only the fiber is postganglionic. Typically, the term neuron applies to the entire cell.)

One type of preganglionic sympathetic fiber does not terminate in a ganglion. These are the axons from central sympathetic neurons that project to the **adrenal medulla**, the interior portion of the adrenal gland. These axons are still referred to as preganglionic fibers, but the target is not a ganglion. The adrenal medulla releases signaling molecules into the bloodstream, rather than using axons to communicate with target structures. The cells in the adrenal medulla that are contacted by the preganglionic fibers are called **chromaffin cells**. These cells are neurosecretory cells that develop from the neural crest along with the sympathetic ganglia, reinforcing the idea that the gland is, functionally, a sympathetic ganglion.

The projections of the sympathetic division of the autonomic nervous system diverge widely, resulting in a broad influence of the system throughout the body. As a response to a threat, the sympathetic system would increase heart rate and breathing rate and cause blood flow to the skeletal muscle to increase and blood flow to the digestive system to decrease. Sweat gland secretion should also increase as part of an integrated response.

All of those physiological changes are going to be required to occur together to run away from the hunting lioness, or the modern equivalent. This divergence is seen in the branching patterns of preganglionic sympathetic neurons—a single preganglionic sympathetic neuron may have 10–20 targets. An axon that leaves a central neuron of the lateral horn in the thoracolumbar spinal cord will pass through the white ramus communicans and enter the sympathetic chain, where it will branch toward a variety of targets. At the level of the spinal cord at which the preganglionic sympathetic fiber exits the spinal cord, a branch will synapse on a neuron in the adjacent chain ganglion.

Some branches will extend up or down to a different level of the chain ganglia. Other branches will pass through the chain ganglia and project through one of the splanchnic nerves to a collateral ganglion. Finally, some branches may project through the splanchnic nerves to the adrenal medulla. All of these branches mean that one preganglionic neuron can influence different regions of the sympathetic system very broadly, by acting on widely distributed organs.

Parasympathetic Division of the Autonomic Nervous System

The parasympathetic division of the autonomic nervous system is named because its central neurons are located on either side of the thoracolumbar region of the spinal cord (*para–* = "beside" or "near"). The parasympathetic system can also be referred to as the **craniosacral system** (or outflow) because the preganglionic neurons are located in nuclei of the brain stem and the lateral horn of the sacral spinal cord.

The connections, or "circuits," of the parasympathetic division are similar to the general layout of the sympathetic division with a few specific differences (Figure 3). The preganglionic fibers from the cranial region travel in cranial nerves, whereas preganglionic fibers from the sacral region travel in spinal nerves. The targets of these fibers are **terminal ganglia**, which are located near—or even within—the target effector. These ganglia are often referred to as **intramural ganglia** when they are found within the walls of the target organ. The postganglionic fiber projects from the terminal ganglia a short distance to the target effector, or to the specific target tissue within the organ. Comparing the relative lengths of axons in the parasympathetic system, the preganglionic fibers are long and the postganglionic fibers are short because the ganglia are close to—and sometimes within—the target effectors.

The cranial component of the parasympathetic system is based in particular nuclei of the brain stem. In the midbrain, the **Eddinger–Westphal nucleus** is part of the oculomotor complex, and axons from those neurons travel with the fibers in the oculomotor nerve (cranial nerve III) that innervate the extraocular muscles. The preganglionic parasympathetic fibers within cranial nerve III terminate in the **ciliary ganglion**, which is located in the posterior orbit. The postganglionic parasympathetic fibers then project to the smooth muscle of the iris to control pupillary size. In the upper medulla, the salivatory nuclei contain neurons with axons that project through the facial and

glossopharyngeal nerves to ganglia that control salivary glands. Tear production is influenced by parasympathetic fibers in the facial nerve, which activate a ganglion, and ultimately the lacrimal (tear) gland.

Neurons in the **dorsal nucleus of the vagus nerve** and the **nucleus ambiguus** project through the vagus nerve (cranial nerve X) to the terminal ganglia of the thoracic and abdominal cavities. Parasympathetic preganglionic fibers primarily influence the heart, bronchi, and esophagus in the thoracic cavity and the stomach, liver, pancreas, gallbladder, and small intestine of the abdominal cavity. The postganglionic fibers from the ganglia activated by the vagus nerve are often incorporated into the structure of the organ, such as the **mesenteric plexus** of the digestive tract organs and the intramural ganglia.

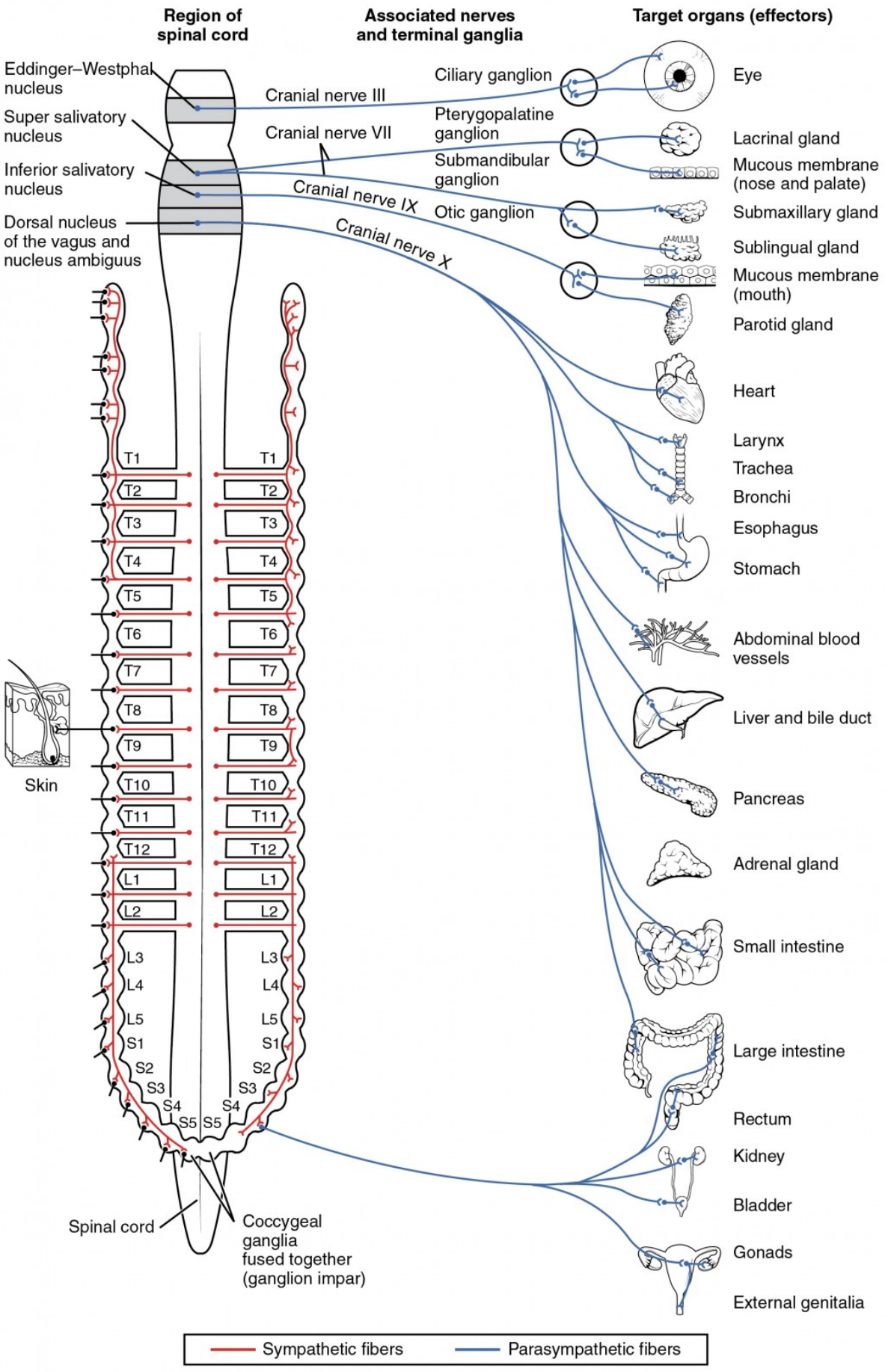

Region of spinal cord
Associated nerves and terminal ganglia
Target organs (effectors)
Eddinger–Westphal nucleus
Super salivatory nucleus
Inferior salivatory nucleus
Dorsal nucleus of the vagus and nucleus ambiguus
Cranial nerve III
Cranial nerve VII
Cranial nerve IX
Cranial nerve X
Ciliary ganglion
Pterygopalatine ganglion
Submandibular ganglion
Otic ganglion
Eye
Lacrinal gland
Mucous membrane (nose and palate)
Submaxillary gland
Sublingual gland
Mucous membrane (mouth)
Parotid gland
Heart
Larynx
Trachea
Bronchi
Esophagus
Stomach
Abdominal blood vessels
Liver and bile duct
Pancreas
Adrenal gland
Small intestine
Large intestine
Rectum
Kidney
Bladder
Gonads
External genitalia
T1
T2
T3
T4
T5
T6
T7
T8
T9
T10
T11
T12
L1
L2
L3
L4
L5
S1
S2
S3
S4
S5
Skin
Spinal cord
Coccygeal ganglia fused together (ganglion impar)
Sympathetic fibers
Parasympathetic fibers

Figure 3. Connections of Parasympathetic Division of the Autonomic Nervous System *Neurons from brain-stem nuclei, or from the lateral horn of the sacral spinal cord, project to terminal ganglia near or within the various organs of the body. Axons from these ganglionic neurons then project the short distance to those target effectors.*

Chemical Signaling in the Autonomic Nervous System

Where an autonomic neuron connects with a target, there is a synapse. The electrical signal of the action potential causes the release of a signaling molecule, which will bind to receptor proteins on the target cell. Synapses of the autonomic system are classified as either **cholinergic**, meaning that **acetylcholine (ACh)** is released, or **adrenergic**, meaning that **norepinephrine** is released. The terms cholinergic and adrenergic refer not only to the signaling molecule that is released but also to the class of receptors that each binds.

The cholinergic system includes two classes of receptor: the **nicotinic receptor** and the **muscarinic receptor**. Both receptor types bind to ACh and cause changes in the target cell. The nicotinic receptor is a **ligand-gated cation channel** and the muscarinic receptor is a **G protein–coupled receptor**. The receptors are named for, and differentiated by, other molecules that bind to them. Whereas nicotine will bind to the nicotinic receptor, and muscarine will bind to the muscarinic receptor, there is no cross-reactivity between the receptors. The situation is similar to locks and keys.

Imagine two locks—one for a classroom and the other for an office—that are opened by two separate keys. The classroom key will not open the office door and the office key will not open the classroom door. This is similar to the specificity of nicotine and muscarine for their receptors. However, a master key can open multiple locks, such as a master key for the Biology Department that opens both the classroom and the office doors. This is similar to ACh that binds to both types of receptors. The molecules that define these receptors are not crucial—they are simply tools for researchers to use in the laboratory. These molecules are **exogenous,** meaning that they are made outside of the human body, so a researcher can use them without any confounding **endogenous** results (results caused by the molecules produced in the body).

The adrenergic system also has two types of receptors, named the **alpha (α)-adrenergic receptor** and **beta (β)-adrenergic receptor**. Unlike cholinergic receptors, these receptor types are not classified by which drugs can bind to them. All of them are G protein–coupled receptors. There are three types of α-adrenergic receptors, termed α_1, α_2, and α_3, and there are two types of β-adrenergic receptors, termed β_1 and β_2. An itional aspect of the adrenergic system is that there is a second signaling molecule called **epinephrine**. The chemical difference between norepinephrine and epinephrine is the ition of a methyl group (CH_3) in epinephrine. The prefix “nor-” actually refers to this chemical difference, in which a methyl group is missing.

The term adrenergic should remind you of the word adrenaline, which is associated with the fight-or-flight response described at the beginning of the chapter. Adrenaline and epinephrine are two names for the same molecule. The adrenal gland (in Latin, *ad–* = “on top of”; *renal* = “kidney”) secretes adrenaline. The ending “-ine” refers to the chemical being derived, or extracted, from the adrenal gland. A similar construction from Greek instead of Latin results in the word epinephrine (*epi–* = “above”; *nephr–* = “kidney”). In scientific usage, epinephrine is preferred in the United States, whereas adrenaline is preferred in Great Britain, because “adrenalin” was once a registered, proprietary drug name in the United States. Though the drug is no longer sold, the convention of referring to this molecule by the two different names persists. Similarly, norepinephrine and noradrenaline are two names for the same molecule.

Having understood the cholinergic and adrenergic systems, their role in the autonomic system is relatively simple to understand. All preganglionic fibers, both sympathetic and parasympathetic, release ACh. All ganglionic neurons—the targets of these preganglionic fibers—have nicotinic receptors in their cell membranes. The nicotinic receptor is a ligand-gated cation channel that results in depolarization of the postsynaptic membrane. The postganglionic parasympathetic fibers also release ACh, but the receptors on their targets are muscarinic receptors, which are G protein–coupled receptors and do not exclusively cause depolarization of the postsynaptic membrane. Postganglionic sympathetic fibers release norepinephrine, except for fibers that project to sweat glands and to blood vessels associated with skeletal muscles, which release ACh (Table 1).

Table 1		
	Sympathetic	Parasympathetic
Preganglionic	Acetylcholine > nicotinic receptor	Acetylcholine > nicotinic receptor
Postganglionic	Norepinephrine > a or B-adrenergic receptors Acetylcholine > muscarinic receptor (associated with sweat glands and the blood vessels associated with skeletal muscles only	Acetylcholine > muscarinic receptor

Signaling molecules can belong to two broad groups. Neurotransmitters are released at synapses, whereas hormones are released into the bloodstream. These are simplistic definitions, but they can help to clarify this point. Acetylcholine can be considered a neurotransmitter because it is released by axons at synapses. The adrenergic system, however, presents a challenge. Postganglionic sympathetic fibers release norepinephrine, which can be considered a neurotransmitter. But the adrenal medulla releases epinephrine and norepinephrine into circulation, so they should be considered hormones.

What are referred to here as synapses may not fit the strictest definition of synapse. Some sources will refer to the connection between a postganglionic fiber and a target effector as neuroeffector junctions; neurotransmitters, as defined above, would be called neuromodulators. The structure of postganglionic connections are not the typical synaptic end bulb that is found at the neuromuscular junction, but rather are chains of swellings along the length of a postganglionic fiber called a **varicosity** (Figure 4).

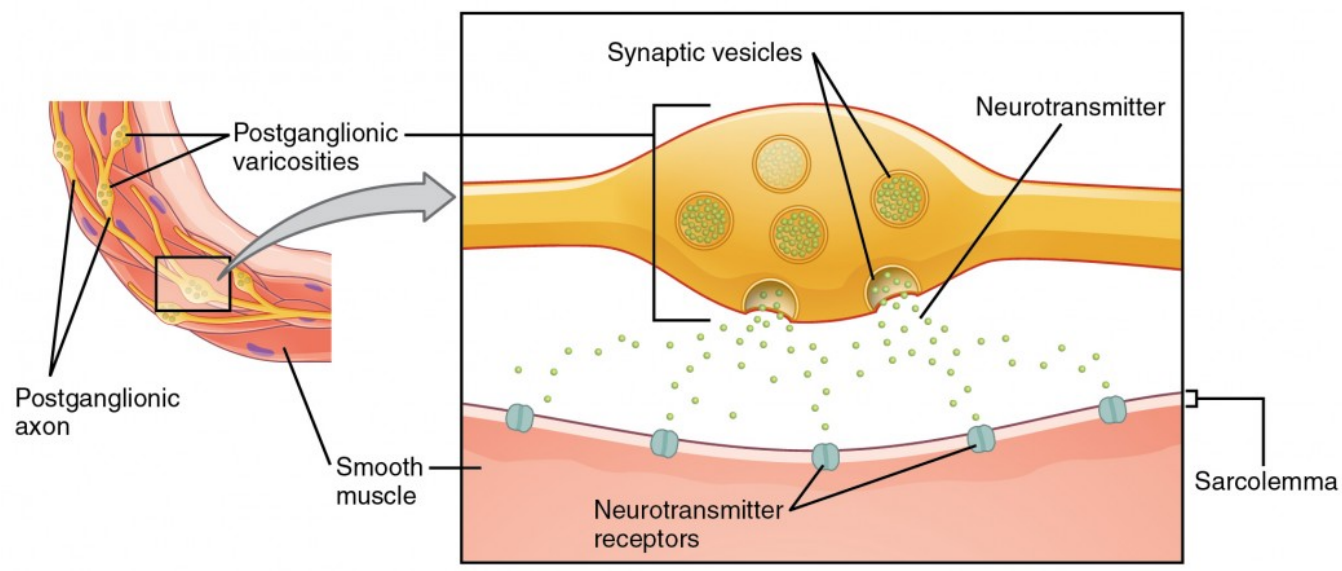


Figure 4. Autonomic Varicosities. *The connection between autonomic fibers and target effectors is not the same as the typical synapse, such as the neuromuscular junction. Instead of a synaptic end bulb, a neurotransmitter is released from swellings along the length of a fiber that makes an extended network of connections in the target effector.*

Everyday Connections: Fight or Flight? What About Fright and Freeze?

The original usage of the epithet “fight or flight” comes from a scientist named Walter Cannon who worked at Harvard in 1915. The concept of homeostasis and the functioning of the sympathetic system had been introduced in France in the previous century. Cannon expanded the idea, and introduced the idea that an animal responds to a threat by preparing to stand and fight or run away. The nature of this response was thoroughly explained in a book on the physiology of pain, hunger, fear, and rage.

When students learn about the sympathetic system and the fight-or-flight response, they often stop and wonder about other responses. If you were faced with a lioness running toward you as pictured at the

beginning of this chapter, would you run or would you stand your ground? Some people would say that they would freeze and not know what to do. So isn't there really more to what the autonomic system does than fight, flight, rest, or digest. What about fear and paralysis in the face of a threat?

The common epithet of "fight or flight" is being enlarged to be "fight, flight, or fright" or even "fight, flight, fright, or freeze." Cannon's original contribution was a catchy phrase to express some of what the nervous system does in response to a threat, but it is incomplete. The sympathetic system is responsible for the physiological responses to emotional states. The name "sympathetic" can be said to mean that (*sym–* = "together"; *–pathos* = "pain," "suffering," or "emotion").

Watch this video to learn more about the nervous system.

Watch this video online: https://youtu.be/RyP8L3qTW9Q

As described in this video, the nervous system has a way to deal with threats and stress that is separate from the conscious control of the somatic nervous system. The system comes from a time when threats were about survival, but in the modern age, these responses become part of stress and anxiety. This video describes how the autonomic system is only part of the response to threats, or stressors. What other organ system gets involved, and what part of the brain coordinates the two systems for the entire response, including epinephrine (adrenaline) and cortisol?

AUTONOMIC REFLEXES AND HOMEOSTASIS

Learning Objectives

- Compare the structure of somatic and autonomic reflex arcs
- Explain the differences in sympathetic and parasympathetic reflexes
- Differentiate between short and long reflexes
- Determine the effect of the autonomic nervous system on the regulation of the various organ systems on the basis of the signaling molecules involved
- Describe the effects of drugs that affect autonomic function

The autonomic nervous system regulates organ systems through circuits that resemble the reflexes described in the somatic nervous system. The main difference between the somatic and autonomic systems is in what target tissues are effectors. Somatic responses are solely based on skeletal muscle contraction. The autonomic system, however, targets cardiac and smooth muscle, as well as glandular tissue. Whereas the basic circuit is a **reflex arc**, there are differences in the structure of those reflexes for the somatic and autonomic systems.

The Structure of Reflexes

One difference between a **somatic reflex**, such as the withdrawal reflex, and a **visceral reflex**, which is an autonomic reflex, is in the **efferent branch**. The output of a somatic reflex is the lower motor neuron in the ventral horn of the spinal cord that projects directly to a skeletal muscle to cause its contraction. The output of a visceral reflex is a two-step pathway starting with the preganglionic fiber emerging from a lateral horn neuron in the spinal cord, or a cranial nucleus neuron in the brain stem, to a ganglion—followed by the postganglionic fiber projecting

to a target effector. The other part of a reflex, the **afferent branch**, is often the same between the two systems. Sensory neurons receiving input from the periphery—with cell bodies in the sensory ganglia, either of a cranial nerve or a dorsal root ganglion adjacent to the spinal cord—project into the CNS to initiate the reflex (Figure 1). The Latin root "effere" means "to carry." Adding the prefix "ef-" suggests the meaning "to carry away," whereas adding the prefix "af-" suggests "to carry toward or inward."

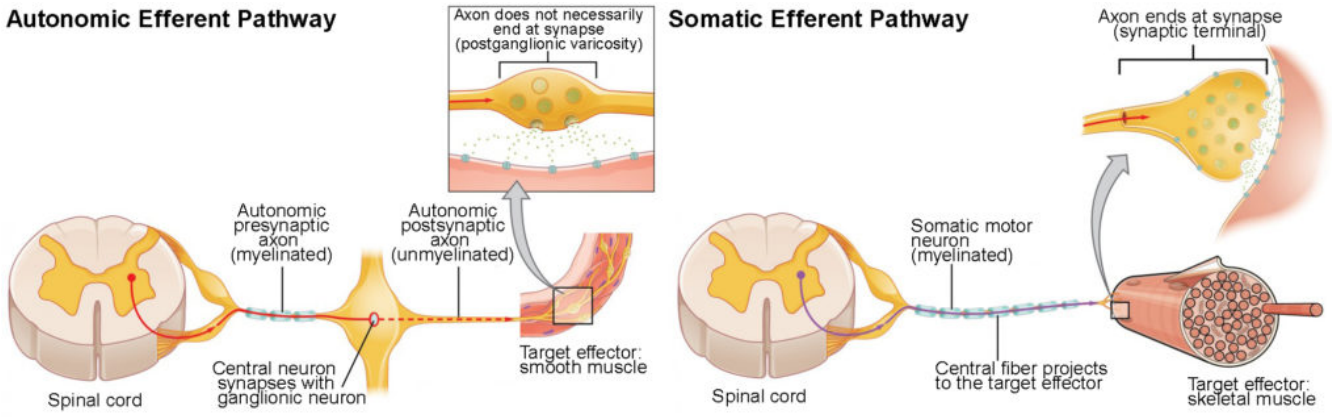


Figure 1. Comparison of Somatic and Visceral Reflexes. *The afferent inputs to somatic and visceral reflexes are essentially the same, whereas the efferent branches are different. Somatic reflexes, for instance, involve a direct connection from the ventral horn of the spinal cord to the skeletal muscle. Visceral reflexes involve a projection from the central neuron to a ganglion, followed by a second projection from the ganglion to the target effector.*

Afferent Branch

The afferent branch of a reflex arc does differ between somatic and visceral reflexes in some instances. Many of the inputs to visceral reflexes are from special or somatic senses, but particular senses are associated with the viscera that are not part of the conscious perception of the environment through the somatic nervous system. For example, there is a specific type of mechanoreceptor, called a **baroreceptor**, in the walls of the aorta and carotid sinuses that senses the stretch of those organs when blood volume or pressure increases. You do not have a conscious perception of having high blood pressure, but that is an important afferent branch of the cardiovascular and, particularly, vasomotor reflexes. The sensory neuron is essentially the same as any other general sensory neuron. The baroreceptor apparatus is part of the ending of a unipolar neuron that has a cell body in a sensory ganglion. The baroreceptors from the carotid arteries have axons in the glossopharyngeal nerve, and those from the aorta have axons in the vagus nerve.

Though visceral senses are not primarily a part of conscious perception, those sensations sometimes make it to conscious awareness. If a visceral sense is strong enough, it will be perceived. The sensory homunculus—the representation of the body in the primary somatosensory cortex—only has a small region allotted for the perception of internal stimuli. If you swallow a large bolus of food, for instance, you will probably feel the lump of that food as it pushes through your esophagus, or even if your stomach is distended after a large meal. If you inhale especially cold air, you can feel it as it enters your larynx and trachea. These sensations are not the same as feeling high blood pressure or blood sugar levels.

When particularly strong visceral sensations rise to the level of conscious perception, the sensations are often felt in unexpected places. For example, strong visceral sensations of the heart will be felt as pain in the left shoulder and left arm. This irregular pattern of projection of conscious perception of visceral sensations is called **referred pain**. Depending on the organ system affected, the referred pain will project to different areas of the body (Figure 2). The location of referred pain is not random, but a definitive explanation of the mechanism has not been established. The most broadly accepted theory for this phenomenon is that the visceral sensory fibers enter into the same level of the spinal cord as the somatosensory fibers of the referred pain location. By this explanation, the visceral sensory fibers from the mediastinal region, where the heart is located, would enter the spinal cord at the same level as the spinal nerves from the shoulder and arm, so the brain misinterprets the sensations from the mediastinal region as being from the axillary and brachial regions. Projections from the medial and inferior divisions of the cervical ganglia do enter the spinal cord at the middle to lower cervical levels, which is where the somatosensory fibers enter.

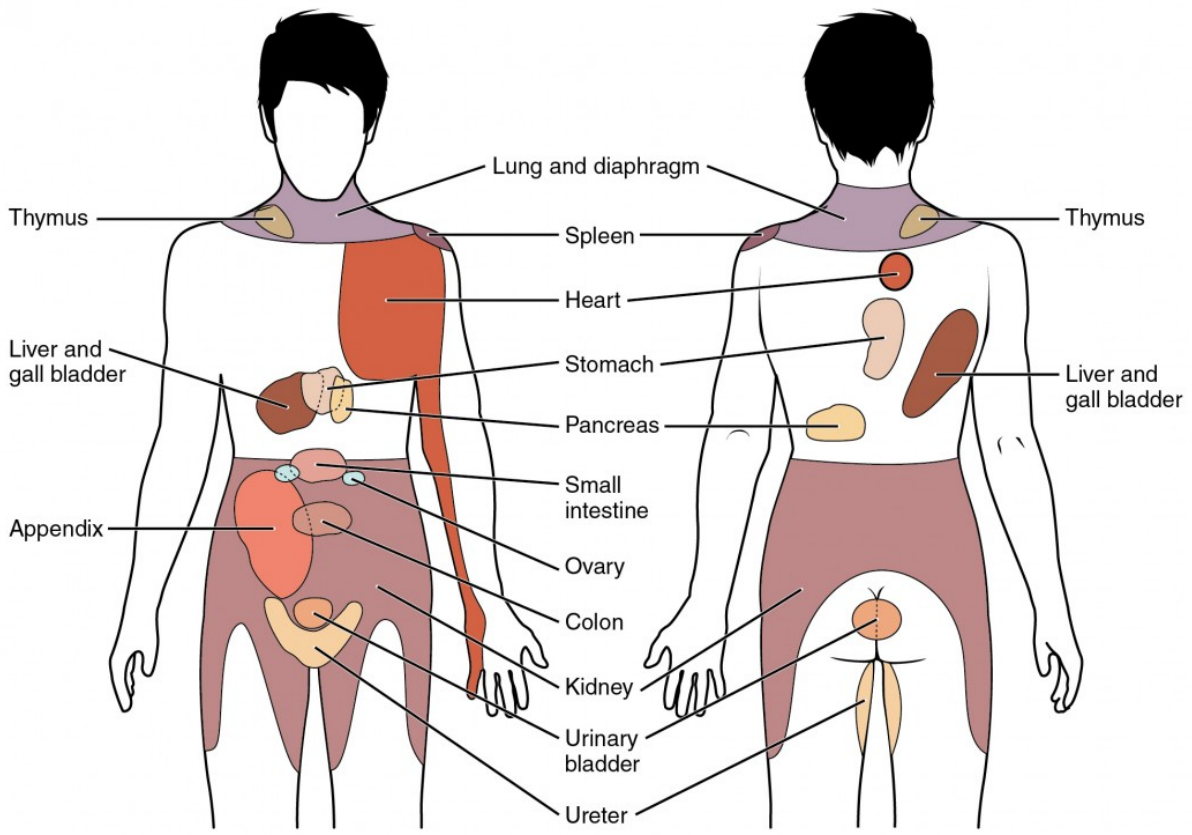


Figure 2. Referred Pain Chart *Conscious perception of visceral sensations map to specific regions of the body, as shown in this chart. Some sensations are felt locally, whereas others are perceived as affecting areas that are quite distant from the involved organ.*

Disorders of the Nervous System: Kehr's Sign

Kehr's sign is the presentation of pain in the left shoulder, chest, and neck regions following rupture of the spleen. The spleen is in the upper-left abdominopelvic quadrant, but the pain is more in the shoulder and neck. How can this be? The sympathetic fibers connected to the spleen are from the celiac ganglion, which would be from the mid-thoracic to lower thoracic region whereas parasympathetic fibers are found in the vagus nerve, which connects in the medulla of the brain stem. However, the neck and shoulder would connect to the spinal cord at the mid-cervical level of the spinal cord. These connections do not fit with the expected correspondence of visceral and somatosensory fibers entering at the same level of the spinal cord.

The incorrect assumption would be that the visceral sensations are coming from the spleen directly. In fact, the visceral fibers are coming from the diaphragm. The nerve connecting to the diaphragm takes a special route. The phrenic nerve is connected to the spinal cord at cervical levels 3 to 5. The motor fibers that make up this nerve are responsible for the muscle contractions that drive ventilation. These fibers have left the spinal cord to enter the phrenic nerve, meaning that spinal cord damage below the mid-cervical level is not fatal by making ventilation impossible. Therefore, the visceral fibers from the diaphragm enter the spinal cord at the same level as the somatosensory fibers from the neck and shoulder.

The diaphragm plays a role in Kehr's sign because the spleen is just inferior to the diaphragm in the upper-left quadrant of the abdominopelvic cavity. When the spleen ruptures, blood spills into this region. The accumulating hemorrhage then puts pressure on the diaphragm. The visceral sensation is actually in the diaphragm, so the referred pain is in a region of the body that corresponds to the diaphragm, not the spleen.

Efferent Branch

The efferent branch of the visceral reflex arc begins with the projection from the central neuron along the preganglionic fiber. This fiber then makes a synapse on the ganglionic neuron that projects to the target effector.

The effector organs that are the targets of the autonomic system range from the iris and ciliary body of the eye to the urinary bladder and reproductive organs. The thoracolumbar output, through the various sympathetic ganglia, reaches all of these organs. The cranial component of the parasympathetic system projects from the eye to part of the intestines. The sacral component picks up with the majority of the large intestine and the pelvic organs of the urinary and reproductive systems.

Short and Long Reflexes

Somatic reflexes involve sensory neurons that connect sensory receptors to the CNS and motor neurons that project back out to the skeletal muscles. Visceral reflexes that involve the thoracolumbar or craniosacral systems share similar connections. However, there are reflexes that do not need to involve any CNS components. A **long reflex** has afferent branches that enter the spinal cord or brain and involve the efferent branches, as previously explained. A **short reflex** is completely peripheral and only involves the local integration of sensory input with motor output (Figure 3).

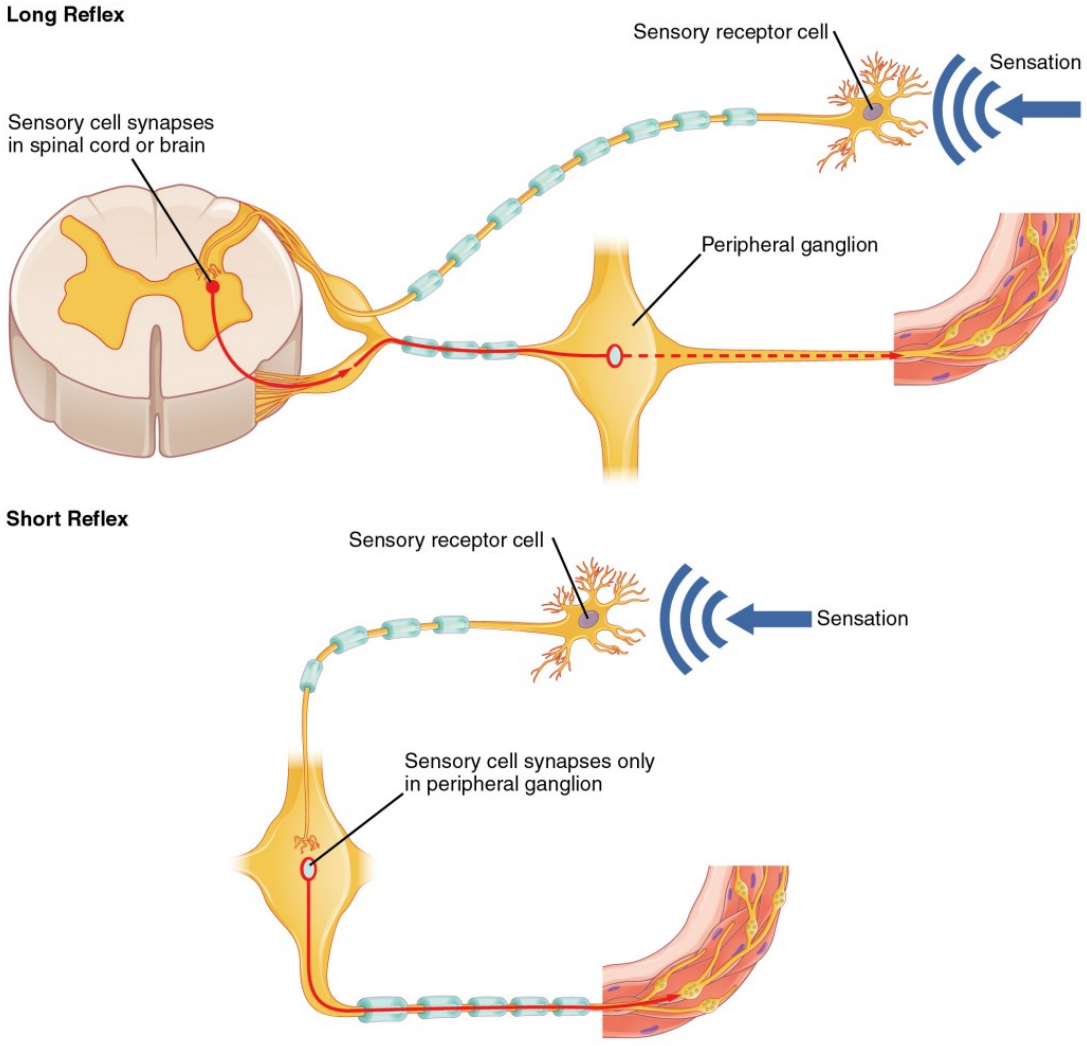


Figure 3. Short and Long Reflexes. *Sensory input can stimulate either a short or a long reflex. A sensory neuron can project to the CNS or to an autonomic ganglion. The short reflex involves the direct stimulation*

of a postganglionic fiber by the sensory neuron, whereas the long reflex involves integration in the spinal cord or brain.

The difference between short and long reflexes is in the involvement of the CNS. Somatic reflexes always involve the CNS, even in a monosynaptic reflex in which the sensory neuron directly activates the motor neuron. That synapse is in the spinal cord or brain stem, so it has to involve the CNS. However, in the autonomic system there is the possibility that the CNS is not involved. Because the efferent branch of a visceral reflex involves two neurons—the central neuron and the ganglionic neuron—a "short circuit" can be possible. If a sensory neuron projects directly to the ganglionic neuron and causes it to activate the effector target, then the CNS is not involved.

A division of the nervous system that is related to the autonomic nervous system is the enteric nervous system. The word enteric refers to the digestive organs, so this represents the nervous tissue that is part of the digestive system. There are a few myenteric plexuses in which the nervous tissue in the wall of the digestive tract organs can directly influence digestive function. If stretch receptors in the stomach are activated by the filling and distension of the stomach, a short reflex will directly activate the smooth muscle fibers of the stomach wall to increase motility to digest the excessive food in the stomach. No CNS involvement is needed because the stretch receptor is directly activating a neuron in the wall of the stomach that causes the smooth muscle to contract. That neuron, connected to the smooth muscle, is a postganglionic parasympathetic neuron that can be controlled by a fiber found in the vagus nerve.

Read this article to learn about a teenager who experiences a series of spells that suggest a stroke. He undergoes endless tests and seeks input from multiple doctors. In the end, one expert, one question, and a simple blood pressure cuff answers the question. Why would the heart have to beat faster when the teenager changes his body position from lying down to sitting, and then to standing?

Balance in Competing Autonomic Reflex Arcs

The autonomic nervous system is important for homeostasis because its two divisions compete at the target effector. The balance of homeostasis is attributable to the competing inputs from the sympathetic and parasympathetic divisions (dual innervation). At the level of the target effector, the signal of which system is sending the message is strictly chemical. A signaling molecule binds to a receptor that causes changes in the target cell, which in turn causes the tissue or organ to respond to the changing conditions of the body.

Competing Neurotransmitters

The postganglionic fibers of the sympathetic and parasympathetic divisions both release neurotransmitters that bind to receptors on their targets. Postganglionic sympathetic fibers release norepinephrine, with a minor exception, whereas postganglionic parasympathetic fibers release ACh. For any given target, the difference in which division of the autonomic nervous system is exerting control is just in what chemical binds to its receptors. The target cells will have adrenergic and muscarinic receptors. If norepinephrine is released, it will bind to the adrenergic receptors present on the target cell, and if ACh is released, it will bind to the muscarinic receptors on the target cell.

In the sympathetic system, there are exceptions to this pattern of dual innervation. The postganglionic sympathetic fibers that contact the blood vessels within skeletal muscle and that contact sweat glands do not release norepinephrine, they release ACh. This does not create any problem because there is no parasympathetic input to the sweat glands. Sweat glands have muscarinic receptors and produce and secrete sweat in response to the presence of ACh.

At most of the other targets of the autonomic system, the effector response is based on which neurotransmitter is released and what receptor is present. For example, regions of the heart that establish heart rate are contacted by postganglionic fibers from both systems. If norepinephrine is released onto those cells, it binds to an adrenergic receptor that causes the cells to depolarize faster, and the heart rate increases. If ACh is released onto those cells, it binds to a muscarinic receptor that causes the cells to hyperpolarize so that they cannot reach threshold as easily, and the heart rate slows. Without this parasympathetic input, the heart would work at a rate of

approximately 100 beats per minute (bpm). The sympathetic system speeds that up, as it would during exercise, to 120–140 bpm, for example. The parasympathetic system slows it down to the resting heart rate of 60–80 bpm.

Another example is in the control of pupillary size (Figure 4). The afferent branch responds to light hitting the retina. Photoreceptors are activated, and the signal is transferred to the retinal ganglion cells that send an action potential along the optic nerve into the diencephalon. If light levels are low, the sympathetic system sends a signal out through the upper thoracic spinal cord to the superior cervical ganglion of the sympathetic chain. The postganglionic fiber then projects to the iris, where it releases norepinephrine onto the radial fibers of the iris (a smooth muscle). When those fibers contract, the pupil dilates—increasing the amount of light hitting the retina. If light levels are too high, the parasympathetic system sends a signal out from the Eddinger–Westphal nucleus through the oculomotor nerve. This fiber synapses in the ciliary ganglion in the posterior orbit. The postganglionic fiber then projects to the iris, where it releases ACh onto the circular fibers of the iris—another smooth muscle. When those fibers contract, the pupil constricts to limit the amount of light hitting the retina.

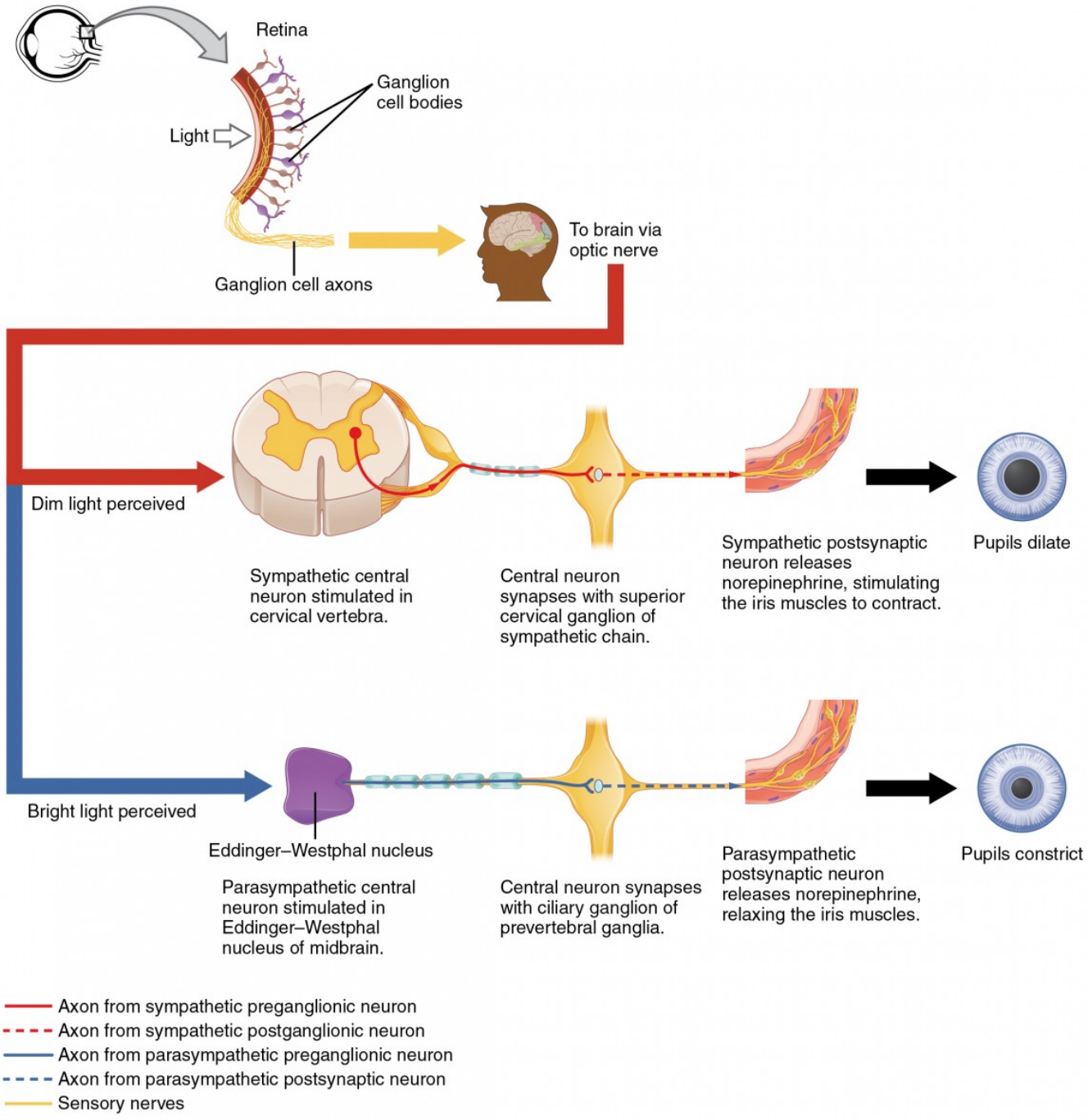


Figure 4. Autonomic Control of Pupillary Size. *Activation of the pupillary reflex comes from the amount of light activating the retinal ganglion cells, as sent along the optic nerve. The output of the sympathetic system projects through the superior cervical ganglion, whereas the parasympathetic system originates out of the midbrain and projects through the oculomotor nerve to the ciliary ganglion, which then projects to the iris. The postganglionic fibers of either division release neurotransmitters onto the smooth muscles of the iris to cause changes in the pupillary size. Norepinephrine results in dilation and ACh results in constriction*

In this example, the autonomic system is controlling how much light hits the retina. It is a homeostatic reflex mechanism that keeps the activation of photoreceptors within certain limits. In the context of avoiding a threat like the lioness on the savannah, the sympathetic response for fight or flight will increase pupillary diameter so that more light hits the retina and more visual information is available for running away. Likewise, the parasympathetic response of rest reduces the amount of light reaching the retina, allowing the photoreceptors to cycle through bleaching and be regenerated for further visual perception; this is what the homeostatic process is attempting to maintain.

Watch this video to learn about the pupillary reflexes.

Watch this video online: https://youtu.be/Yj5-cJgVX3c

The pupillary light reflex involves sensory input through the optic nerve and motor response through the oculomotor nerve to the ciliary ganglion, which projects to the circular fibers of the iris. As shown in this short animation, pupils will constrict to limit the amount of light falling on the retina under bright lighting conditions. What constitutes the afferent and efferent branches of the competing reflex (dilation)?

Autonomic Tone

Organ systems are balanced between the input from the sympathetic and parasympathetic divisions. When something upsets that balance, the homeostatic mechanisms strive to return it to its regular state. For each organ system, there may be more of a sympathetic or parasympathetic tendency to the resting state, which is known as the **autonomic tone** of the system. For example, the heart rate was described above. Because the resting heart rate is the result of the parasympathetic system slowing the heart down from its intrinsic rate of 100 bpm, the heart can be said to be in parasympathetic tone.

In a similar fashion, another aspect of the cardiovascular system is primarily under sympathetic control. Blood pressure is partially determined by the contraction of smooth muscle in the walls of blood vessels. These tissues have adrenergic receptors that respond to the release of norepinephrine from postganglionic sympathetic fibers by constricting and increasing blood pressure. The hormones released from the adrenal medulla—epinephrine and norepinephrine—will also bind to these receptors. Those hormones travel through the bloodstream where they can easily interact with the receptors in the vessel walls. The parasympathetic system has no significant input to the systemic blood vessels, so the sympathetic system determines their tone.

There are a limited number of blood vessels that respond to sympathetic input in a different fashion. Blood vessels in skeletal muscle, particularly those in the lower limbs, are more likely to dilate. It does not have an overall effect on blood pressure to alter the tone of the vessels, but rather allows for blood flow to increase for those skeletal muscles that will be active in the fight-or-flight response. The blood vessels that have a parasympathetic projection are limited to those in the erectile tissue of the reproductive organs. Acetylcholine released by these postganglionic parasympathetic fibers cause the vessels to dilate, leading to the engorgement of the erectile tissue.

Homeostatic Imbalances: Orthostatic Hypotension

Have you ever stood up quickly and felt dizzy for a moment? This is because, for one reason or another, blood is not getting to your brain so it is briefly deprived of oxygen. When you change position from sitting or lying down to standing, your cardiovascular system has to adjust for a new challenge, keeping blood pumping up into the head while gravity is pulling more and more blood down into the legs.

The reason for this is a sympathetic reflex that maintains the output of the heart in response to postural change. When a person stands up, proprioceptors indicate that the body is changing position. A signal goes to the CNS, which then sends a signal to the upper thoracic spinal cord neurons of the sympathetic division. The

sympathetic system then causes the heart to beat faster and the blood vessels to constrict. Both changes will make it possible for the cardiovascular system to maintain the rate of blood delivery to the brain. Blood is being pumped superiorly through the internal branch of the carotid arteries into the brain, against the force of gravity. Gravity is not increasing while standing, but blood is more likely to flow down into the legs as they are extended for standing. This sympathetic reflex keeps the brain well oxygenated so that cognitive and other neural processes are not interrupted.

Sometimes this does not work properly. If the sympathetic system cannot increase cardiac output, then blood pressure into the brain will decrease, and a brief neurological loss can be felt. This can be brief, as a slight "wooziness" when standing up too quickly, or a loss of balance and neurological impairment for a period of time. The name for this is orthostatic hypotension, which means that blood pressure goes below the homeostatic set point when standing. It can be the result of standing up faster than the reflex can occur, which may be referred to as a benign "head rush," or it may be the result of an underlying cause.

There are two basic reasons that orthostatic hypotension can occur. First, blood volume is too low and the sympathetic reflex is not effective. This hypovolemia may be the result of dehydration or medications that affect fluid balance, such as diuretics or vasodilators. Both of these medications are meant to lower blood pressure, which may be necessary in the case of systemic hypertension, and regulation of the medications may alleviate the problem. Sometimes increasing fluid intake or water retention through salt intake can improve the situation.

The second underlying cause of orthostatic hypotension is autonomic failure. There are several disorders that result in compromised sympathetic functions. The disorders range from diabetes to multiple system atrophy (a loss of control over many systems in the body), and ing the underlying condition can improve the hypotension. For example, with diabetes, peripheral nerve damage can occur, which would affect the postganglionic sympathetic fibers. Getting blood glucose levels under control can improve neurological deficits associated with diabetes.

Self-Check Questions

Visit your course online to take a quiz to check your understanding of Autonomic Reflexes and Homeostasis:

CENTRAL CONTROL

Learning Objectives

- Describe the role of higher centers of the brain in autonomic regulation
- Explain the connection of the hypothalamus to homeostasis
- Describe the regions of the CNS that link the autonomic system with emotion
- Describe the pathways important to descending control of the autonomic system

The pupillary light reflex (Figure 1) begins when light hits the retina and causes a signal to travel along the optic nerve. This is visual sensation, because the afferent branch of this reflex is simply sharing the special sense pathway. Bright light hitting the retina leads to the parasympathetic response, through the oculomotor nerve, followed by the postganglionic fiber from the ciliary ganglion, which stimulates the circular fibers of the iris to contract and constrict the pupil. When light hits the retina in one eye, both pupils contract. When that light is

removed, both pupils dilate again back to the resting position. When the stimulus is unilateral (presented to only one eye), the response is bilateral (both eyes). The same is not true for somatic reflexes. If you touch a hot radiator, you only pull that arm back, not both. Central control of autonomic reflexes is different than for somatic reflexes. The hypothalamus, along with other CNS locations, controls the autonomic system.

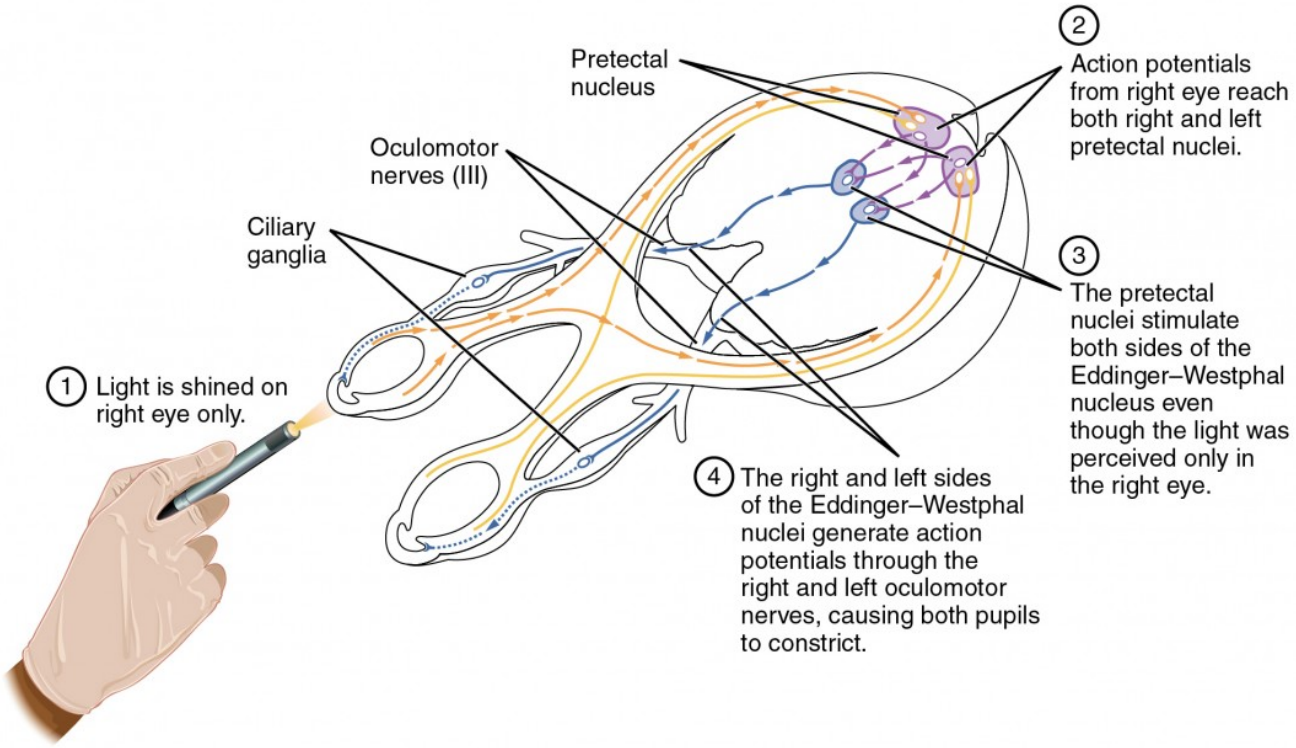


Figure 1. Pupillary Reflex Pathways. *The pupil is under competing autonomic control in response to light levels hitting the retina. The sympathetic system will dilate the pupil when the retina is not receiving enough light, and the parasympathetic system will constrict the pupil when too much light hits the retina.*

Forebrain Structures

Autonomic control is based on the visceral reflexes, composed of the afferent and efferent branches. These homeostatic mechanisms are based on the balance between the two divisions of the autonomic system, which results in tone for various organs that is based on the predominant input from the sympathetic or parasympathetic systems. Coordinating that balance requires integration that begins with forebrain structures like the hypothalamus and continues into the brain stem and spinal cord.

The Hypothalamus

The hypothalamus is the control center for many homeostatic mechanisms. It regulates both autonomic function and endocrine function. The roles it plays in the pupillary reflexes demonstrates the importance of this control center. The optic nerve projects primarily to the thalamus, which is the necessary relay to the occipital cortex for conscious visual perception. Another projection of the optic nerve, however, goes to the hypothalamus.

The hypothalamus then uses this visual system input to drive the pupillary reflexes. If the retina is activated by high levels of light, the hypothalamus stimulates the parasympathetic response. If the optic nerve message shows that low levels of light are falling on the retina, the hypothalamus activates the sympathetic response. Output from the hypothalamus follows two main tracts, the **dorsal longitudinal fasciculus** and the **medial forebrain bundle** (Figure 2). Along these two tracts, the hypothalamus can influence the Eddinger–Westphal nucleus of the oculomotor complex or the lateral horns of the thoracic spinal cord.

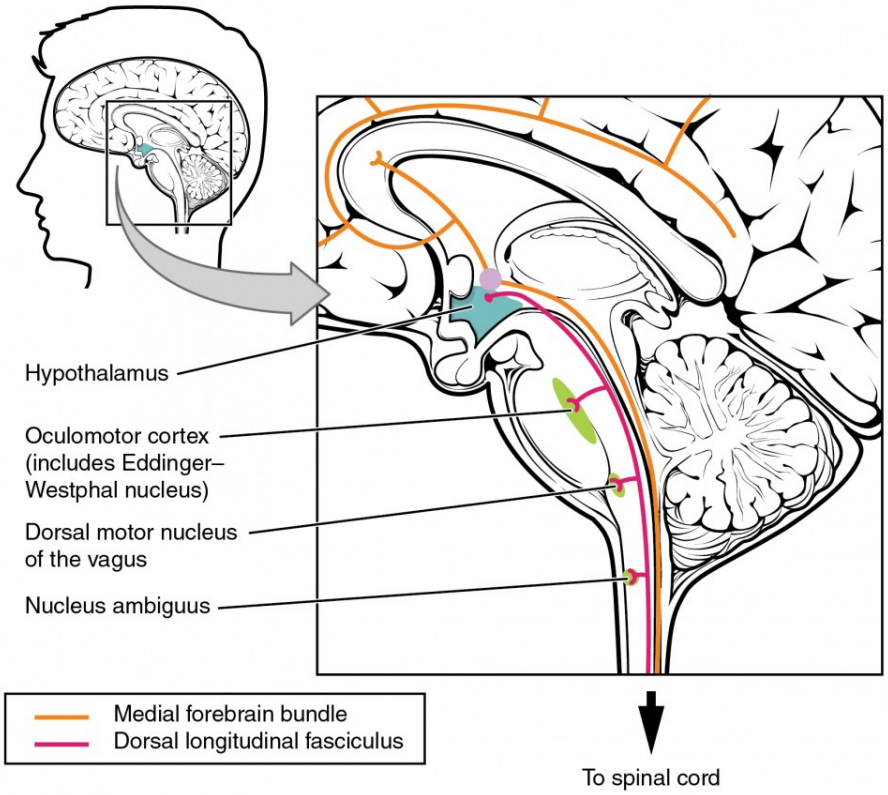


Figure 2. Fiber Tracts of the Central Autonomic System. *The hypothalamus is the source of most of the central control of autonomic function. It receives input from cerebral structures and projects to brain stem and spinal cord structures to regulate the balance of sympathetic and parasympathetic input to the organ systems of the body. The main pathways for this are the medial forebrain bundle and the dorsal longitudinal fasciculus.*

These two tracts connect the hypothalamus with the major parasympathetic nuclei in the brain stem and the preganglionic (central) neurons of the thoracolumbar spinal cord. The hypothalamus also receives input from other areas of the forebrain through the medial forebrain bundle. The olfactory cortex, the septal nuclei of the basal forebrain, and the amygdala project into the hypothalamus through the medial forebrain bundle. These forebrain structures inform the hypothalamus about the state of the nervous system and can influence the regulatory processes of homeostasis. A good example of this is found in the amygdala, which is found beneath the cerebral cortex of the temporal lobe and plays a role in our ability to remember and feel emotions.

The Amygdala

The amygdala is a group of nuclei in the medial region of the temporal lobe that is part of the **limbic lobe** (Figure 3). The limbic lobe includes structures that are involved in emotional responses, as well as structures that contribute to memory function. The limbic lobe has strong connections with the hypothalamus and influences the state of its activity on the basis of emotional state. For example, when you are anxious or scared, the amygdala will send signals to the hypothalamus along the medial forebrain bundle that will stimulate the sympathetic fight-or-flight response. The hypothalamus will also stimulate the release of stress hormones through its control of the endocrine system in response to amygdala input.

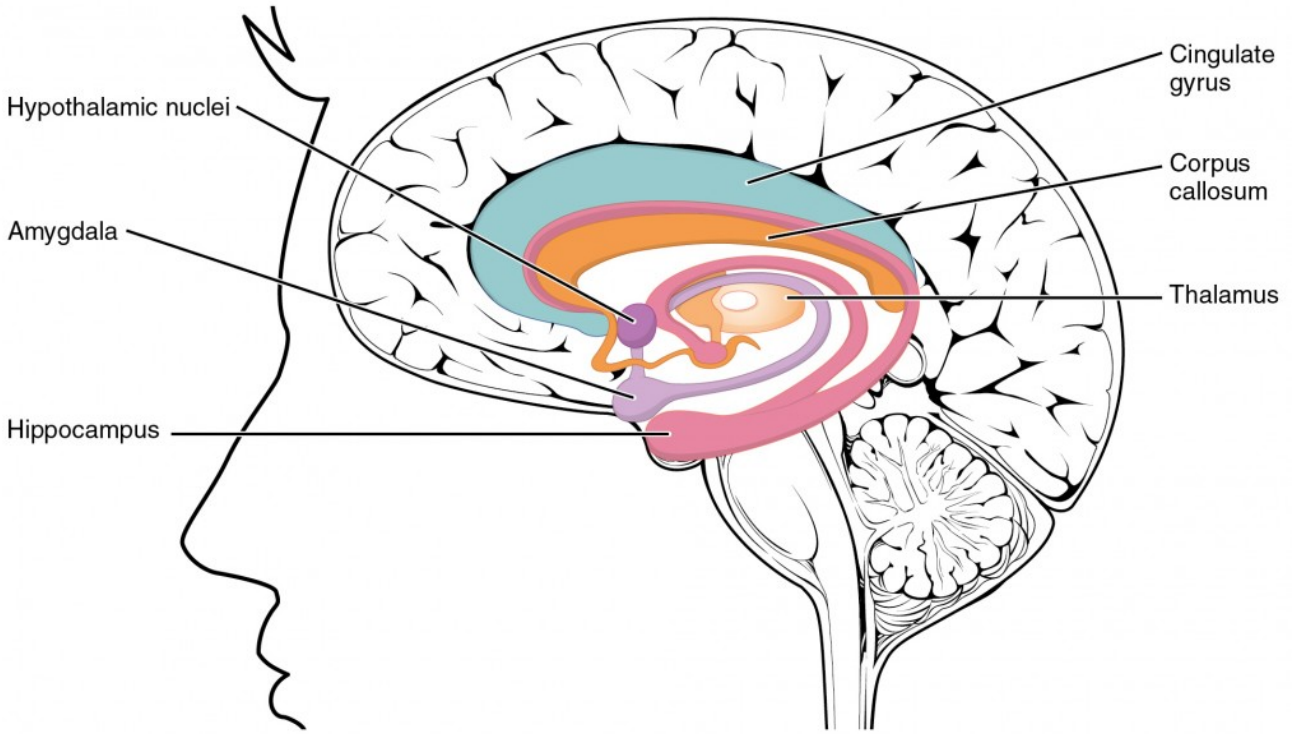


Figure 3 The Limbic Lobe. *Structures arranged around the edge of the cerebrum constitute the limbic lobe, which includes the amygdala, hippocampus, and cingulate gyrus, and connects to the hypothalamus.*

The Medulla

The medulla contains nuclei referred to as the **cardiovascular center**, which controls the smooth and cardiac muscle of the cardiovascular system through autonomic connections. When the homeostasis of the cardiovascular system shifts, such as when blood pressure changes, the coordination of the autonomic system can be accomplished within this region. Furthermore, when descending inputs from the hypothalamus stimulate this area, the sympathetic system can increase activity in the cardiovascular system, such as in response to anxiety or stress. The preganglionic sympathetic fibers that are responsible for increasing heart rate are referred to as the **cardiac accelerator nerves**, whereas the preganglionic sympathetic fibers responsible for constricting blood vessels compose the **vasomotor nerves**.

Several brain stem nuclei are important for the visceral control of major organ systems. One brain stem nucleus involved in cardiovascular function is the solitary nucleus. It receives sensory input about blood pressure and cardiac function from the glossopharyngeal and vagus nerves, and its output will activate sympathetic stimulation of the heart or blood vessels through the upper thoracic lateral horn. Another brain stem nucleus important for visceral control is the dorsal motor nucleus of the vagus nerve, which is the motor nucleus for the parasympathetic functions ascribed to the vagus nerve, including decreasing the heart rate, relaxing bronchial tubes in the lungs, and activating digestive function through the enteric nervous system. The nucleus ambiguus, which is named for its ambiguous histology, also contributes to the parasympathetic output of the vagus nerve and targets muscles in the pharynx and larynx for swallowing and speech, as well as contributing to the parasympathetic tone of the heart along with the dorsal motor nucleus of the vagus.

Everyday Connections: Exercise and the Autonomic System

In addition to its association with the fight-or-flight response and rest-and-digest functions, the autonomic system is responsible for certain everyday functions. For example, it comes into play when homeostatic mechanisms dynamically change, such as the physiological changes that accompany exercise. Getting on the treadmill and putting in a good workout will cause the heart rate to increase, breathing to be stronger and deeper, sweat glands to activate, and the digestive system to suspend activity. These are the same

physiological changes associated with the fight-or-flight response, but there is nothing chasing you on that treadmill.

This is not a simple homeostatic mechanism at work because “maintaining the internal environment” would mean getting all those changes back to their set points. Instead, the sympathetic system has become active during exercise so that your body can cope with what is happening. A homeostatic mechanism is dealing with the conscious decision to push the body away from a resting state. The heart, actually, is moving away from its homeostatic set point. Without any input from the autonomic system, the heart would beat at approximately 100 bpm, and the parasympathetic system slows that down to the resting rate of approximately 70 bpm. But in the middle of a good workout, you should see your heart rate at 120–140 bpm. You could say that the body is stressed because of what you are doing to it. Homeostatic mechanisms are trying to keep blood pH in the normal range, or to keep body temperature under control, but those are in response to the choice to exercise.

Watch this video to learn about physical responses to emotion.

Watch this video online: https://youtu.be/SS_qMHPI0XM

The autonomic system, which is important for regulating the homeostasis of the organ systems, is also responsible for our physiological responses to emotions such as fear. The video summarizes the extent of the body’s reactions and describes several effects of the autonomic system in response to fear. On the basis of what you have already studied about autonomic function, which effect would you expect to be associated with parasympathetic, rather than sympathetic, activity?

Self-Check Questions

Visit your course online to take a quiz to check your understanding of Central Control:

DRUGS THAT AFFECT THE AUTONOMIC SYSTEM

Learning Objectives

- List the classes of pharmaceuticals that interact with the autonomic nervous system
- Differentiate between cholinergic and adrenergic compounds
- Differentiate between sympathomimetic and sympatholytic drugs
- Relate the consequences of nicotine abuse with respect to autonomic control of the cardiovascular system

An important way to understand the effects of native neurochemicals in the autonomic system is in considering the effects of pharmaceutical drugs. This can be considered in terms of how drugs change autonomic function. These effects will primarily be based on how drugs act at the receptors of the autonomic system neurochemistry. The signaling molecules of the nervous system interact with proteins in the cell membranes of various target cells. In fact, no effect can be attributed to just the signaling molecules themselves without considering the receptors. A chemical that the body produces to interact with those receptors is called an **endogenous chemical**, whereas a chemical introduced to the system from outside is an **exogenous chemical**. Exogenous chemicals may be of a natural origin, such as a plant extract, or they may be synthetically produced in a pharmaceutical laboratory.

Broad Autonomic Effects

One important drug that affects the autonomic system broadly is not a pharmaceutical therapeutic agent associated with the system. This drug is nicotine. The effects of nicotine on the autonomic nervous system are important in considering the role smoking can play in health.

All ganglionic neurons of the autonomic system, in both sympathetic and parasympathetic ganglia, are activated by ACh released from preganglionic fibers. The ACh receptors on these neurons are of the nicotinic type, meaning that they are ligand-gated ion channels. When the neurotransmitter released from the preganglionic fiber binds to the receptor protein, a channel opens to allow positive ions to cross the cell membrane. The result is depolarization of the ganglia. Nicotine acts as an ACh analog at these synapses, so when someone takes in the drug, it binds to these ACh receptors and activates the ganglionic neurons, causing them to depolarize.

Ganglia of both divisions are activated equally by the drug. For many target organs in the body, this results in no net change. The competing inputs to the system cancel each other out and nothing significant happens. For example, the sympathetic system will cause sphincters in the digestive tract to contract, limiting digestive propulsion, but the parasympathetic system will cause the contraction of other muscles in the digestive tract, which will try to push the contents of the digestive system along. The end result is that the food does not really move along and the digestive system has not appreciably changed.

The system in which this can be problematic is in the cardiovascular system, which is why smoking is a risk factor for cardiovascular disease. First, there is no significant parasympathetic regulation of blood pressure. Only a limited number of blood vessels are affected by parasympathetic input, so nicotine will preferentially cause the vascular tone to become more sympathetic, which means blood pressure will be increased. Second, the autonomic control of the heart is special. Unlike skeletal or smooth muscles, cardiac muscle is intrinsically active, meaning that it generates its own action potentials. The autonomic system does not cause the heart to beat, it just speeds it up (sympathetic) or slows it down (parasympathetic). The mechanisms for this are not mutually exclusive, so the heart receives conflicting signals, and the rhythm of the heart can be affected (Figure 1).

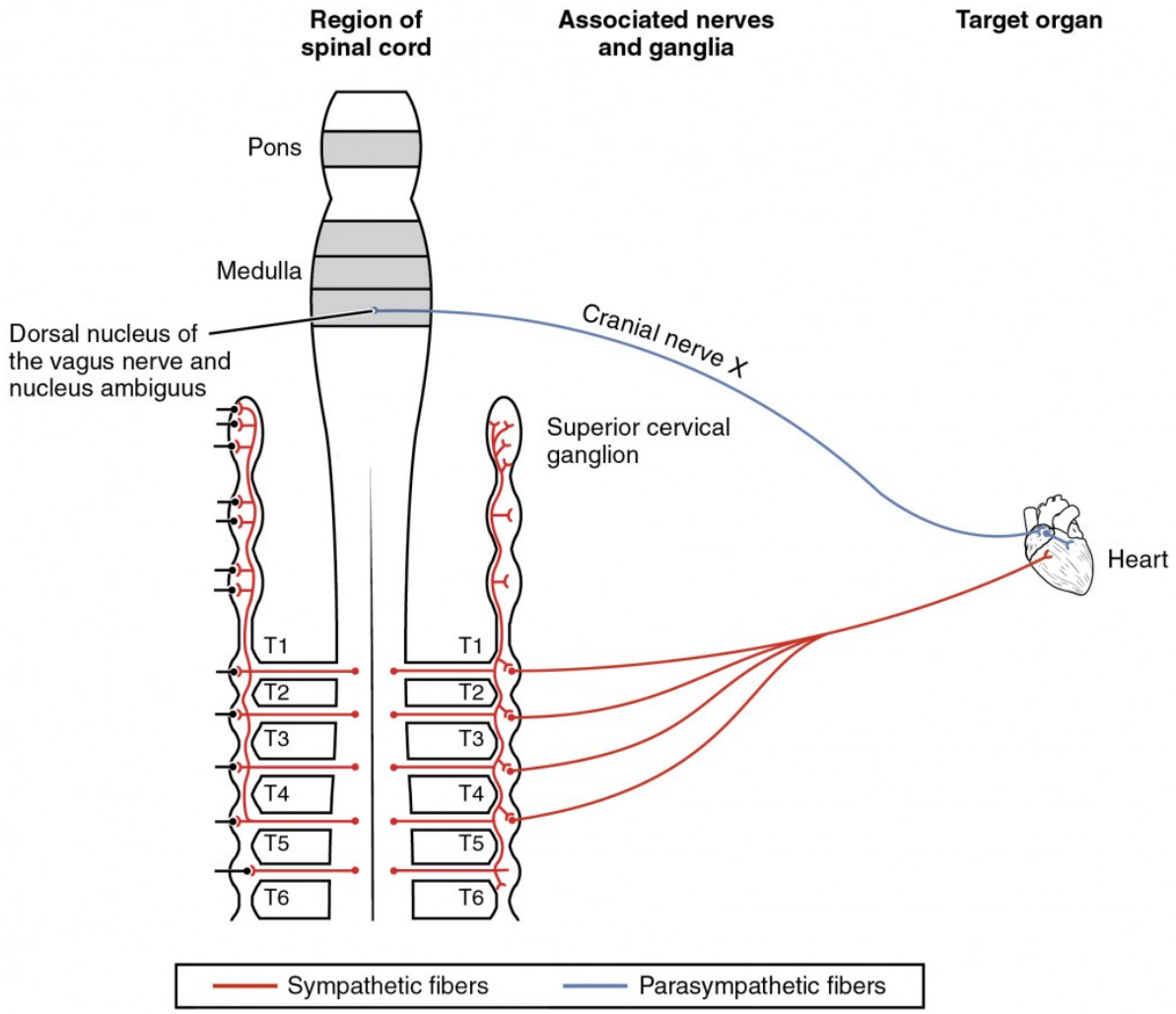


Figure 1. Autonomic Connections to Heart and Blood Vessels *The nicotinic receptor is found on all autonomic ganglia, but the cardiovascular connections are particular, and do not conform to the usual competitive projections that would just cancel each other out when stimulated by nicotine. The opposing signals to the heart would both depolarize and hyperpolarize the heart cells that establish the rhythm of the heartbeat, likely causing arrhythmia. Only the sympathetic system governs systemic blood pressure so nicotine would cause an increase.*

Sympathetic Effect

The neurochemistry of the sympathetic system is based on the adrenergic system. Norepinephrine and epinephrine influence target effectors by binding to the α-adrenergic or β-adrenergic receptors. Drugs that affect the sympathetic system affect these chemical systems. The drugs can be classified by whether they enhance the functions of the sympathetic system or interrupt those functions. A drug that enhances adrenergic function is known as a **sympathomimetic drug**, whereas a drug that interrupts adrenergic function is a **sympatholytic drug**.

Sympathomimetic Drugs

When the sympathetic system is not functioning correctly or the body is in a state of homeostatic imbalance, these drugs act at postganglionic terminals and synapses in the sympathetic efferent pathway. These drugs either bind to particular adrenergic receptors and mimic norepinephrine at the synapses between sympathetic postganglionic fibers and their targets, or they increase the production and release of norepinephrine from postganglionic fibers. Also, to increase the effectiveness of adrenergic chemicals released from the fibers, some of these drugs may block the removal or reuptake of the neurotransmitter from the synapse.

A common sympathomimetic drug is phenylephrine, which is a common component of decongestants. It can also be used to dilate the pupil and to raise blood pressure. Phenylephrine is known as an α_1-adrenergic **agonist**, meaning that it binds to a specific adrenergic receptor, stimulating a response. In this role, phenylephrine will bind to the adrenergic receptors in bronchioles of the lungs and cause them to dilate. By opening these structures, accumulated mucus can be cleared out of the lower respiratory tract. Phenylephrine is often paired with other pharmaceuticals, such as analgesics, as in the "sinus" version of many over-the-counter drugs, such as Tylenol Sinus® or Excedrin Sinus®, or in expectorants for chest congestion such as in Robitussin CF®.

A related molecule, called pseudoephedrine, was much more commonly used in these applications than was phenylephrine, until the molecule became useful in the illicit production of amphetamines. Phenylephrine is not as effective as a drug because it can be partially broken down in the digestive tract before it is ever absorbed. Like the adrenergic agents, phenylephrine is effective in dilating the pupil, known as **mydriasis** (Figure 2). Phenylephrine is used during an eye exam in an ophthalmologist's or optometrist's office for this purpose. It can also be used to increase blood pressure in situations in which cardiac function is compromised, such as under anesthesia or during septic shock.

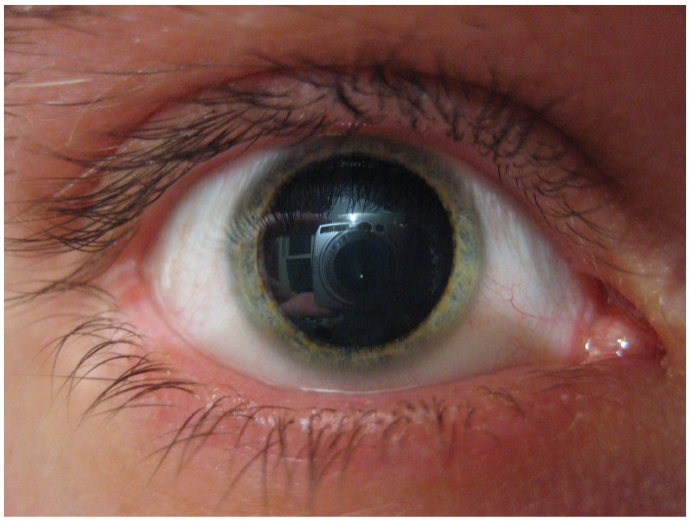


Figure 2. Mydriasis. *The sympathetic system causes pupillary dilation when norepinephrine binds to an adrenergic receptor in the radial fibers of the iris smooth muscle. Phenylephrine mimics this action by binding to the same receptor when drops are applied onto the surface of the eye in a doctor's office. (credit: Corey Theiss)*

Other drugs that enhance adrenergic function are not associated with therapeutic uses, but affect the functions of the sympathetic system in a similar fashion. Cocaine primarily interferes with the uptake of dopamine at the synapse and can also increase adrenergic function. Caffeine is an antagonist to a different neurotransmitter receptor, called the adenosine receptor. Adenosine will suppress adrenergic activity, specifically the release of norepinephrine at synapses, so caffeine indirectly increases adrenergic activity. There is some evidence that caffeine can aid in the therapeutic use of drugs, perhaps by potentiating (increasing) sympathetic function, as is suggested by the inclusion of caffeine in over-the-counter analgesics such as Excedrin®.

Sympatholytic Drugs

Drugs that interfere with sympathetic function are referred to as sympatholytic, or sympathoplegic, drugs. They primarily work as an **antagonist** to the adrenergic receptors. They block the ability of norepinephrine or epinephrine to bind to the receptors so that the effect is "cut" or "takes a blow," to refer to the endings "-lytic" and "-plegic," respectively. The various drugs of this class will be specific to α-adrenergic or β-adrenergic receptors, or to their receptor subtypes.

Possibly the most familiar type of sympatholytic drug are the β-blockers. These drugs are often used to treat cardiovascular disease because they block the β-receptors associated with vasoconstriction and cardioacceleration. By allowing blood vessels to dilate, or keeping heart rate from increasing, these drugs can improve cardiac function in a compromised system, such as for a person with congestive heart failure or who has previously suffered a heart attack. A couple of common versions of β-blockers are metaprolol, which specifically blocks the β_2-receptor, and propanolol, which nonspecifically blocks β-receptors. There are other drugs that are α-blockers and can affect the sympathetic system in a similar way.

Other uses for sympatholytic drugs are as antianxiety medications. A common example of this is clonidine, which is an α-blocker. The sympathetic system is tied to anxiety to the point that the sympathetic response can be referred to as "fight, flight, or fright." Clonidine is used for other treatments aside from hypertension and anxiety, including pain conditions and attention deficit hyperactivity disorder.

Parasympathetic Effects

Drugs affecting parasympathetic functions can be classified into those that increase or decrease activity at postganglionic terminals. Parasympathetic postganglionic fibers release ACh, and the receptors on the targets are muscarinic receptors. There are several types of muscarinic receptors, M1–M5, but the drugs are not usually specific to the specific types. Parasympathetic drugs can be either muscarinic agonists or antagonists, or have indirect effects on the cholinergic system. Drugs that enhance cholinergic effects are called **parasympathomimetic drugs**, whereas those that inhibit cholinergic effects are referred to as **anticholinergic drugs**.

Pilocarpine is a nonspecific muscarinic agonist commonly used to treat disorders of the eye. It reverses mydriasis, such as is caused by phenylephrine, and can be administered after an eye exam. Along with constricting the pupil through the smooth muscle of the iris, pilocarpine will also cause the ciliary muscle to contract. This will open perforations at the base of the cornea, allowing for the drainage of aqueous humor from the anterior compartment of the eye and, therefore, reducing intraocular pressure related to glaucoma.

Atropine and scopolamine are part of a class of muscarinic antagonists that come from the *Atropa* genus of plants that include belladonna or deadly nightshade (Figure 3). The name of one of these plants, belladonna, refers to the fact that extracts from this plant were used cosmetically for dilating the pupil. The active chemicals from this plant block the muscarinic receptors in the iris and allow the pupil to dilate, which is considered attractive because it makes the eyes appear larger. Humans are instinctively attracted to anything with larger eyes, which comes from the fact that the ratio of eye-to-head size is different in infants (or baby animals) and can elicit an emotional response. The cosmetic use of belladonna extract was essentially acting on this response. Atropine is no longer used in this cosmetic capacity for reasons related to the other name for the plant, which is deadly nightshade. Suppression of parasympathetic function, especially when it becomes systemic, can be fatal. Autonomic regulation is disrupted and anticholinergic symptoms develop. The berries of this plant are highly toxic, but can be mistaken for other berries. The antidote for atropine or scopolamine poisoning is pilocarpine.

Figure 3. Belladonna Plant *The plant from the genus Atropa, which is known as belladonna or deadly nightshade, was used cosmetically to dilate pupils, but can be fatal when ingested. The berries on the plant may seem attractive as a fruit, but they contain the same anticholinergic compounds as the rest of the plant.*

Table 1. Sympathetic and Parasympathetic Effects of Different Drug Types

Drug type	Example(s)	Sympathetic effect	Parasympathetic effect	Overall result
Nicotinic agonists	Nicotene	Mimic ACh at preganglionic synapses, causing activation of postganglionic fibers and the release of norepinephrine onto the target organ	Mimic ACh at preganglionic synapses, causing activation of postganglionic fibers and the release of ACh onto the target organ	Most conflicting signals cancel each other out, but cardiovascular system is susceptible to hypertension and arrhythmias
Sympathomimetic drugs	Phenylephrine	Bind to adrenergic receptors or mimics	No effect	Increase sympathetic tone

Table 1. Sympathetic and Parasympathetic Effects of Different Drug Types				
Drug type	Example(s)	Sympathetic effect	Parasympathetic effect	Overall result
		sympathetic action in some other way		
Sympatholytic drugs	B-blockers such as propanolol or metaprolol; a-blockers such as clondine	Block binding to adrenergic drug or decrease adrenergic signals	No effect	Increase parasympathetic tone

Disorders of the Autonomic Nervous System

Approximately 33 percent of people experience a mild problem with motion sickness, whereas up to 66 percent experience motion sickness under extreme conditions, such as being on a tossing boat with no view of the horizon. Connections between regions in the brain stem and the autonomic system result in the symptoms of nausea, cold sweats, and vomiting.

The part of the brain responsible for vomiting, or emesis, is known as the area postrema. It is located next to the fourth ventricle and is not restricted by the blood–brain barrier, which allows it to respond to chemicals in the bloodstream—namely, toxins that will stimulate emesis. There are significant connections between this area, the solitary nucleus, and the dorsal motor nucleus of the vagus nerve. These autonomic system and nuclei connections are associated with the symptoms of motion sickness.

Motion sickness is the result of conflicting information from the visual and vestibular systems. If motion is perceived by the visual system without the complementary vestibular stimuli, or through vestibular stimuli without visual confirmation, the brain stimulates emesis and the associated symptoms. The area postrema, by itself, appears to be able to stimulate emesis in response to toxins in the blood, but it is also connected to the autonomic system and can trigger a similar response to motion.

Autonomic drugs are used to combat motion sickness. Though it is often described as a dangerous and deadly drug, scopolamine is used to treat motion sickness. A popular treatment for motion sickness is the transdermal scopolamine patch. Scopolamine is one of the substances derived from the *Atropa* genus along with atropine. At higher doses, those substances are thought to be poisonous and can lead to an extreme sympathetic syndrome. However, the transdermal patch regulates the release of the drug, and the concentration is kept very low so that the dangers are avoided. For those who are concerned about using "The Most Dangerous Drug," as some websites will call it, antihistamines such as dimenhydrinate (Dramamine®) can be used.

Watch this video to learn about the side effects of 3-D movies.

Watch this video online: https://youtu.be/6J0nTOpFEKE

As discussed in this video, movies that are shot in 3-D can cause motion sickness, which elicits the autonomic symptoms of nausea and sweating. The disconnection between the perceived motion on the screen and the lack of any change in equilibrium stimulates these symptoms. Why do you think sitting close to the screen or right in the middle of the theater makes motion sickness during a 3-D movie worse?

GLOSSARY: THE AUTONOMIC NERVOUS SYSTEM

acetylcholine (ACh): neurotransmitter that binds at a motor end-plate to trigger depolarization

adrenal medulla: interior portion of the adrenal (or suprarenal) gland that releases epinephrine and norepinephrine into the bloodstream as hormones

adrenergic: synapse where norepinephrine is released, which binds to α- or β-adrenergic receptors

afferent branch: component of a reflex arc that represents the input from a sensory neuron, for either a special or general sense

agonist: any exogenous substance that binds to a receptor and produces a similar effect to the endogenous ligand

alpha (α)-adrenergic receptor: one of the receptors to which epinephrine and norepinephrine bind, which comes in three subtypes: α_1, α_2, and α_3

antagonist: any exogenous substance that binds to a receptor and produces an opposing effect to the endogenous ligand

anticholinergic drugs: drugs that interrupt or reduce the function of the parasympathetic system

autonomic tone: tendency of an organ system to be governed by one division of the autonomic nervous system over the other, such as heart rate being lowered by parasympathetic input at rest

baroreceptor: mechanoreceptor that senses the stretch of blood vessels to indicate changes in blood pressure

beta (β)-adrenergic receptor: one of the receptors to which epinephrine and norepinephrine bind, which comes in two subtypes: β_1 and β_2

cardiac accelerator nerves: preganglionic sympathetic fibers that cause the heart rate to increase when the cardiovascular center in the medulla initiates a signal

cardiovascular center: region in the medulla that controls the cardiovascular system through cardiac accelerator nerves and vasomotor nerves, which are components of the sympathetic division of the autonomic nervous system

celiac ganglion: one of the collateral ganglia of the sympathetic system that projects to the digestive system

central neuron: specifically referring to the cell body of a neuron in the autonomic system that is located in the central nervous system, specifically the lateral horn of the spinal cord or a brain stem nucleus

cholinergic: synapse at which acetylcholine is released and binds to the nicotinic or muscarinic receptor

chromaffin cells: neuroendocrine cells of the adrenal medulla that release epinephrine and norepinephrine into the bloodstream as part of sympathetic system activity

ciliary ganglion: one of the terminal ganglia of the parasympathetic system, located in the posterior orbit, axons from which project to the iris

collateral ganglia: ganglia outside of the sympathetic chain that are targets of sympathetic preganglionic fibers, which are the celiac, inferior mesenteric, and superior mesenteric ganglia

craniosacral system: alternate name for the parasympathetic division of the autonomic nervous system that is based on the anatomical location of central neurons in brain-stem nuclei and the lateral horn of the sacral spinal cord; also referred to as craniosacral outflow

dorsal longitudinal fasciculus: major output pathway of the hypothalamus that descends through the gray matter of the brain stem and into the spinal cord

dorsal nucleus of the vagus nerve: location of parasympathetic neurons that project through the vagus nerve to terminal ganglia in the thoracic and abdominal cavities

Eddinger–Westphal nucleus: location of parasympathetic neurons that project to the ciliary ganglion

efferent branch: component of a reflex arc that represents the output, with the target being an effector, such as muscle or glandular tissue

endogenous chemical: substance produced and released within the body to interact with a receptor protein

endogenous: describes substance made in the human body

epinephrine: signaling molecule released from the adrenal medulla into the bloodstream as part of the sympathetic response

exogenous chemical: substance from a source outside the body, whether it be another organism such as a plant or from the synthetic processes of a laboratory, that binds to a transmembrane receptor protein

exogenous: describes substance made outside of the human body

fight-or-flight response: set of responses induced by sympathetic activity that lead to either fleeing a threat or standing up to it, which in the modern world is often associated with anxious feelings

G protein–coupled receptor: membrane protein complex that consists of a receptor protein that binds to a signaling molecule—a G protein—that is activated by that binding and in turn activates an effector protein (enzyme) that creates a second-messenger molecule in the cytoplasm of the target cell

ganglionic neuron: specifically refers to the cell body of a neuron in the autonomic system that is located in a ganglion

gray rami communicantes: (singular = ramus communicans) unmyelinated structures that provide a short connection from a sympathetic chain ganglion to the spinal nerve that contains the postganglionic sympathetic fiber

greater splanchnic nerve: nerve that contains fibers of the central sympathetic neurons that do not synapse in the chain ganglia but project onto the celiac ganglion

inferior mesenteric ganglion: one of the collateral ganglia of the sympathetic system that projects to the digestive system

intramural ganglia: terminal ganglia of the parasympathetic system that are found within the walls of the target effector

lesser splanchnic nerve: nerve that contains fibers of the central sympathetic neurons that do not synapse in the chain ganglia but project onto the inferior mesenteric ganglion

ligand-gated cation channel: ion channel, such as the nicotinic receptor, that is specific to positively charged ions and opens when a molecule such as a neurotransmitter binds to it

limbic lobe: structures arranged around the edges of the cerebrum that are involved in memory and emotion

long reflex: reflex arc that includes the central nervous system

medial forebrain bundle: fiber pathway that extends anteriorly into the basal forebrain, passes through the hypothalamus, and extends into the brain stem and spinal cord

mesenteric plexus: nervous tissue within the wall of the digestive tract that contains neurons that are the targets of autonomic preganglionic fibers and that project to the smooth muscle and glandular tissues in the digestive organ

muscarinic receptor: type of acetylcholine receptor protein that is characterized by also binding to muscarine and is a metabotropic receptor

mydriasis: dilation of the pupil; typically the result of disease, trauma, or drugs

nicotinic receptor: type of acetylcholine receptor protein that is characterized by also binding to nicotine and is an ionotropic receptor

norepinephrine: signaling molecule released as a neurotransmitter by most postganglionic sympathetic fibers as part of the sympathetic response, or as a hormone into the bloodstream from the adrenal medulla

nucleus ambiguus: brain-stem nucleus that contains neurons that project through the vagus nerve to terminal ganglia in the thoracic cavity; specifically associated with the heart

parasympathetic division: division of the autonomic nervous system responsible for restful and digestive functions

parasympathomimetic drugs: drugs that enhance or mimic the function of the parasympathetic system

paravertebral ganglia: autonomic ganglia superior to the sympathetic chain ganglia

postganglionic fiber: axon from a ganglionic neuron in the autonomic nervous system that projects to and synapses with the target effector; sometimes referred to as a postganglionic neuron

preganglionic fiber: axon from a central neuron in the autonomic nervous system that projects to and synapses with a ganglionic neuron; sometimes referred to as a preganglionic neuron

prevertebral ganglia: autonomic ganglia that are anterior to the vertebral column and functionally related to the sympathetic chain ganglia

referred pain: the conscious perception of visceral sensation projected to a different region of the body, such as the left shoulder and arm pain as a sign for a heart attack

reflex arc: circuit of a reflex that involves a sensory input and motor output, or an afferent branch and an efferent branch, and an integrating center to connect the two branches

rest and digest: set of functions associated with the parasympathetic system that lead to restful actions and digestion

short reflex: reflex arc that does not include any components of the central nervous system

somatic reflex: reflex involving skeletal muscle as the effector, under the control of the somatic nervous system

superior cervical ganglion: one of the paravertebral ganglia of the sympathetic system that projects to the head

superior mesenteric ganglion: one of the collateral ganglia of the sympathetic system that projects to the digestive system

sympathetic chain ganglia: series of ganglia adjacent to the vertebral column that receive input from central sympathetic neurons

sympathetic division: division of the autonomic nervous system associated with the fight-or-flight response

sympatholytic drug: drug that interrupts, or “lyses,” the function of the sympathetic system

sympathomimetic drug: drug that enhances or mimics the function of the sympathetic system

target effector: organ, tissue, or gland that will respond to the control of an autonomic or somatic or endocrine signal

terminal ganglia: ganglia of the parasympathetic division of the autonomic system, which are located near or within the target effector, the latter also known as intramural ganglia

thoracolumbar system: alternate name for the sympathetic division of the autonomic nervous system that is based on the anatomical location of central neurons in the lateral horn of the thoracic and upper lumbar spinal cord

varicosity: structure of some autonomic connections that is not a typical synaptic end bulb, but a string of swellings along the length of a fiber that makes a network of connections with the target effector

vasomotor nerves: preganglionic sympathetic fibers that cause the constriction of blood vessels in response to signals from the cardiovascular center

visceral reflex: reflex involving an internal organ as the effector, under the control of the autonomic nervous system

white rami communicantes: (singular = ramus communicans) myelinated structures that provide a short connection from a sympathetic chain ganglion to the spinal nerve that contains the preganglionic sympathetic fiber

MODULE 16: THE BRAIN AND CRANIAL NERVES

INTRODUCTION TO THE BRAIN AND CRANIAL NERVES

Learning Objectives

- Describe the components of the somatic nervous system
- Name the modalities and submodalities of the sensory systems
- Distinguish between general and special senses
- Describe regions of the central nervous system that contribute to somatic functions
- Explain the stimulus-response motor pathway

The somatic nervous system is traditionally considered a division within the peripheral nervous system. However, this misses an important point: somatic refers to a functional division, whereas peripheral refers to an anatomic division. The somatic nervous system is responsible for our conscious perception of the environment and for our voluntary responses to that perception by means of skeletal muscles. Peripheral sensory neurons receive input from environmental stimuli, but the neurons that produce motor responses originate in the central nervous system.

The distinction between the structures (i.e., anatomy) of the peripheral and central nervous systems and functions (i.e., physiology) of the somatic and autonomic systems can most easily be demonstrated through a simple reflex action. When you

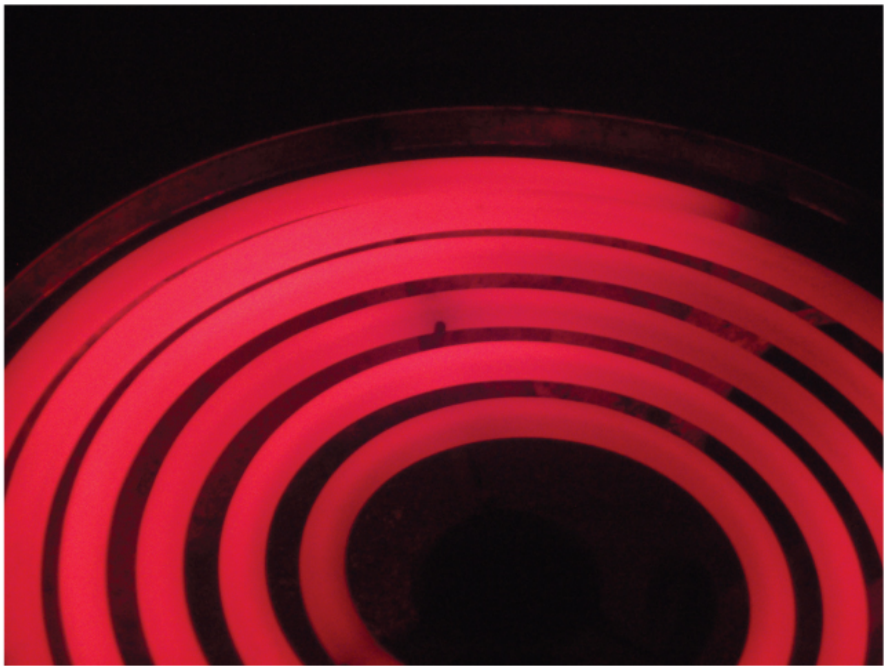


Figure 1. Too Hot to Touch. *When high temperature is sensed in the skin, a reflexive withdrawal is initiated by the muscles of the arm. Sensory neurons are activated by a stimulus, which is sent to the central nervous system, and a motor response is sent out to the skeletal muscles that control this movement.*

touch a hot stove, you pull your hand away. Sensory receptors in the skin sense extreme temperature and the early signs of tissue damage. This triggers an action potential, which travels along the sensory fiber from the skin, through the dorsal spinal root to the spinal cord, and directly activates a ventral horn motor neuron. That neuron sends a signal along its axon to excite the biceps brachii, causing contraction of the muscle and flexion of the forearm at the elbow to withdraw the hand from the hot stove. The withdrawal reflex has more components, such as inhibiting the opposing muscle and balancing posture while the arm is forcefully withdrawn, which will be further explored at the end of this chapter.

The basic withdrawal reflex explained above includes sensory input (the painful stimulus), central processing (the synapse in the spinal cord), and motor output (activation of a ventral motor neuron that causes contraction of the biceps brachii). Expanding the explanation of the withdrawal reflex can include inhibition of the opposing muscle, or cross extension, either of which increase the complexity of the example by involving more central neurons. A collateral branch of the sensory axon would inhibit another ventral horn motor neuron so that the triceps brachii do not contract and slow the withdrawal down. The cross extensor reflex provides a counterbalancing movement on the other side of the body, which requires another collateral of the sensory axon to activate contraction of the extensor muscles in the contralateral limb.

A more complex example of somatic function is conscious muscle movement. For example, reading of this text starts with visual sensory input to the retina, which then projects to the thalamus, and on to the cerebral cortex. A sequence of regions of the cerebral cortex process the visual information, starting in the primary visual cortex of the occipital lobe, and resulting in the conscious perception of these letters. Subsequent cognitive processing results in understanding of the content. As you continue reading, regions of the cerebral cortex in the frontal lobe plan how to move the eyes to follow the lines of text. The output from the cortex causes activity in motor neurons in the brain stem that cause movement of the extraocular muscles through the third, fourth, and sixth cranial nerves. This example also includes sensory input (the retinal projection to the thalamus), central processing (the thalamus and subsequent cortical activity), and motor output (activation of neurons in the brain stem that lead to coordinated contraction of extraocular muscles).

SENSORY PERCEPTION: TASTE AND OLFACTION

Learning Objectives

- Describe different types of sensory receptors
- Describe the structures responsible for the special senses of taste, smell, hearing, balance, and vision
- Distinguish how different tastes are transduced
- Describe the means of mechanoreception for hearing and balance
- List the supporting structures around the eye and describe the structure of the eyeball
- Describe the processes of phototransduction

A major role of sensory receptors is to help us learn about the environment around us, or about the state of our internal environment. Stimuli from varying sources, and of different types, are received and changed into the electrochemical signals of the nervous system. This occurs when a stimulus changes the cell membrane potential of a sensory neuron. The stimulus causes the sensory cell to produce an action potential that is relayed into the central nervous system (CNS), where it is integrated with other sensory information—or sometimes higher cognitive functions—to become a conscious perception of that stimulus. The central integration may then lead to a motor response.

Describing sensory function with the term sensation or perception is a deliberate distinction. Sensation is the activation of sensory receptor cells at the level of the stimulus. Perception is the central processing of sensory stimuli into a meaningful pattern. Perception is dependent on sensation, but not all sensations are perceived. Receptors are the cells or structures that detect sensations. A receptor cell is changed directly by a stimulus. A transmembrane protein receptor is a protein in the cell membrane that mediates a physiological change in a neuron, most often through the opening of ion channels or changes in the cell signaling processes. Transmembrane receptors are activated by chemicals called ligands.

For example, a molecule in food can serve as a ligand for taste receptors. Other transmembrane proteins, which are not accurately called receptors, are sensitive to mechanical or thermal changes. Physical changes in these proteins increase ion flow across the membrane, and can generate an action potential or a graded potential in the sensory neurons.

Sensory Receptors

Stimuli in the environment activate specialized receptor cells in the peripheral nervous system. Different types of stimuli are sensed by different types of receptor cells. Receptor cells can be classified into types on the basis of three different criteria: cell type, position, and function. Receptors can be classified structurally on the basis of cell type and their position in relation to stimuli they sense. They can also be classified functionally on the basis of the **transduction** of stimuli, or how the mechanical stimulus, light, or chemical changed the cell membrane potential.

Structural Receptor Types

The cells that interpret information about the environment can be either (1) a neuron that has a **free nerve ending**, with dendrites embedded in tissue that would receive a sensation; (2) a neuron that has an **encapsulated ending** in which the sensory nerve endings are encapsulated in connective tissue that enhances their sensitivity; or (3) a specialized **receptor cell**, which has distinct structural components that interpret a specific type of stimulus (Figure 1).

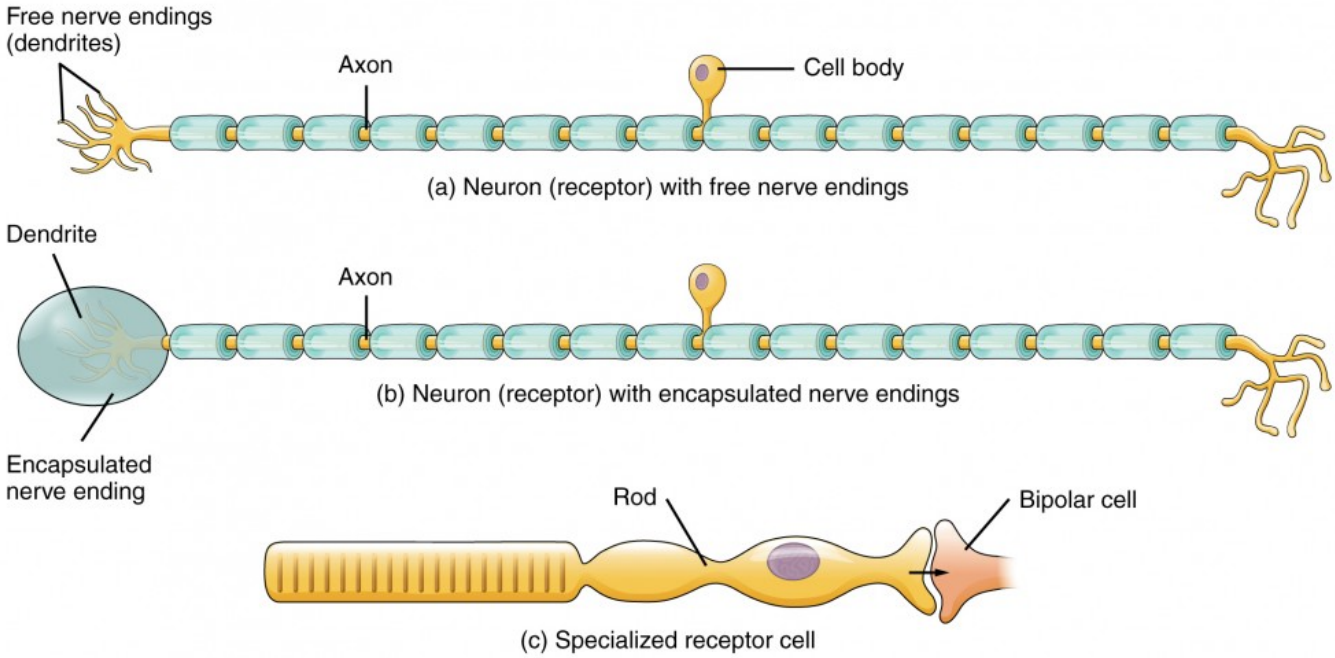


Figure 1. Receptor Classification by Cell Type. *Receptor cell types can be classified on the basis of their structure. Sensory neurons can have either (a) free nerve endings or (b) encapsulated endings. Photoreceptors in the eyes, such as rod cells, are examples of (c) specialized receptor cells. These cells release neurotransmitters onto a bipolar cell, which then synapses with the optic nerve neurons.*

The pain and temperature receptors in the dermis of the skin are examples of neurons that have free nerve endings. Also located in the dermis of the skin are lamellated corpuscles, neurons with encapsulated nerve endings that respond to pressure and touch. The cells in the retina that respond to light stimuli are an example of a specialized receptor, a **photoreceptor**.

Another way that receptors can be classified is based on their location relative to the stimuli. An **exteroceptor** is a receptor that is located near a stimulus in the external environment, such as the somatosensory receptors that are located in the skin. An **interoceptor** is one that interprets stimuli from internal organs and tissues, such as the receptors that sense the increase in blood pressure in the aorta or carotid sinus. Finally, a **proprioceptor** is a receptor located near a moving part of the body, such as a muscle, that interprets the positions of the tissues as they move.

Functional Receptor Types

A third classification of receptors is by how the receptor transduces stimuli into membrane potential changes. Stimuli are of three general types. Some stimuli are ions and macromolecules that affect transmembrane receptor proteins when these chemicals diffuse across the cell membrane. Some stimuli are physical variations in the environment that affect receptor cell membrane potentials. Other stimuli include the electromagnetic radiation from visible light.

For humans, the only electromagnetic energy that is perceived by our eyes is visible light. Some other organisms have receptors that humans lack, such as the heat sensors of snakes, the ultraviolet light sensors of bees, or magnetic receptors in migratory birds. Receptor cells can be further categorized on the basis of the type of stimuli they transduce. Chemical stimuli can be interpreted by a **chemoreceptor** that interprets chemical stimuli, such as an object's taste or smell. **Osmoreceptors** respond to solute concentrations of body fluids. Additionally, pain is primarily a chemical sense that interprets the presence of chemicals from tissue damage, or similar intense stimuli, through a **nociceptor**.

Physical stimuli, such as pressure and vibration, as well as the sensation of sound and body position (balance), are interpreted through a **mechanoreceptor**. Another physical stimulus that has its own type of receptor is temperature, which is sensed through a **thermoreceptor** that is either sensitive to temperatures above (heat) or below (cold) normal body temperature.

Sensory Modalities

Ask anyone what the senses are, and they are likely to list the five major senses—taste, smell, touch, hearing, and sight. However, these are not all of the senses. The most obvious omission from this list is balance. Also, what is referred to simply as touch can be further subdivided into pressure, vibration, stretch, and hair-follicle position, on the basis of the type of mechanoreceptors that perceive these touch sensations. Other overlooked senses include temperature perception by thermoreceptors and pain perception by nociceptors. Within the realm of physiology, senses can be classified as either general or specific.

A **general sense** is one that is distributed throughout the body and has receptor cells within the structures of other organs. Mechanoreceptors in the skin, muscles, or the walls of blood vessels are examples of this type. General senses often contribute to the sense of touch, as described above, or to **proprioception** (body movement) and **kinesthesia** (body movement), or to a **visceral sense**, which is most important to autonomic functions.

A **special sense** is one that has a specific organ devoted to it, namely the eye, inner ear, tongue, or nose. Each of the senses is referred to as a **sensory modality**. Modality refers to the way that information is encoded, which is similar to the idea of transduction. The main sensory modalities can be described on the basis of how each is transduced. The chemical senses are taste and smell. The general sense that is usually referred to as touch includes chemical sensation in the form of nociception, or pain. Pressure, vibration, muscle stretch, and the movement of hair by an external stimulus, are all sensed by mechanoreceptors. Hearing and balance are also sensed by mechanoreceptors. Finally, vision involves the activation of photoreceptors.

Listing all the different sensory modalities, which can number as many as 17, involves separating the five major senses into more specific categories, or **submodalities**, of the larger sense. An individual sensory modality represents the sensation of a specific type of stimulus. For example, the general sense of touch, which is known

as **somatosensation**, can be separated into light pressure, deep pressure, vibration, itch, pain, temperature, or hair movement.

Gustation (Taste)

Only a few recognized submodalities exist within the sense of taste, or **gustation**. Until recently, only four tastes were recognized: sweet, salty, sour, and bitter. Research at the turn of the 20th century led to recognition of the fifth taste, umami, during the mid-1980s. **Umami** is a Japanese word that means “delicious taste,” and is often translated to mean savory. Very recent research has suggested that there may also be a sixth taste for fats, or lipids.

Gustation is the special sense associated with the tongue. The surface of the tongue, along with the rest of the oral cavity, is lined by a stratified squamous epithelium. Raised bumps called **papillae** (singular = *papilla*) contain the structures for gustatory transduction. There are four types of papillae, based on their appearance (Figure 2): circumvallate, foliate, filiform, and fungiform. Within the structure of the papillae are **taste buds** that contain specialized **gustatory receptor cells** for the transduction of taste stimuli. These receptor cells are sensitive to the chemicals contained within foods that are ingested, and they release neurotransmitters based on the amount of the chemical in the food. Neurotransmitters from the gustatory cells can activate sensory neurons in the facial, glossopharyngeal, and vagus cranial nerves.

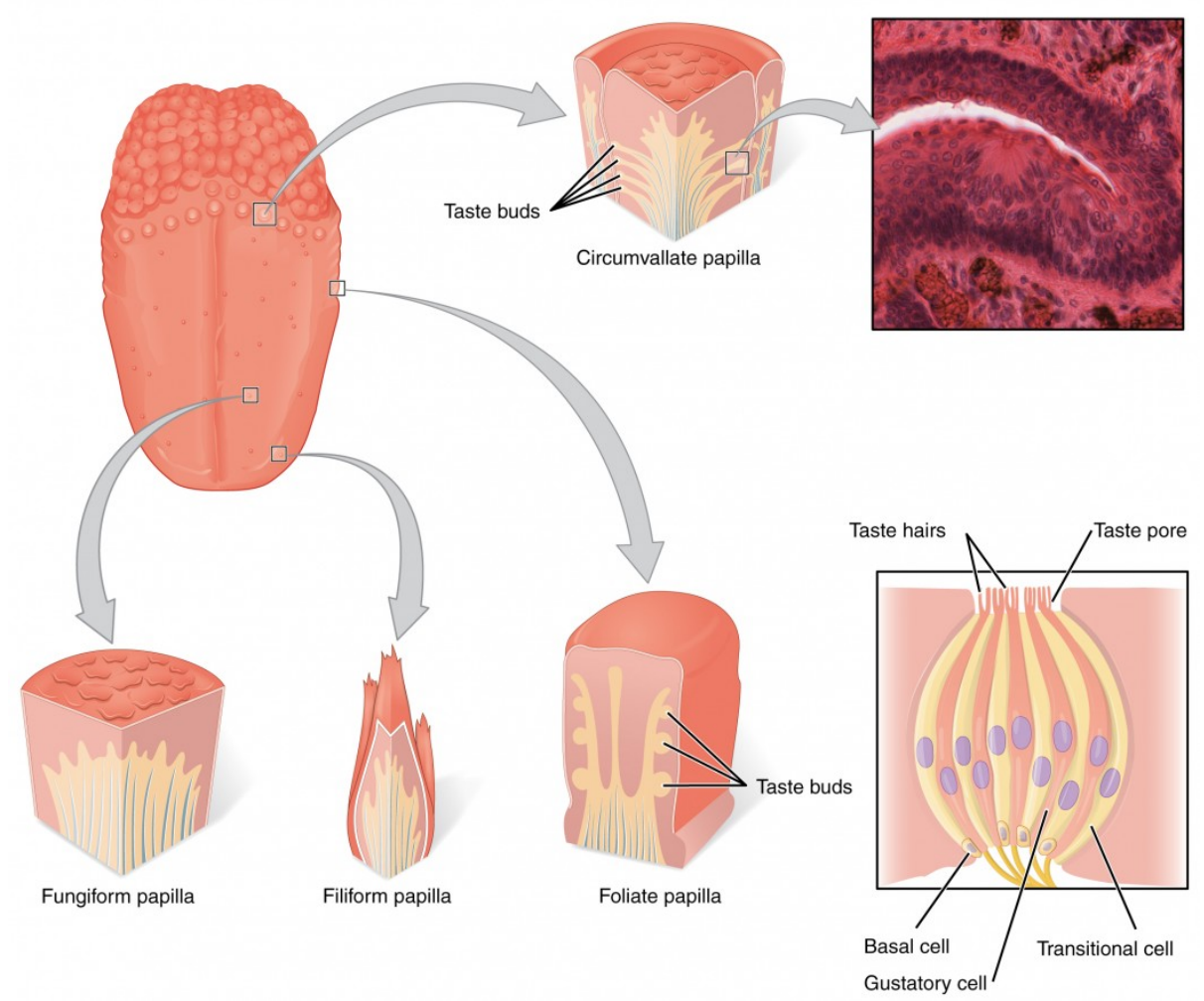


Figure 2. The Tongue. *The tongue is covered with small bumps, called papillae, which contain taste buds that are sensitive to chemicals in ingested food or drink. Different types of papillae are found in different regions of the tongue. The taste buds contain specialized gustatory receptor cells that respond to chemical stimuli dissolved in the saliva. These receptor cells activate sensory neurons that are part of the facial and glossopharyngeal nerves. LM × 1600. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

Salty taste is simply the perception of sodium ions (Na^+) in the saliva. When you eat something salty, the salt crystals dissociate into the component ions Na^+ and Cl^-, which dissolve into the saliva in your mouth. The Na^+ concentration becomes high outside the gustatory cells, creating a strong concentration gradient that drives the diffusion of the ion into the cells. The entry of Na^+ into these cells results in the depolarization of the cell membrane and the generation of a receptor potential.

Sour taste is the perception of H^+ concentration. Just as with sodium ions in salty flavors, these hydrogen ions enter the cell and trigger depolarization. Sour flavors are, essentially, the perception of acids in our food. Increasing hydrogen ion concentrations in the saliva (lowering saliva pH) triggers progressively stronger graded potentials in the gustatory cells. For example, orange juice—which contains citric acid—will taste sour because it has a pH value of approximately 3. Of course, it is often sweetened so that the sour taste is masked. The first two tastes (salty and sour) are triggered by the cations Na^+ and H^+. The other tastes result from food molecules binding to a G protein–coupled receptor. A G protein signal transduction system ultimately leads to depolarization of the gustatory cell.

The sweet taste is the sensitivity of gustatory cells to the presence of glucose dissolved in the saliva. Other monosaccharides such as fructose, or artificial sweeteners such as aspartame (NutraSweet™), saccharine, or sucralose (Splenda™) also activate the sweet receptors. The affinity for each of these molecules varies, and some will taste sweeter than glucose because they bind to the G protein–coupled receptor differently.

Bitter taste is similar to sweet in that food molecules bind to G protein–coupled receptors. However, there are a number of different ways in which this can happen because there are a large diversity of bitter-tasting molecules. Some bitter molecules depolarize gustatory cells, whereas others hyperpolarize gustatory cells. Likewise, some bitter molecules increase G protein activation within the gustatory cells, whereas other bitter molecules decrease G protein activation. The specific response depends on which molecule is binding to the receptor. One major group of bitter-tasting molecules are alkaloids. **Alkaloids** are nitrogen-containing molecules that often have a basic pH. Alkaloids are commonly found in bitter-tasting plant products, such as coffee, hops (in beer), tannins (in wine), tea, and aspirin. By containing toxic alkaloids, the plant is less susceptible to microbe infection and less attractive to herbivores. Therefore, the function of bitter taste may primarily be related to stimulating the gag reflex to avoid ingesting poisons. Because of this, many bitter foods that are normally ingested are often combined with a sweet component to make them more palatable (cream and sugar in coffee, for example). The highest concentration of bitter receptors appear to be in the posterior tongue, where a gag reflex could still spit out poisonous food.

The taste known as umami is often referred to as the savory taste. Like sweet and bitter, it is based on the activation of G protein–coupled receptors by a specific molecule. The molecule that activates this receptor is the amino acid L-glutamate. Therefore, the umami flavor is often perceived while eating protein-rich foods. Not surprisingly, dishes that contain meat are often described as savory.

Once the gustatory cells are activated by the taste molecules, they release neurotransmitters onto the dendrites of sensory neurons. These neurons are part of the facial and glossopharyngeal cranial nerves, as well as a component within the vagus nerve dedicated to the gag reflex. The facial nerve connects to taste buds in the anterior third of the tongue. The glossopharyngeal nerve connects to taste buds in the posterior two thirds of the tongue. The vagus nerve connects to taste buds in the extreme posterior of the tongue, verging on the pharynx, which are more sensitive to noxious stimuli such as bitterness.

Watch this video to learn about Dr. Danielle Reed of the Monell Chemical Senses Center in Philadelphia, Pennsylvania, who became interested in science at an early age because of her sensory experiences. She recognized that her sense of taste was unique compared with other people she knew. Now, she studies the genetic differences between people and their sensitivities to taste stimuli.

Watch this video online: https://youtu.be/eX7LvKO9txc

In the video, there is a brief image of a person sticking out their tongue, which has been covered with a colored dye. This is how Dr. Reed is able to visualize and count papillae on the surface of the tongue. People fall into two groups known as “tasters” and “non-tasters” based on the density of papillae on their tongue, which also indicates the number of taste buds. Non-tasters can taste food, but they are not as sensitive to certain tastes, such as bitterness. Dr. Reed discovered that she is a non-taster, which explains why she

perceived bitterness differently than other people she knew. Are you very sensitive to tastes? Can you see any similarities among the members of your family?

Olfaction (Smell)

Like taste, the sense of smell, or **olfaction**, is also responsive to chemical stimuli. The olfactory receptor neurons are located in a small region within the superior nasal cavity (Figure 3). This region is referred to as the **olfactory epithelium** and contains bipolar sensory neurons. Each **olfactory sensory neuron** has dendrites that extend from the apical surface of the epithelium into the mucus lining the cavity. As airborne molecules are inhaled through the nose, they pass over the olfactory epithelial region and dissolve into the mucus. These **odorant molecules** bind to proteins that keep them dissolved in the mucus and help transport them to the olfactory dendrites. The odorant–protein complex binds to a receptor protein within the cell membrane of an olfactory dendrite. These receptors are G protein–coupled, and will produce a graded membrane potential in the olfactory neurons.

The axon of an olfactory neuron extends from the basal surface of the epithelium, through an olfactory foramen in the cribriform plate of the ethmoid bone, and into the brain. The group of axons called the olfactory tract connect to the **olfactory bulb** on the ventral surface of the frontal lobe. From there, the axons split to travel to several brain regions. Some travel to the cerebrum, specifically to the primary olfactory cortex that is located in the inferior and medial areas of the temporal lobe. Others project to structures within the limbic system and hypothalamus, where smells become associated with long-term memory and emotional responses. This is how certain smells trigger emotional memories, such as the smell of food associated with one's birthplace. Smell is the one sensory modality that does not synapse in the thalamus before connecting to the cerebral cortex. This intimate connection between the olfactory system and the cerebral cortex is one reason why smell can be a potent trigger of memories and emotion.

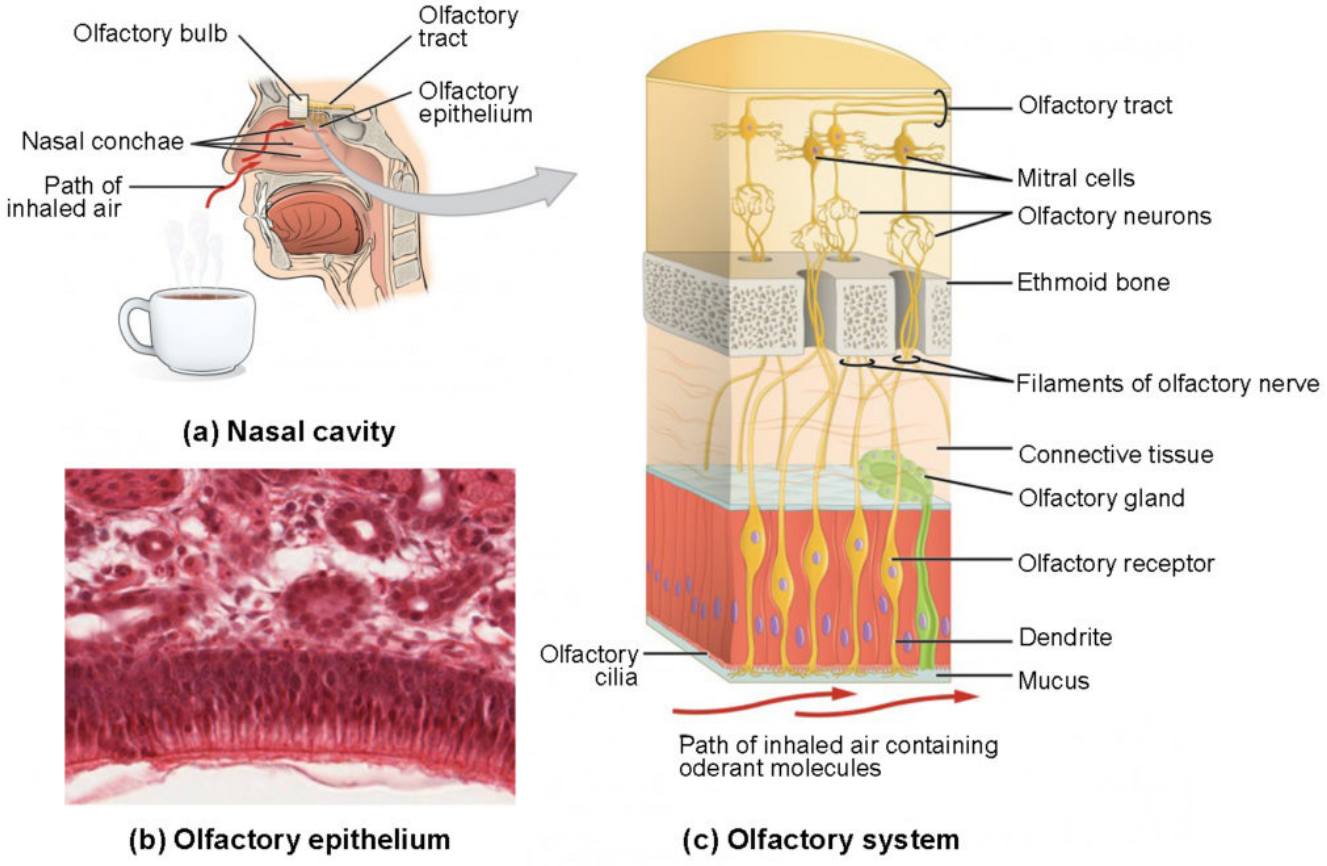


Figure 3. The Olfactory System *(a) The olfactory system begins in the peripheral structures of the nasal cavity. (b) Axons of the olfactory receptor neurons project through the cribriform plate of the ethmoid bone and synapse with the neurons of the olfactory*

bulb (tissue source: simian).LM × 812. (Micrograph provided by the Regents of University of Michigan Medical School © 2012) (c) The olfactory receptor neurons are within the olfactory epithelium.

The nasal epithelium, including the olfactory cells, can be harmed by airborne toxic chemicals. Therefore, the olfactory neurons are regularly replaced within the nasal epithelium, after which the axons of the new neurons must find their appropriate connections in the olfactory bulb. These new axons grow along the axons that are already in place in the cranial nerve.

Disorders of the Olfactory System: Anosmia

Blunt force trauma to the face, such as that common in many car accidents, can lead to the loss of the olfactory nerve, and subsequently, loss of the sense of smell. This condition is known as **anosmia**. When the frontal lobe of the brain moves relative to the ethmoid bone, the olfactory tract axons may be sheared apart. Professional fighters often experience anosmia because of repeated trauma to face and head. In addition, certain pharmaceuticals, such as antibiotics, can cause anosmia by killing all the olfactory neurons at once. If no axons are in place within the olfactory nerve, then the axons from newly formed olfactory neurons have no guide to lead them to their connections within the olfactory bulb. There are temporary causes of anosmia, as well, such as those caused by inflammatory responses related to respiratory infections or allergies. Loss of the sense of smell can result in food tasting bland. A person with an impaired sense of smell may require additional spice and seasoning levels for food to be tasted. Anosmia may also be related to some presentations of mild depression, because the loss of enjoyment of food may lead to a general sense of despair. The ability of olfactory neurons to replace themselves decreases with age, leading to age-related anosmia. This explains why some elderly people salt their food more than younger people do. However, this increased sodium intake can increase blood volume and blood pressure, increasing the risk of cardiovascular diseases in the elderly.

AUDITION AND SOMATOSENSATION

Audition (Hearing)

Hearing, or **audition**, is the transduction of sound waves into a neural signal that is made possible by the structures of the ear (Figure 1). The large, fleshy structure on the lateral aspect of the head is known as the **auricle**. Some sources will also refer to this structure as the pinna, though that term is more appropriate for a structure that can be moved, such as the external ear of a cat. The C-shaped curves of the auricle direct sound waves toward the auditory canal. The canal enters the skull through the external auditory meatus of the temporal bone. At the end of the auditory canal is the **tympanic membrane**, or ear drum, which vibrates after it is struck by sound waves. The auricle, ear canal, and tympanic membrane are often referred to as the **external ear**.

The **middle ear** consists of a space spanned by three small bones called the **ossicles**. The three ossicles are the **malleus**, **incus**, and **stapes**, which are Latin names that roughly translate to hammer, anvil, and stirrup. The malleus is attached to the tympanic membrane and articulates with the incus. The incus, in turn, articulates with the stapes. The stapes is then attached to the **inner ear**, where the sound waves will be transduced into a neural signal. The middle ear is connected to the pharynx through the Eustachian tube, which helps equilibrate air pressure across the tympanic membrane. The tube is normally closed but will pop open when the muscles of the pharynx contract during swallowing or yawning.

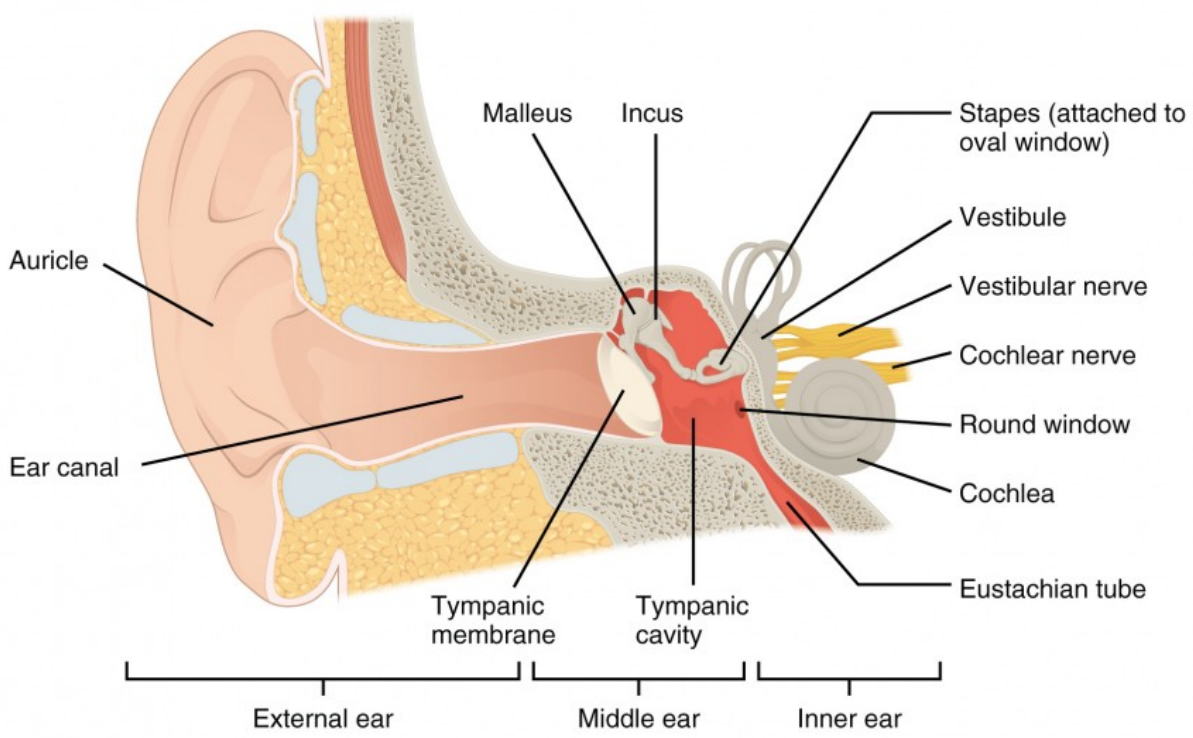


Figure 1. Structures of the Ear *The external ear contains the auricle, ear canal, and tympanic membrane. The middle ear contains the ossicles and is connected to the pharynx by the Eustachian tube. The inner ear contains the cochlea and vestibule, which are responsible for audition and equilibrium, respectively.*

The inner ear is often described as a bony labyrinth, as it is composed of a series of canals embedded within the temporal bone. It has two separate regions, the **cochlea** and the **vestibule**, which are responsible for hearing and balance, respectively. The neural signals from these two regions are relayed to the brain stem through separate fiber bundles. However, these two distinct bundles travel together from the inner ear to the brain stem as the vestibulocochlear nerve. Sound is transduced into neural signals within the cochlear region of the inner ear, which contains the sensory neurons of the **spiral ganglia**. These ganglia are located within the spiral-shaped cochlea of the inner ear. The cochlea is attached to the stapes through the **oval window**. The oval window is located at the beginning of a fluid-filled tube within the cochlea called the **scala vestibuli**. The scala vestibuli extends from the oval window, travelling above the **cochlear duct**, which is the central cavity of the cochlea that contains the sound-transducing neurons.

At the uppermost tip of the cochlea, the scala vestibuli curves over the top of the cochlear duct. The fluid-filled tube, now called the **scala tympani**, returns to the base of the cochlea, this time travelling under the cochlear duct. The scala tympani ends at the **round window**, which is covered by a membrane that contains the fluid within the scala. As vibrations of the ossicles travel through the oval window, the fluid of the scala vestibuli and scala tympani moves in a wave-like motion. The frequency of the fluid waves match the frequencies of the sound waves (Figure 2). The membrane covering the round window will bulge out or pucker in with the movement of the fluid within the scala tympani.

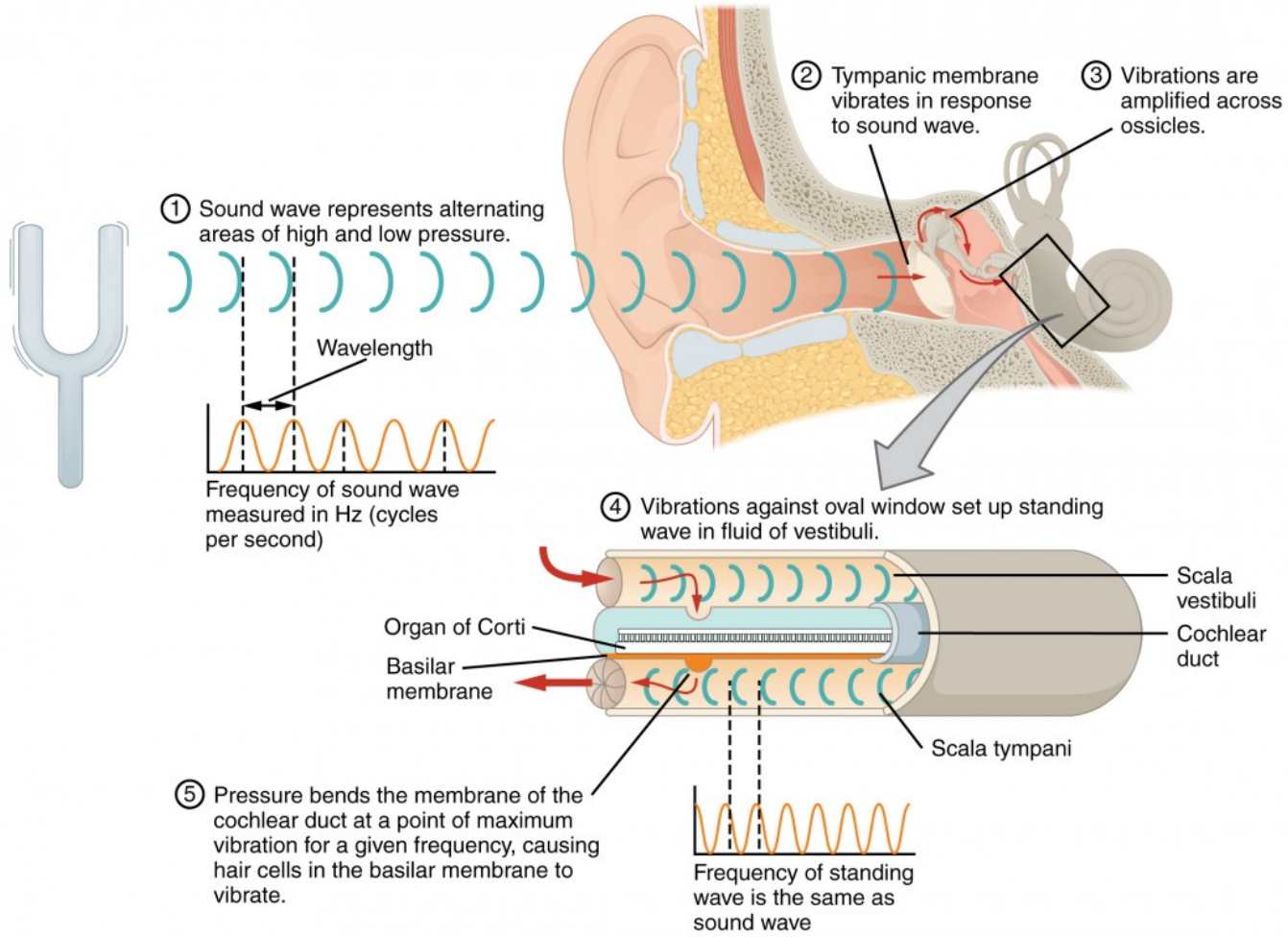


Figure 2. Transmission of Sound Waves to Cochlea *A sound wave causes the tympanic membrane to vibrate. This vibration is amplified as it moves across the malleus, incus, and stapes. The amplified vibration is picked up by the oval window causing pressure waves in the fluid of the scala vestibuli and scala tympani. The complexity of the pressure waves is determined by the changes in amplitude and frequency of the sound waves entering the ear.*

A cross-sectional view of the cochlea shows that the scala vestibuli and scala tympani run along both sides of the cochlear duct (Figure 3. The cochlear duct contains several **organs of Corti**, which tranduce the wave motion of the two scala into neural signals. The organs of Corti lie on top of the **basilar membrane**, which is the side of the cochlear duct located between the organs of Corti and the scala tympani. As the fluid waves move through the scala vestibuli and scala tympani, the basilar membrane moves at a specific spot, depending on the frequency of the waves. Higher frequency waves move the region of the basilar membrane that is close to the base of the cochlea. Lower frequency waves move the region of the basilar membrane that is near the tip of the cochlea.

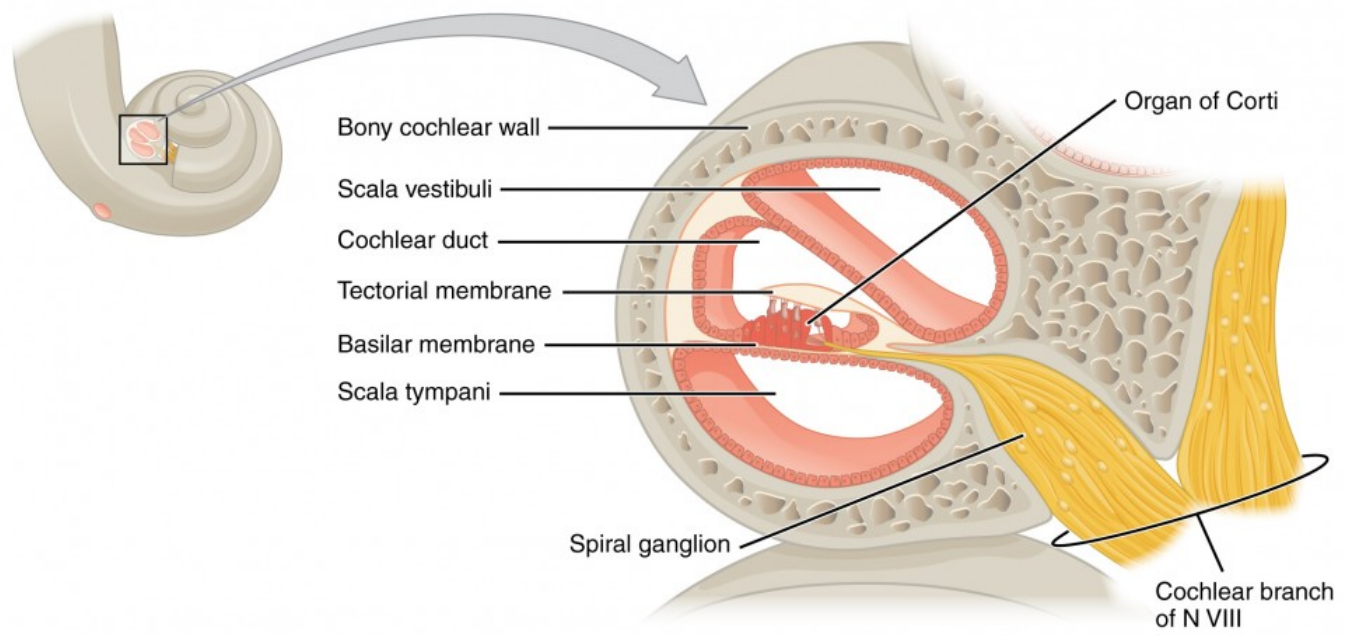


Figure 3. Cross Section of the Cochlea *The three major spaces within the cochlea are highlighted. The scala tympani and scala vestibuli lie on either side of the cochlear duct. The organ of Corti, containing the mechanoreceptor hair cells, is adjacent to the scala tympani, where it sits atop the basilar membrane.*

The organs of Corti contain **hair cells**, which are named for the hair-like **stereocilia** extending from the cell's apical surfaces (Figure 4). The stereocilia are an array of microvilli-like structures arranged from tallest to shortest. Protein fibers tether adjacent hairs together within each array, such that the array will bend in response to movements of the basilar membrane. The stereocilia extend up from the hair cells to the overlying **tectorial membrane**, which is attached medially to the organ of Corti. When the pressure waves from the scala move the basilar membrane, the tectorial membrane slides across the stereocilia. This bends the stereocilia either toward or away from the tallest member of each array.

When the stereocilia bend toward the tallest member of their array, tension in the protein tethers opens ion channels in the hair cell membrane. This will depolarize the hair cell membrane, triggering nerve impulses that travel down the afferent nerve fibers attached to the hair cells. When the stereocilia bend toward the shortest member of their array, the tension on the tethers slackens and the ion channels close. When no sound is present, and the stereocilia are standing straight, a small amount of tension still exists on the tethers, keeping the membrane potential of the hair cell slightly depolarized.

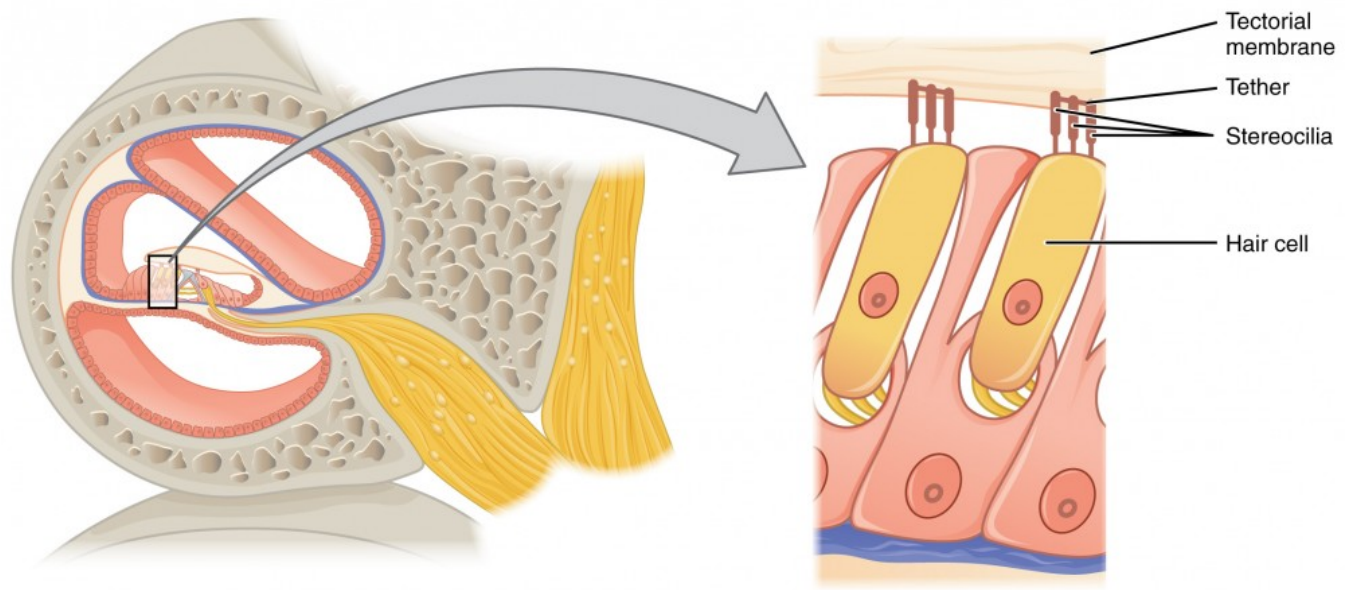


Figure 4. Hair Cell *The hair cell is a mechanoreceptor with an array of stereocilia emerging from its apical surface. The stereocilia are tethered together by proteins that open ion channels when the array is bent toward the tallest member of their array, and closed when the array is bent toward the shortest member of their array.*

View the University of Michigan WebScope at to explore the tissue sample in Figure 5 in greater detail. The basilar membrane is the thin membrane that extends from the central core of the cochlea to the edge. What is anchored to this membrane so that they can be activated by movement of the fluids within the cochlea?

As stated above, a given region of the basilar membrane will only move if the incoming sound is at a specific frequency. Because the tectorial membrane only moves where the basilar membrane moves, the hair cells in this region will also only respond to sounds of this specific frequency. Therefore, as the frequency of a sound changes, different hair cells are activated all along the basilar membrane.

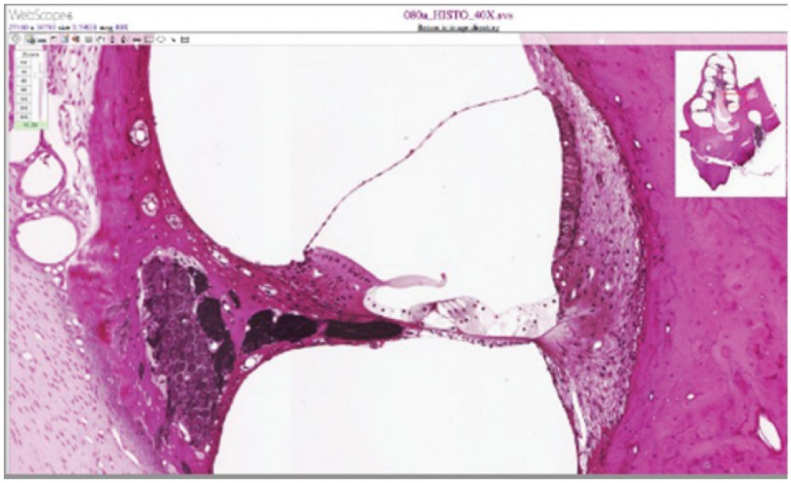


Figure 5. Cochlea and Organ of Corti *LM × 412. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

The cochlea encodes auditory stimuli for frequencies between 20 and 20,000 Hz, which is the range of sound that human ears can detect. The unit of Hertz measures the frequency of sound waves in terms of cycles produced per second. Frequencies as low as 20 Hz are detected by hair cells at the apex, or tip, of the cochlea. Frequencies in the higher ranges of 20 KHz are encoded by hair cells at the base of the cochlea, close to the round and oval windows (Figure 6). Most auditory stimuli contain a mixture of sounds at a variety of frequencies and intensities (represented by the amplitude of the sound wave). The hair cells along the length of the cochlear duct, which are each sensitive to a particular frequency, allow the cochlea to separate auditory stimuli by frequency, just as a prism separates visible light into its component colors.

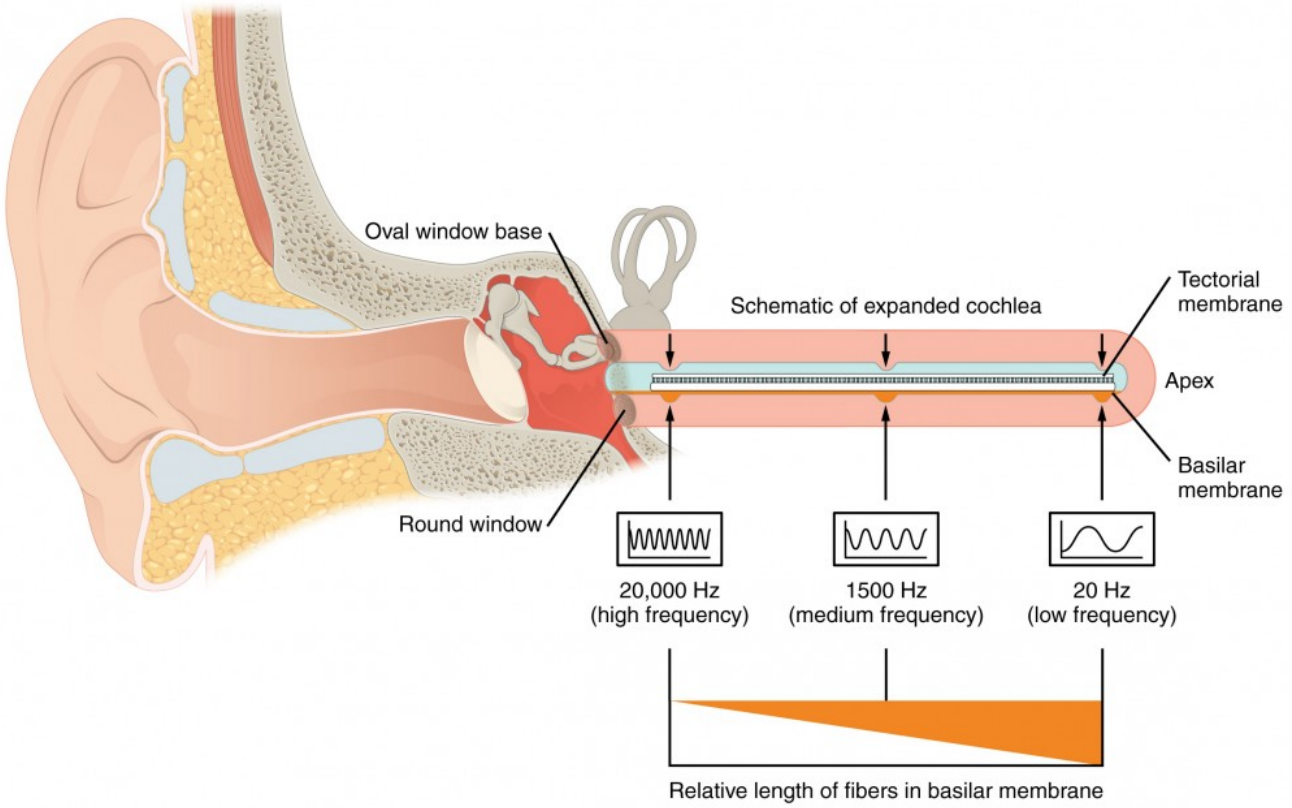


Figure 6. Frequency Coding in the Cochlea *The standing sound wave generated in the cochlea by the movement of the oval window deflects the basilar membrane on the basis of the frequency of sound. Therefore, hair cells at the base of the cochlea are activated only by high frequencies, whereas those at the apex of the cochlea are activated only by low frequencies.*

Watch this video to learn more about how the structures of the ear convert sound waves into a neural signal by moving the "hairs," or stereocilia, of the cochlear duct. Specific locations along the length of the duct encode specific frequencies, or pitches. The brain interprets the meaning of the sounds we hear as music, speech, noise, etc.

Watch this video online: https://youtu.be/GGqfRvCkt-w

Which ear structures are responsible for the amplification and transfer of sound from the external ear to the inner ear?

Watch this animation to learn more about the inner ear and to see the cochlea unroll, with the base at the back of the image and the apex at the front.

Watch this video online: https://youtu.be/dyenMluFaUw

Specific wavelengths of sound cause specific regions of the basilar membrane to vibrate, much like the keys of a piano produce sound at different frequencies. Based on the animation, where do frequencies—from high to low pitches—cause activity in the hair cells within the cochlear duct?

Equilibrium (Balance)

Along with audition, the inner ear is responsible for encoding information about **equilibrium**, the sense of balance. A similar mechanoreceptor—a hair cell with stereocilia—senses head position, head movement, and whether our bodies are in motion. These cells are located within the vestibule of the inner ear. Head position is sensed by the **utricle** and **saccule**, whereas head movement is sensed by the **semicircular canals**. The neural signals generated in the **vestibular ganglion** are transmitted through the vestibulocochlear nerve to the brain stem and

cerebellum. The utricle and saccule are both largely composed of **macula** tissue (plural = maculae). The macula is composed of hair cells surrounded by support cells. The stereocilia of the hair cells extend into a viscous gel called the **otolith** (Figure 7).

The otolith contains calcium carbonate crystals, making it denser and giving it greater inertia than the macula. Therefore, gravity will cause the otolith to move separately from the macula in response to head movements. Tilting the head causes the otolith to slide over the macula in the direction of gravity. The moving otolith layer, in turn, bends the sterocilia to cause some hair cells to depolarize as others hyperpolarize. The exact tilt of the head is interpreted by the brain on the basis of the pattern of hair-cell depolarization.

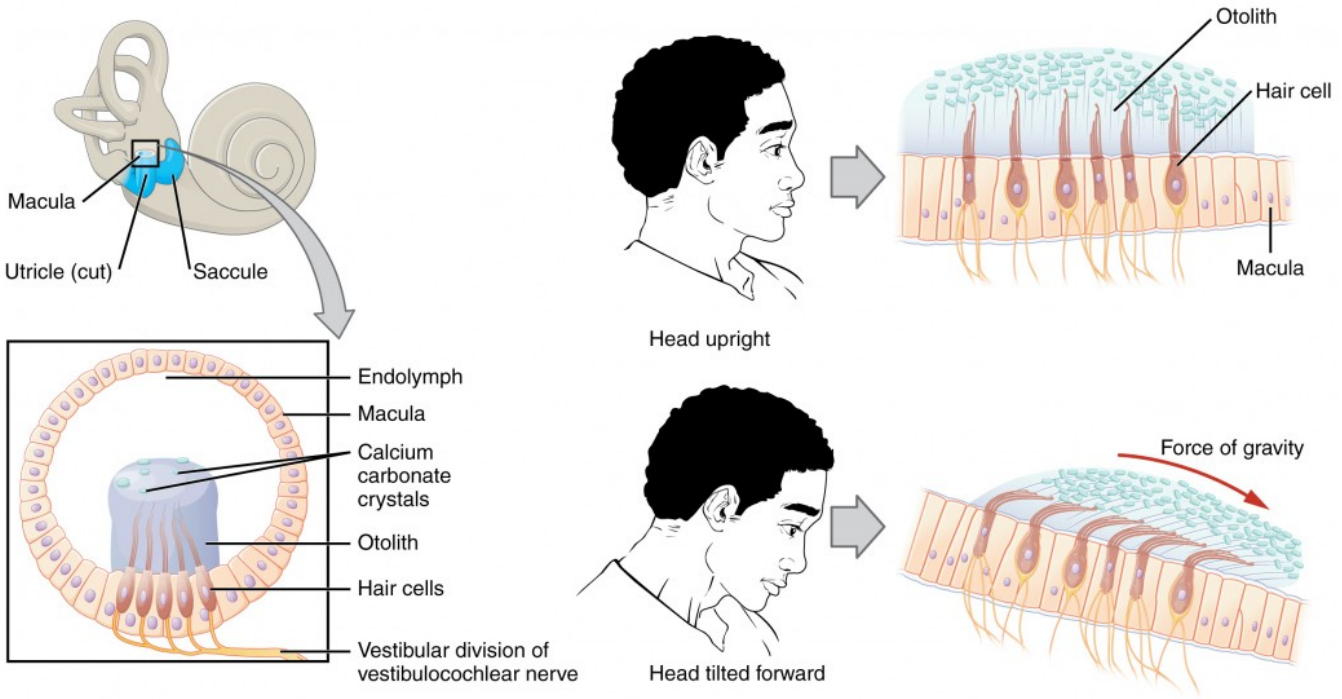


Figure 7. Linear Acceleration Coding by Maculae *The maculae are specialized for sensing linear acceleration, such as when gravity acts on the tilting head, or if the head starts moving in a straight line. The difference in inertia between the hair cell stereocilia and the otolith in which they are embedded leads to a shearing force that causes the stereocilia to bend in the direction of that linear acceleration.*

The semicircular canals are three ring-like extensions of the vestibule. One is oriented in the horizontal plane, whereas the other two are oriented in the vertical plane. The anterior and posterior vertical canals are oriented at approximately 45 degrees relative to the sagittal plane (Figure 8).

The base of each semicircular canal, where it meets with the vestibule, connects to an enlarged region known as the **ampulla**. The ampulla contains the hair cells that respond to rotational movement, such as turning the head while saying “no.” The stereocilia of these hair cells extend into the **cupula**, a membrane that attaches to the top of the ampulla. As the head rotates in a plane parallel to the semicircular canal, the fluid lags, deflecting the cupula in the direction opposite to the head movement. The semicircular canals contain several ampullae, with some oriented horizontally and others oriented vertically. By comparing the relative movements of both the horizontal and vertical ampullae, the vestibular system can detect the direction of most head movements within three-dimensional (3-D) space.

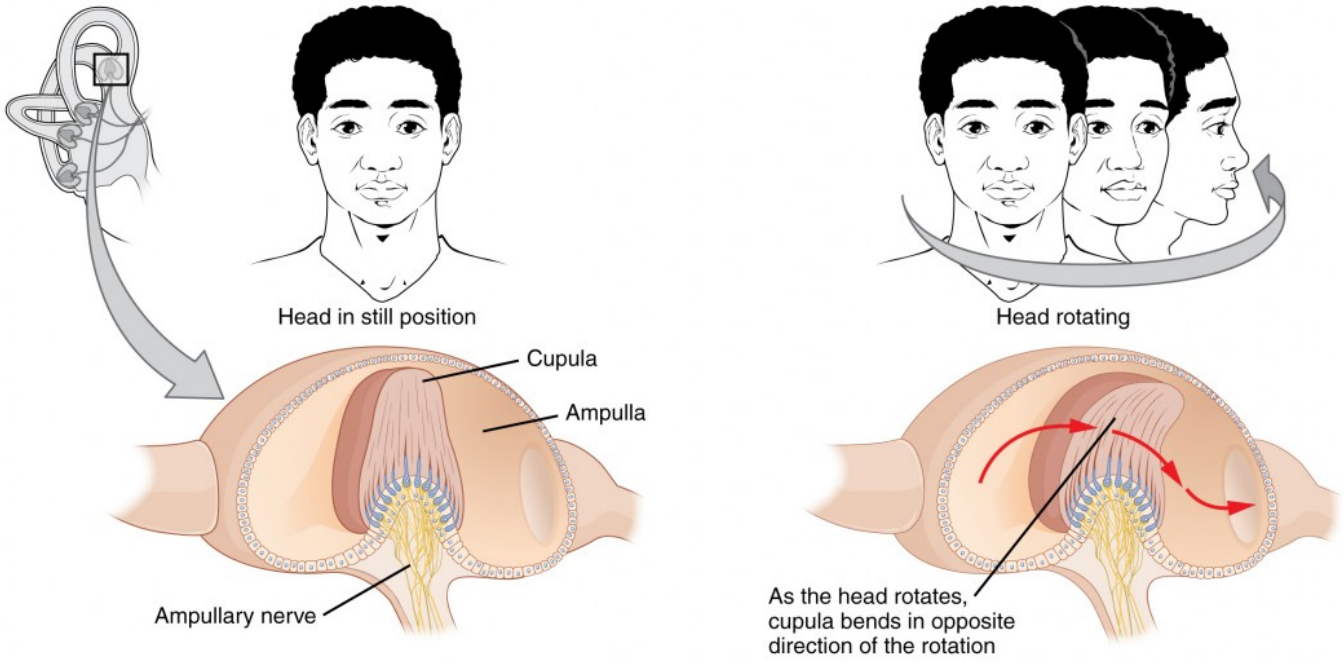


Figure 8. Rotational Coding by Semicircular Canals *Rotational movement of the head is encoded by the hair cells in the base of the semicircular canals. As one of the canals moves in an arc with the head, the internal fluid moves in the opposite direction, causing the cupula and stereocilia to bend. The movement of two canals within a plane results in information about the direction in which the head is moving, and activation of all six canals can give a very precise indication of head movement in three dimensions.*

Somatosensation (Touch)

Somatosensation is considered a general sense, as opposed to the special senses discussed in this section. Somatosensation is the group of sensory modalities that are associated with touch, proprioception, and interoception. These modalities include pressure, vibration, light touch, tickle, itch, temperature, pain, proprioception, and kinesthesia. This means that its receptors are not associated with a specialized organ, but are instead spread throughout the body in a variety of organs. Many of the somatosensory receptors are located in the skin, but receptors are also found in muscles, tendons, joint capsules, ligaments, and in the walls of visceral organs. Two types of somatosensory signals that are transduced by free nerve endings are pain and temperature. These two modalities use thermoreceptors and nociceptors to transduce temperature and pain stimuli, respectively. Temperature receptors are stimulated when local temperatures differ from body temperature.

Some thermoreceptors are sensitive to just cold and others to just heat. Nociception is the sensation of potentially damaging stimuli. Mechanical, chemical, or thermal stimuli beyond a set threshold will elicit painful sensations. Stressed or damaged tissues release chemicals that activate receptor proteins in the nociceptors.

For example, the sensation of heat associated with spicy foods involves **capsaicin**, the active molecule in hot peppers. Capsaicin molecules bind to a transmembrane ion channel in nociceptors that is sensitive to temperatures above 37°C. The dynamics of capsaicin binding with this transmembrane ion channel is unusual in that the molecule remains bound for a long time. Because of this, it will decrease the ability of other stimuli to elicit pain sensations through the activated nociceptor. For this reason, capsaicin can be used as a topical analgesic, such as in products such as Icy Hot™. If you drag your finger across a textured surface, the skin of your finger will vibrate. Such low frequency vibrations are sensed by mechanoreceptors called Merkel cells, also known as type I cutaneous mechanoreceptors. Merkel cells are located in the stratum basale of the epidermis.

Deep pressure and vibration is transduced by lamellated (Pacinian) corpuscles, which are receptors with encapsulated endings found deep in the dermis, or subcutaneous tissue. Light touch is transduced by the encapsulated endings known as tactile (Meissner) corpuscles. Follicles are also wrapped in a plexus of nerve endings known as the hair follicle plexus. These nerve endings detect the movement of hair at the surface of the skin, such as when an insect may be walking along the skin. Stretching of the skin is transduced by stretch

receptors known as bulbous corpuscles. Bulbous corpuscles are also known as Ruffini corpuscles, or type II cutaneous mechanoreceptors.

Other somatosensory receptors are found in the joints and muscles. Stretch receptors monitor the stretching of tendons, muscles, and the components of joints. For example, have you ever stretched your muscles before or after exercise and noticed that you can only stretch so far before your muscles spasm back to a less stretched state? This spasm is a reflex that is initiated by stretch receptors to avoid muscle tearing. Such stretch receptors can also prevent over-contraction of a muscle. In skeletal muscle tissue, these stretch receptors are called muscle spindles. Golgi tendon organs similarly transduce the stretch levels of tendons. Bulbous corpuscles are also present in joint capsules, where they measure stretch in the components of the skeletal system within the joint. The types of nerve endings, their locations, and the stimuli they transduce are presented in Table 1.

Table 1. Mechanoreceptors of Somatosensation

Name	Historical (eponymous) name	Location(s)	Stimuli
Free nerve endings	[No corresponding eponymous name]	Dermis, cornea, tongue, joint capsules, visceral organs	Pain, temperature, mechanical deformation
Mechanoreceptors	Merkel's discs	Epidermal-dermal junction, mucosal membranes	Low frequency vibration (5-15 Hz)
Bulbous corpuscle	Ruffini's corpuscle	Dermis, joint capsules	Stretch
Tactile corpuscle	Messiner's corpuscle	Papillary dermis, especially in the fingertips and lips	Light touch, vibrations below 50 Hz
Lamellated corpuscle	Pacinian corpuscle	Deep dermis, subcutaneous tissue	Deep pressure, high-frequency vibration (around 250 Hz)
Hair folicle plexus	[No corresponding eponymous name]	Wrapped around hair follicles in the dermis	Movement of hair
Muscle spindle	[No corresponding eponymous name]	In line with skeletal muscle fibers	Muscle contraction and stretch
Tendon stretch organ	Golgi tendon organ	In line with tendons	Stretch of tendons

VISION

Vision is the special sense of sight that is based on the transduction of light stimuli received through the eyes. The eyes are located within either orbit in the skull. The bony orbits surround the eyeballs, protecting them and anchoring the soft tissues of the eye (Figure 1). The eyelids, with lashes at their leading edges, help to protect the eye from abrasions by blocking particles that may land on the surface of the eye. The inner surface of each lid is a thin membrane known as the **palpebral conjunctiva**. The conjunctiva extends over the white areas of the eye (the sclera), connecting the eyelids to the eyeball. Tears are produced by the **lacrimal gland**, located beneath the

lateral edges of the nose. Tears produced by this gland flow through the **lacrimal duct** to the medial corner of the eye, where the tears flow over the conjunctiva, washing away foreign particles.

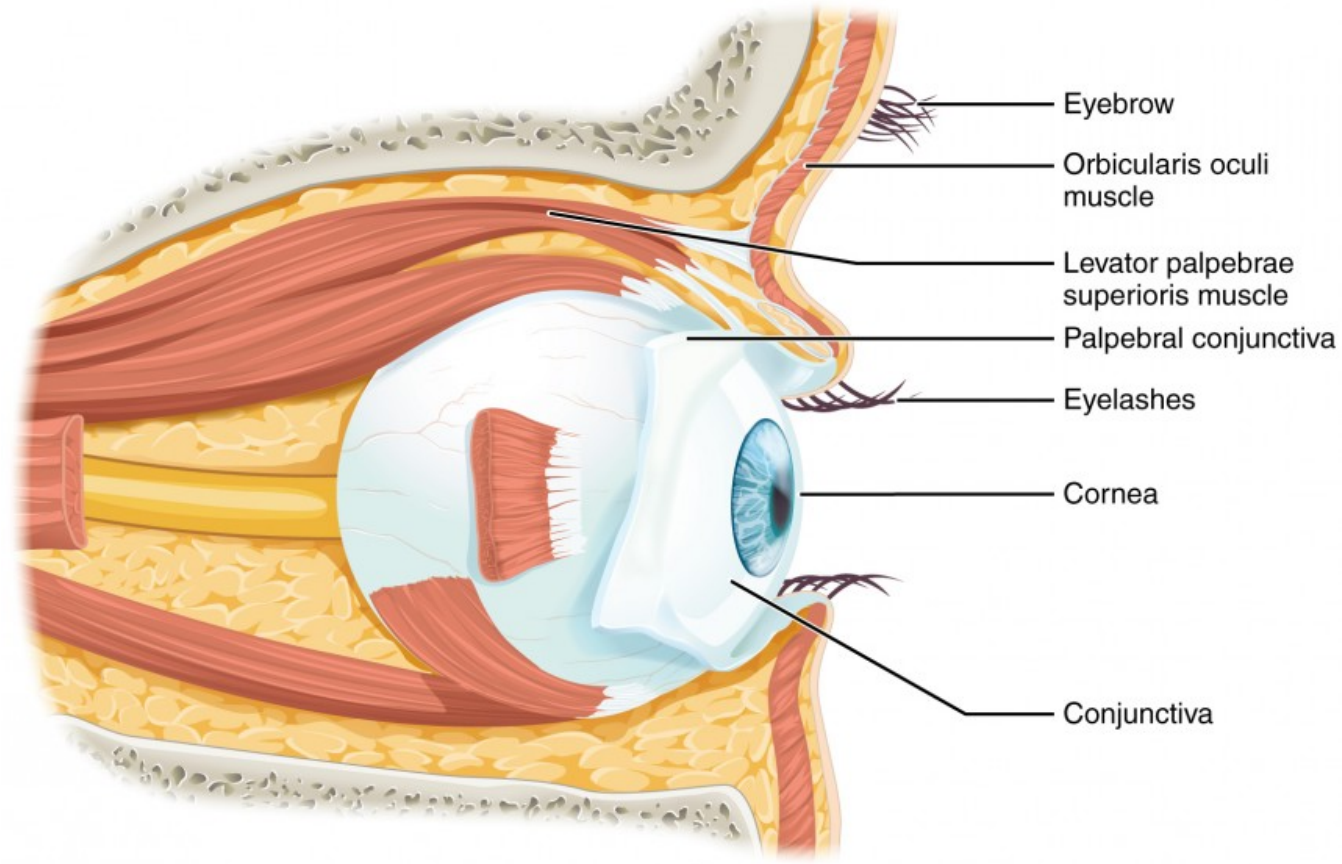


Figure 1. The Eye in the Orbit *The eye is located within the orbit and surrounded by soft tissues that protect and support its function. The orbit is surrounded by cranial bones of the skull.*

Movement of the eye within the orbit is accomplished by the contraction of six **extraocular muscles** that originate from the bones of the orbit and insert into the surface of the eyeball (Figure 2). Four of the muscles are arranged at the cardinal points around the eye and are named for those locations. They are the **superior rectus**, **medial rectus**, **inferior rectus**, and **lateral rectus**. When each of these muscles contract, the eye to moves toward the contracting muscle. For example, when the superior rectus contracts, the eye rotates to look up.

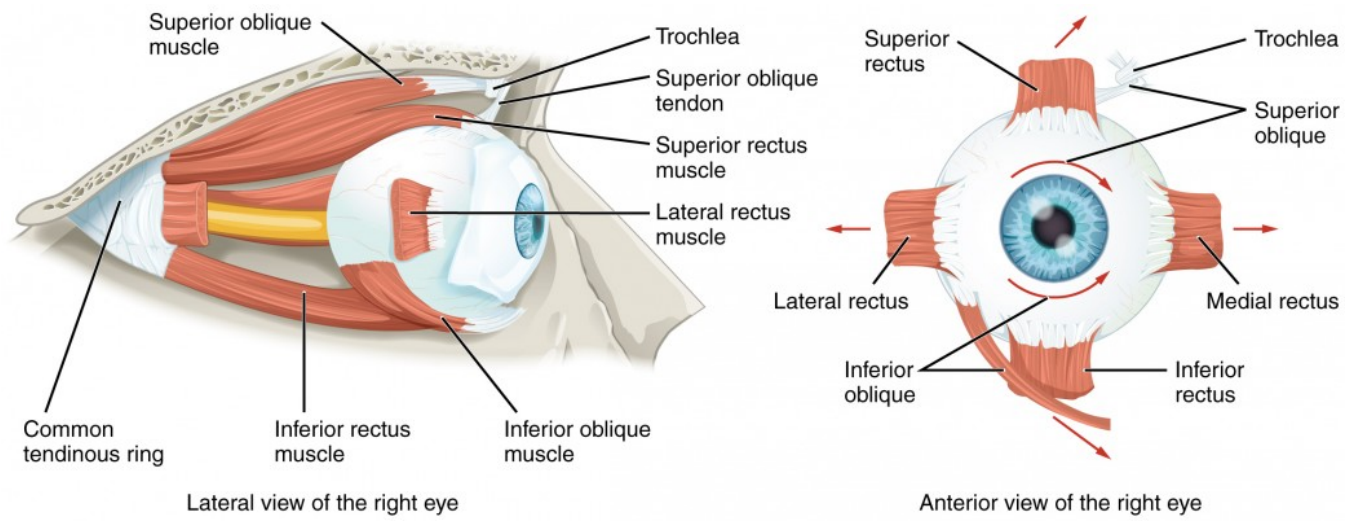


Figure 2. Extraocular Muscles *The extraocular muscles move the eye within the orbit.*

The **superior oblique** originates at the posterior orbit, near the origin of the four rectus muscles. However, the tendon of the oblique muscles threads through a pulley-like piece of cartilage known as the **trochlea**. The tendon inserts obliquely into the superior surface of the eye. The angle of the tendon through the trochlea means that contraction of the superior oblique rotates the eye medially.

The **inferior oblique** muscle originates from the floor of the orbit and inserts into the inferolateral surface of the eye. When it contracts, it laterally rotates the eye, in opposition to the superior oblique. Rotation of the eye by the two oblique muscles is necessary because the eye is not perfectly aligned on the sagittal plane.

When the eye looks up or down, the eye must also rotate slightly to compensate for the superior rectus pulling at approximately a 20-degree angle, rather than straight up. The same is true for the inferior rectus, which is compensated by contraction of the inferior oblique. A seventh muscle in the orbit is the **levator palpebrae superioris**, which is responsible for elevating and retracting the upper eyelid, a movement that usually occurs in concert with elevation of the eye by the superior rectus (see Figure 1). The extraocular muscles are innervated by three cranial nerves. The lateral rectus, which causes abduction of the eye, is innervated by the abducens nerve. The superior oblique is innervated by the trochlear nerve. All of the other muscles are innervated by the oculomotor nerve, as is the levator palpebrae superioris. The motor nuclei of these cranial nerves connect to the brain stem, which coordinates eye movements.

The eye itself is a hollow sphere composed of three layers of tissue. The outermost layer is the **fibrous tunic**, which includes the white **sclera** and clear **cornea**. The sclera accounts for five sixths of the surface of the eye, most of which is not visible, though humans are unique compared with many other species in having so much of the "white of the eye" visible (Figure 3). The transparent cornea covers the anterior tip of the eye and allows light to enter the eye.

The middle layer of the eye is the **vascular tunic**, which is mostly composed of the choroid, ciliary body, and iris. The **choroid** is a layer of highly vascularized connective tissue that provides a blood supply to the eyeball. The choroid is posterior to the **ciliary body**, a muscular structure that is attached to the **lens** by **zonule fibers**. These two structures bend the lens, allowing it to focus light on the back of the eye. Overlaying the ciliary body, and visible in the anterior eye, is the **iris**—the colored part of the eye. The iris is a smooth muscle that opens or closes the **pupil**, which is the hole at the center of the eye that allows light to enter. The iris constricts the pupil in response to bright light and dilates the pupil in response to dim light.

The innermost layer of the eye is the **neural tunic**, or **retina**, which contains the nervous tissue responsible for photoreception. The eye is also divided into two cavities: the anterior cavity and the posterior cavity. The anterior cavity is the space between the cornea and lens, including the iris and ciliary body. It is filled with a watery fluid called the **aqueous humor**. The posterior cavity is the space behind the lens that extends to the posterior side of the interior eyeball, where the retina is located. The posterior cavity is filled with a more viscous fluid called the **vitreous humor**. The retina is composed of several layers and contains specialized cells for the initial processing of visual stimuli. The photoreceptors (rods and cones) change their membrane potential when stimulated by light energy. The change in membrane potential alters the amount of neurotransmitter that the

photoreceptor cells release onto **bipolar cells** in the **outer synaptic layer**. It is the bipolar cell in the retina that connects a photoreceptor to a **retinal ganglion cell (RGC)** in the **inner synaptic layer**. There, **amacrine cells** additionally contribute to retinal processing before an action potential is produced by the RGC. The axons of RGCs, which lie at the innermost layer of the retina, collect at the **optic disc** and leave the eye as the **optic nerve** (see Figure 3). Because these axons pass through the retina, there are no photoreceptors at the very back of the eye, where the optic nerve begins. This creates a "blind spot" in the retina, and a corresponding blind spot in our visual field.

Note that the photoreceptors in the retina (rods and cones) are located behind the axons, RGCs, bipolar cells, and retinal blood vessels. A significant amount of light is absorbed by these structures before the light reaches the photoreceptor cells. However, at the exact center of the retina is a small area known as the **fovea**. At the fovea, the retina lacks the supporting cells and blood vessels, and only contains photoreceptors. Therefore, **visual acuity**, or the sharpness of vision, is greatest at the fovea. This is because the fovea is where the least amount of incoming light is absorbed by other retinal structures (see Figure 3).

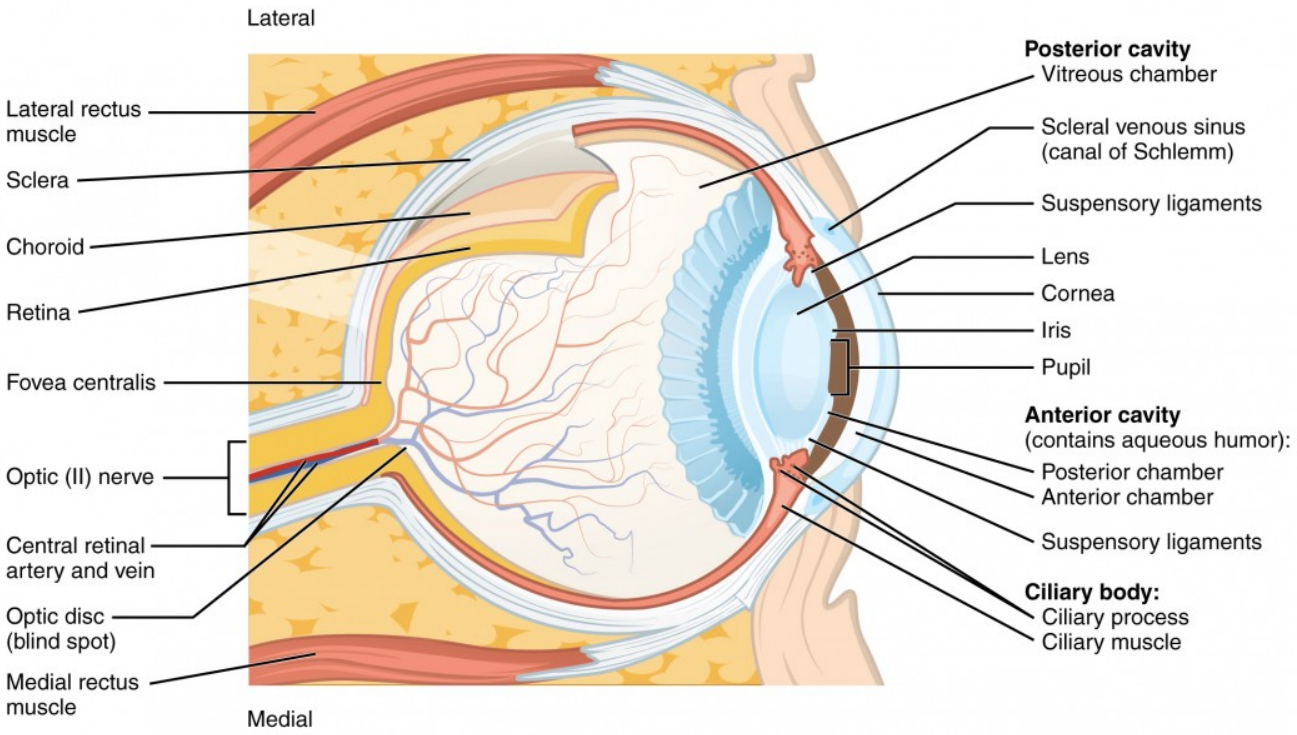


Figure 3. Structure of the Eye *The sphere of the eye can be divided into anterior and posterior chambers. The wall of the eye is composed of three layers: the fibrous tunic, vascular tunic, and neural tunic. Within the neural tunic is the retina, with three layers of cells and two synaptic layers in between. The center of the retina has a small indentation known as the fovea.*

As one moves in either direction from this central point of the retina, visual acuity drops significantly. In addition, each photoreceptor cell of the fovea is connected to a single RGC. Therefore, this RGC does not have to integrate inputs from multiple photoreceptors, which reduces the accuracy of visual transduction. Toward the edges of the retina, several photoreceptors converge on RGCs (through the bipolar cells) up to a ratio of 50 to 1.

The difference in visual acuity between the fovea and peripheral retina is easily evidenced by looking directly at a word in the middle of this paragraph. The visual stimulus in the middle of the field of view falls on the fovea and is in the sharpest focus. Without moving your eyes off that word, notice that words at the beginning or end of the paragraph are not in focus. The images in your peripheral vision are focused by the peripheral retina, and have vague, blurry edges and words that are not as clearly identified. As a result, a large part of the neural function of the eyes is concerned with moving the eyes and head so that important visual stimuli are centered on the fovea. Light falling on the retina causes chemical changes to pigment molecules in the photoreceptors, ultimately leading to a change in the activity of the RGCs.

Photoreceptor cells have two parts, the **inner segment** and the **outer segment** (Figure 4). The inner segment contains the nucleus and other common organelles of a cell, whereas the outer segment is a specialized region in

which photoreception takes place. There are two types of photoreceptors—rods and cones—which differ in the shape of their outer segment. The rod-shaped outer segments of the **rod photoreceptor** contain a stack of membrane-bound discs that contain the photosensitive pigment **rhodopsin**. The cone-shaped outer segments of the **cone photoreceptor** contain their photosensitive pigments in infoldings of the cell membrane. There are three cone photopigments, called **opsins**, which are each sensitive to a particular wavelength of light. The wavelength of visible light determines its color. The pigments in human eyes are specialized in perceiving three different primary colors: red, green, and blue.

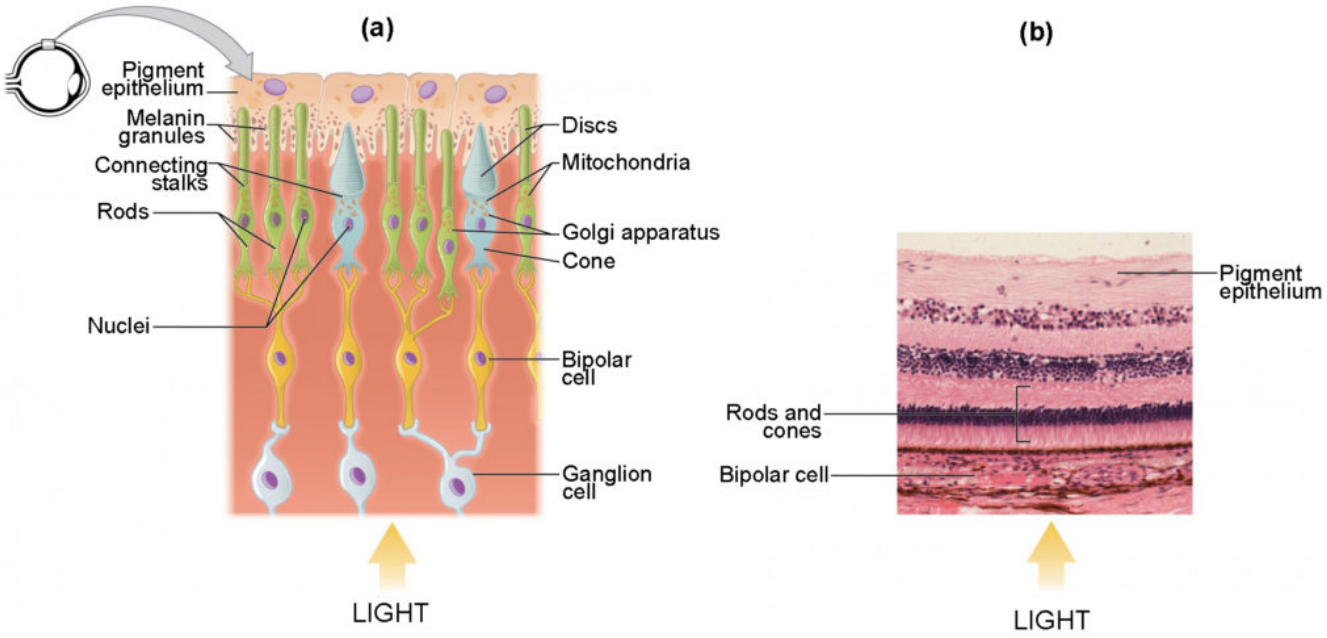


Figure 4. Photoreceptor *(a) All photoreceptors have inner segments containing the nucleus and other important organelles and outer segments with membrane arrays containing the photosensitive opsin molecules. Rod outer segments are long columnar shapes with stacks of membrane-bound discs that contain the rhodopsin pigment. Cone outer segments are short, tapered shapes with folds of membrane in place of the discs in the rods. (b) Tissue of the retina shows a dense layer of nuclei of the rods and cones. LM × 800. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)*

At the molecular level, visual stimuli cause changes in the photopigment molecule that lead to changes in membrane potential of the photoreceptor cell. A single unit of light is called a **photon**, which is described in physics as a packet of energy with properties of both a particle and a wave. The energy of a photon is represented by its wavelength, with each wavelength of visible light corresponding to a particular color. Visible light is electromagnetic radiation with a wavelength between 380 and 720 nm. Longer wavelengths of less than 380 nm fall into the infrared range, whereas shorter wavelengths of more than 720 nm fall into the ultraviolet range. Light with a wavelength of 380 nm is blue whereas light with a wavelength of 720 nm is dark red. All other colors fall between red and blue at various points along the wavelength scale.

Opsin pigments are actually transmembrane proteins that contain a cofactor known as **retinal**. Retinal is a hydrocarbon molecule related to vitamin A. When a photon hits retinal, the long hydrocarbon chain of the molecule is biochemically altered. Specifically, photons cause some of the double-bonded carbons within the chain to switch from a *cis* to a *trans* conformation. This process is called **photoisomerization**. Before interacting with a photon, retinal's flexible double-bonded carbons are in the *cis* conformation. This molecule is referred to as 11-*cis*-retinal. A photon interacting with the molecule causes the flexible double-bonded carbons to change to the *trans*– conformation, forming all-*trans*-retinal, which has a straight hydrocarbon chain (Figure 5).

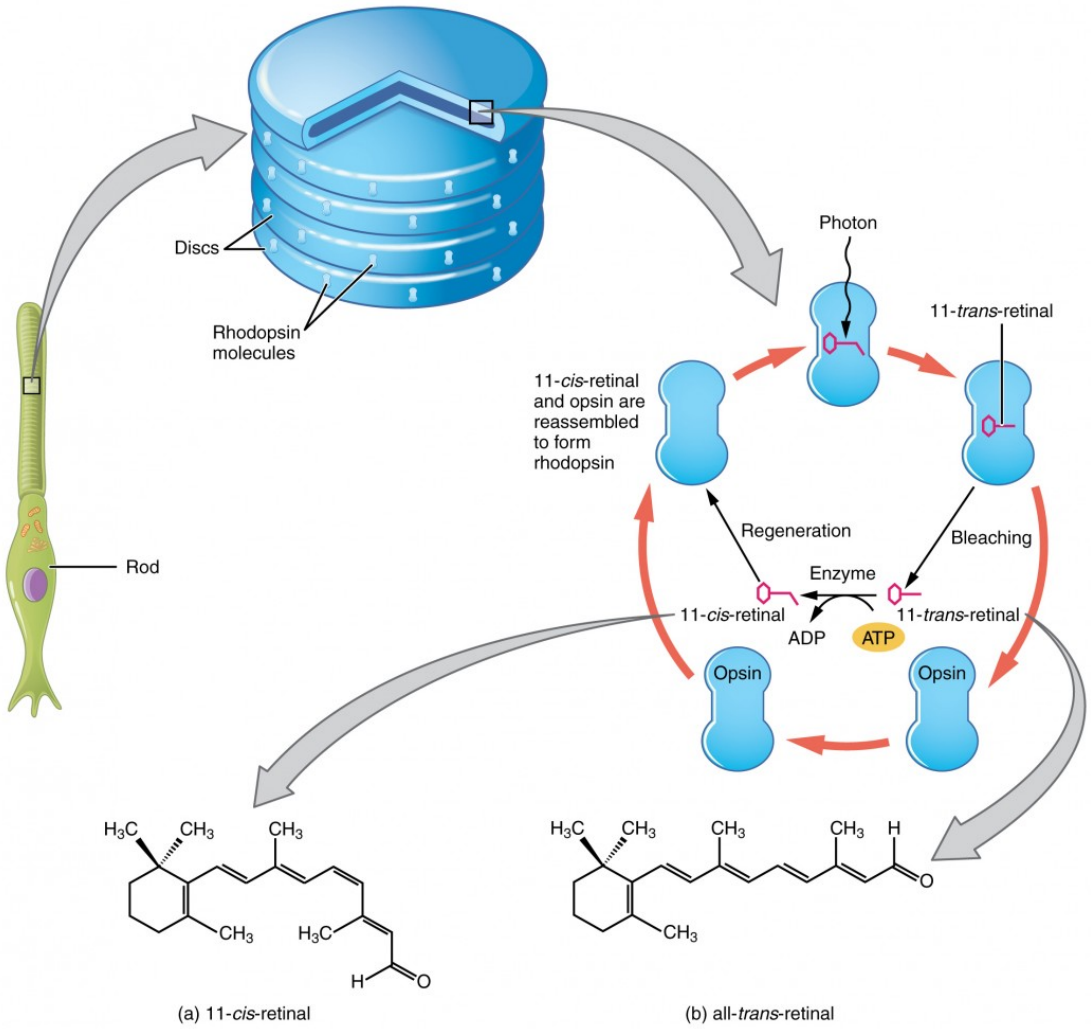


Figure 5. Retinal Isomers *The retinal molecule has two isomers, (a) one before a photon interacts with it and (b) one that is altered through photoisomerization.*

The shape change of retinal in the photoreceptors initiates visual transduction in the retina. Activation of retinal and the opsin proteins result in activation of a G protein. The G protein changes the membrane potential of the photoreceptor cell, which then releases less neurotransmitter into the outer synaptic layer of the retina. Until the retinal molecule is changed back to the 11-*cis*-retinal shape, the opsin cannot respond to light energy, which is called bleaching. When a large group of photopigments is bleached, the retina will send information as if opposing visual information is being perceived. After a bright flash of light, afterimages are usually seen in negative. The photoisomerization is reversed by a series of enzymatic changes so that the retinal responds to more light energy.

The opsins are sensitive to limited wavelengths of light. Rhodopsin, the photopigment in rods, is most sensitive to light at a wavelength of 498 nm. The three color opsins have peak sensitivities of 564 nm, 534 nm, and 420 nm corresponding roughly to the primary colors of red, green, and blue (Figure 6). The absorbance of rhodopsin in the rods is much more sensitive than in the cone opsins; specifically, rods are sensitive to vision in low light conditions, and cones are sensitive to brighter conditions.

In normal sunlight, rhodopsin will be constantly bleached while the cones are active. In a darkened room, there is not enough light to activate cone opsins, and vision is entirely dependent on rods. Rods are so sensitive to light that a single photon can result in an action potential from a rod's corresponding RGC.

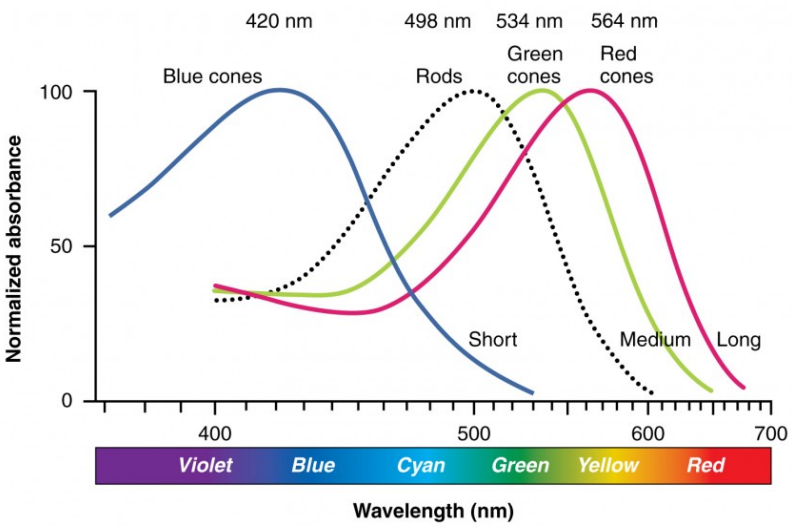


Figure 6. Comparison of Color Sensitivity of Photopigments *Comparing the peak sensitivity and absorbance spectra of the four photopigments suggests that they are most sensitive to particular wavelengths.*

The three types of cone opsins, being sensitive to different wavelengths of light, provide us with color vision. By comparing the activity of the three different cones, the brain can extract color information from visual stimuli. For example, a bright blue light that has a wavelength of approximately 450 nm would activate the "red" cones minimally, the "green" cones marginally, and the "blue" cones predominantly. The relative activation of the three different cones is calculated by the brain, which perceives the color as blue. However, cones cannot react to low-intensity light, and rods do not sense the color of light. Therefore, our low-light vision is—in essence—in grayscale. In other words, in a dark room, everything appears as a shade of gray. If you think that you can see colors in the dark, it is most likely because your brain knows what color something is and is relying on that memory.

Watch this video to learn more about a transverse section through the brain that depicts the visual pathway from the eye to the occipital cortex.

Watch this video online: https://youtu.be/wbVdlIc5DPE

The first half of the pathway is the projection from the RGCs through the optic nerve to the lateral geniculate nucleus in the thalamus on either side. This first fiber in the pathway synapses on a thalamic cell that then projects to the visual cortex in the occipital lobe where "seeing," or visual perception, takes place. This video gives an abbreviated overview of the visual system by concentrating on the pathway from the eyes to the occipital lobe. The video makes the statement (at 0:45) that "specialized cells in the retina called ganglion cells convert the light rays into electrical signals." What aspect of retinal processing is simplified by that statement? Explain your answer.

Sensory Nerves

Once any sensory cell transduces a stimulus into a nerve impulse, that impulse has to travel along axons to reach the CNS. In many of the special senses, the axons leaving the sensory receptors have a **topographical** arrangement, meaning that the location of the sensory receptor relates to the location of the axon in the nerve. For example, in the retina, axons from RGCs in the fovea are located at the center of the optic nerve, where they are surrounded by axons from the more peripheral RGCs.

Spinal Nerves

Generally, spinal nerves contain afferent axons from sensory receptors in the periphery, such as from the skin, mixed with efferent axons travelling to the muscles or other effector organs. As the spinal nerve nears the spinal

cord, it splits into dorsal and ventral roots. The dorsal root contains only the axons of sensory neurons, whereas the ventral roots contain only the axons of the motor neurons. Some of the branches will synapse with local neurons in the dorsal root ganglion, posterior (dorsal) horn, or even the anterior (ventral) horn, at the level of the spinal cord where they enter. Other branches will travel a short distance up or down the spine to interact with neurons at other levels of the spinal cord. A branch may also turn into the posterior (dorsal) column of the white matter to connect with the brain. For the sake of convenience, we will use the terms ventral and dorsal in reference to structures within the spinal cord that are part of these pathways. This will help to underscore the relationships between the different components. Typically, spinal nerve systems that connect to the brain are **contralateral**, in that the right side of the body is connected to the left side of the brain and the left side of the body to the right side of the brain.

Cranial Nerves

Cranial nerves convey specific sensory information from the head and neck directly to the brain. For sensations below the neck, the right side of the body is connected to the left side of the brain and the left side of the body to the right side of the brain. Whereas spinal information is contralateral, cranial nerve systems are mostly **ipsilateral**, meaning that a cranial nerve on the right side of the head is connected to the right side of the brain. Some cranial nerves contain only sensory axons, such as the olfactory, optic, and vestibulocochlear nerves. Other cranial nerves contain both sensory and motor axons, including the trigeminal, facial, glossopharyngeal, and vagus nerves (however, the vagus nerve is not associated with the somatic nervous system). The general senses of somatosensation for the face travel through the trigeminal system.

CENTRAL PROCESSING

Learning Objectives

- Describe the pathways that sensory systems follow into the central nervous system
- Differentiate between the two major ascending pathways in the spinal cord
- Describe the pathway of somatosensory input from the face and compare it to the ascending pathways in the spinal cord
- Explain topographical representations of sensory information in at least two systems
- Describe two pathways of visual processing and the functions associated with each

Sensory Pathways

Specific regions of the CNS coordinate different somatic processes using sensory inputs and motor outputs of peripheral nerves. A simple case is a reflex caused by a synapse between a dorsal sensory neuron axon and a motor neuron in the ventral horn. More complex arrangements are possible to integrate peripheral sensory information with higher processes. The important regions of the CNS that play a role in somatic processes can be separated into the spinal cord brain stem, diencephalon, cerebral cortex, and subcortical structures.

Spinal Cord and Brain Stem

A sensory pathway that carries peripheral sensations to the brain is referred to as an **ascending pathway**, or ascending tract. Each of the various sensory modalities follows a specific pathway through the CNS. Tactile and other somatosensory stimuli activate receptors in the skin, muscles, tendons, and joints throughout the entire body. However, the somatosensory pathways are divided into two separate systems on the basis of the location of the receptor neurons.

Somatosensory stimuli from below the neck pass along the sensory pathways of the spinal cord, whereas somatosensory stimuli from the head and neck travel through the cranial nerves—specifically, the trigeminal system. The **dorsal column system** (sometimes referred to as the dorsal column–medial lemniscus) and the **spinothalamic tract** are two major pathways that bring sensory information to the brain (Figure 1). The sensory pathways in each of these systems are composed of three successive neurons.

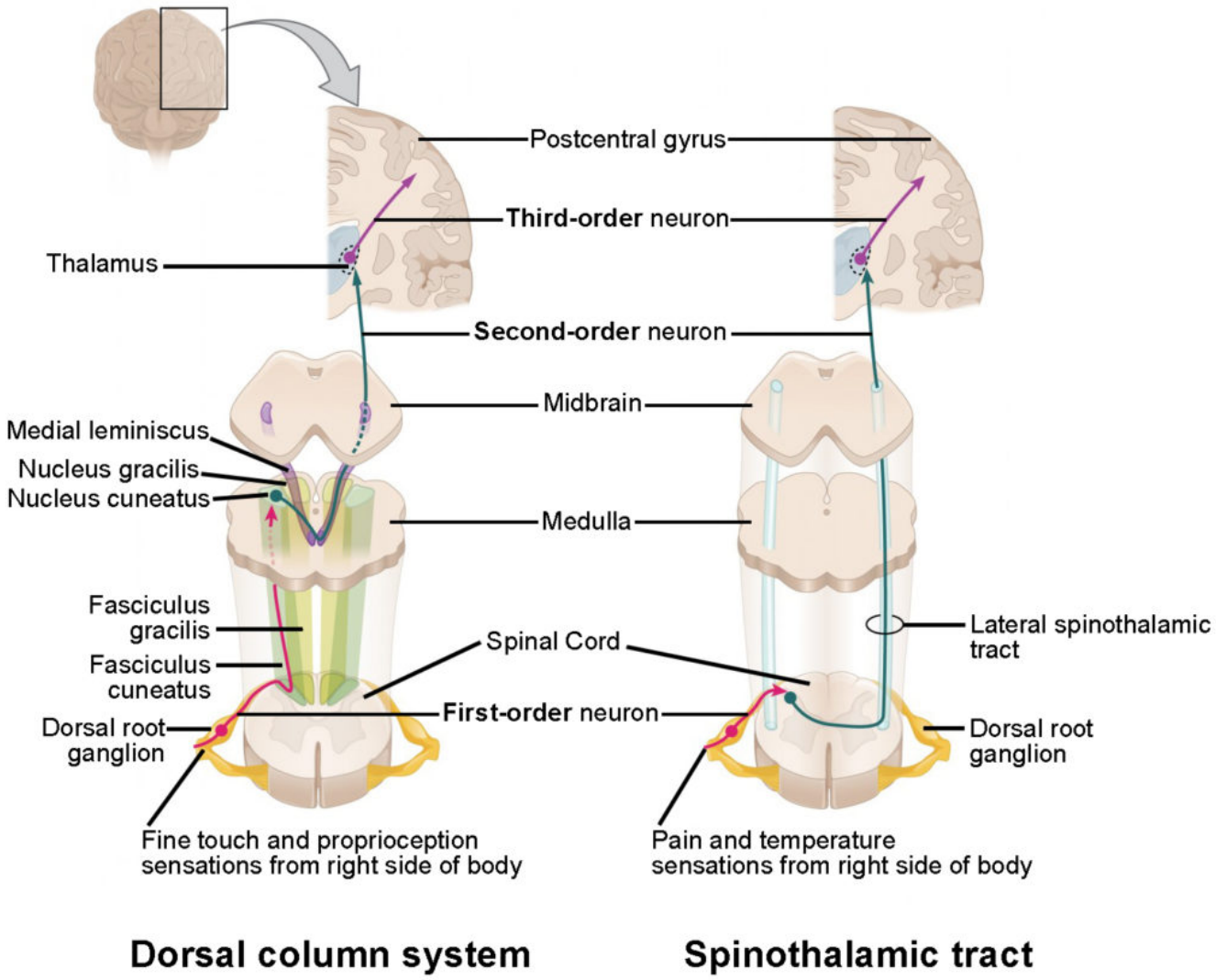


Figure 1. Ascending Sensory Pathways of the Spinal Cord. *The dorsal column system and spinothalamic tract are the major ascending pathways that connect the periphery with the brain.*

Dorsal Column System

The dorsal column system begins with the axon of a dorsal root ganglion neuron entering the dorsal root and joining the dorsal column white matter in the spinal cord. As axons of this pathway enter the dorsal column, they

take on a positional arrangement so that axons from lower levels of the body position themselves medially, whereas axons from upper levels of the body position themselves laterally.

The dorsal column is separated into two component tracts, the **fasciculus gracilis** that contains axons from the legs and lower body, and the **fasciculus cuneatus** that contains axons from the upper body and arms. The axons in the dorsal column terminate in the nuclei of the medulla, where each synapses with the second neuron in their respective pathway. The **nucleus gracilis** is the target of fibers in the fasciculus gracilis, whereas the **nucleus cuneatus** is the target of fibers in the fasciculus cuneatus.

The second neuron in the system projects from one of the two nuclei and then **decussates**, or crosses the midline of the medulla. These axons then continue to ascend the brain stem as a bundle called the **medial lemniscus**. These axons terminate in the thalamus, where each synapses with the third neuron in their respective pathway.

The third neuron in the system projects its axons to the postcentral gyrus of the cerebral cortex, where somatosensory stimuli are initially processed and the conscious perception of the stimulus occurs.

Spinothalamic Tract

The spinothalamic tract also begins with neurons in a dorsal root ganglion. These neurons extend their axons to the dorsal horn, where they synapse with the second neuron in their respective pathway. The name “spinothalamic” comes from this second neuron, which has its cell body in the spinal cord gray matter and connects to the thalamus. Axons from these second neurons then decussate within the spinal cord and ascend to the brain and enter the thalamus, where each synapses with the third neuron in its respective pathway.

The neurons in the thalamus then project their axons to the spinothalamic tract, which synapses in the postcentral gyrus of the cerebral cortex. These two systems are similar in that they both begin with dorsal root ganglion cells, as with most general sensory information.

The dorsal column system is primarily responsible for touch sensations and proprioception, whereas the spinothalamic tract pathway is primarily responsible for pain and temperature sensations. Another similarity is that the second neurons in both of these pathways are contralateral, because they project across the midline to the other side of the brain or spinal cord. In the dorsal column system, this decussation takes place in the brain stem; in the spinothalamic pathway, it takes place in the spinal cord at the same spinal cord level at which the information entered. The third neurons in the two pathways are essentially the same. In both, the second neuron synapses in the thalamus, and the thalamic neuron projects to the somatosensory cortex.

Somatosensory Information

The trigeminal pathway carries somatosensory information from the face, head, mouth, and nasal cavity. As with the previously discussed nerve tracts, the sensory pathways of the trigeminal pathway each involve three successive neurons.

First, axons from the trigeminal ganglion enter the brain stem at the level of the pons. These axons project to one of three locations. The **spinal trigeminal nucleus** of the medulla receives information similar to that carried by spinothalamic tract, such as pain and temperature sensations. Other axons go to either the **chief sensory nucleus** in the pons or the **mesencephalic nuclei** in the midbrain. These nuclei receive information like that carried by the dorsal column system, such as touch, pressure, vibration, and proprioception.

Axons from the second neuron decussate and ascend to the thalamus along the trigeminothalamic tract. In the thalamus, each axon synapses with the third neuron in its respective pathway.

Axons from the third neuron then project from the thalamus to the primary somatosensory cortex of the cerebrum. The sensory pathway for gustation travels along the facial and glossopharyngeal cranial nerves, which synapse with neurons of the **solitary nucleus** in the brain stem.

Axons from the solitary nucleus then project to the **ventral posterior nucleus** of the thalamus.

Finally, axons from the ventral posterior nucleus project to the gustatory cortex of the cerebral cortex, where taste is processed and consciously perceived.

The sensory pathway for audition travels along the vestibulocochlear nerve, which synapses with neurons in the cochlear nuclei of the superior medulla. Within the brain stem, input from either ear is combined to extract location information from the auditory stimuli. Whereas the initial auditory stimuli received at the cochlea strictly represent the frequency—or pitch—of the stimuli, the locations of sounds can be determined by comparing information arriving at both ears.

Sound localization is a feature of central processing in the auditory nuclei of the brain stem. Sound localization is achieved by the brain calculating the **interaural time difference** and the **interaural intensity difference**. A sound originating from a specific location will arrive at each ear at different times, unless the sound is directly in front of the listener. If the sound source is slightly to the left of the listener, the sound will arrive at the left ear microseconds before it arrives at the right ear (Figure 2). This time difference is an example of an interaural time difference. Also, the sound will be slightly louder in the left ear than in the right ear because some of the sound waves reaching the opposite ear are blocked by the head. This is an example of an interaural intensity difference.

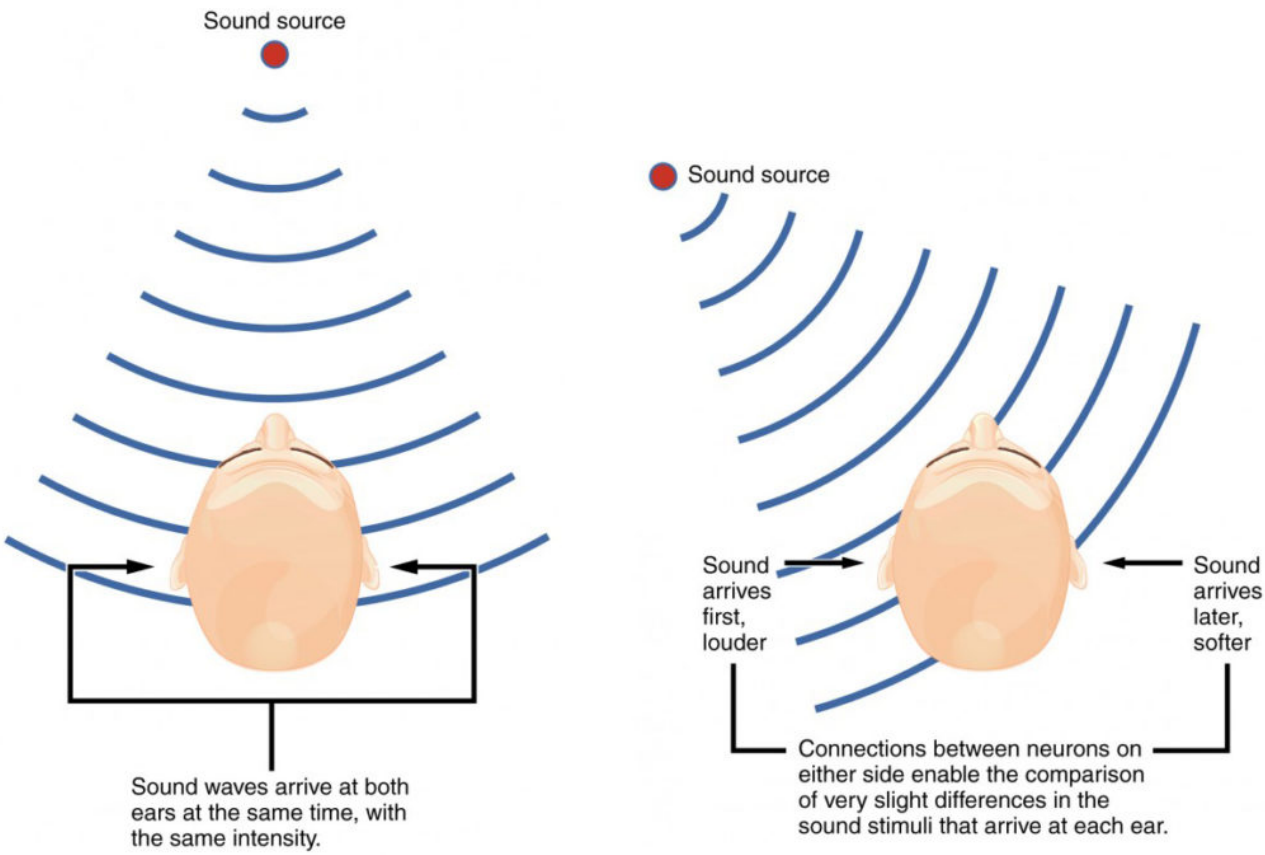


Figure 2. Auditory Brain Stem Mechanisms of Sound Localization. *Localizing sound in the horizontal plane is achieved by processing in the medullary nuclei of the auditory system. Connections between neurons on either side are able to compare very slight differences in sound stimuli that arrive at either ear and represent interaural time and intensity differences.*

Auditory processing continues on to a nucleus in the midbrain called the **inferior colliculus**. Axons from the inferior colliculus project to two locations, the thalamus and the **superior colliculus**. The **medial geniculate nucleus** of the thalamus receives the auditory information and then projects that information to the auditory cortex in the temporal lobe of the cerebral cortex. The superior colliculus receives input from the visual and somatosensory systems, as well as the ears, to initiate stimulation of the muscles that turn the head and neck toward the auditory stimulus.

Balance is coordinated through the vestibular system, the nerves of which are composed of axons from the vestibular ganglion that carries information from the utricle, saccule, and semicircular canals. The system contributes to controlling head and neck movements in response to vestibular signals. An important function of the vestibular system is coordinating eye and head movements to maintain visual attention. Most of the axons terminate in the **vestibular nuclei** of the medulla. Some axons project from the vestibular ganglion directly to the

cerebellum, with no intervening synapse in the vestibular nuclei. The cerebellum is primarily responsible for initiating movements on the basis of equilibrium information.

Neurons in the vestibular nuclei project their axons to targets in the brain stem. One target is the reticular formation, which influences respiratory and cardiovascular functions in relation to body movements. A second target of the axons of neurons in the vestibular nuclei is the spinal cord, which initiates the spinal reflexes involved with posture and balance. To assist the visual system, fibers of the vestibular nuclei project to the oculomotor, trochlear, and abducens nuclei to influence signals sent along the cranial nerves. These connections constitute the pathway of the **vestibulo-ocular reflex (VOR)**, which compensates for head and body movement by stabilizing images on the retina (Figure 3). Finally, the vestibular nuclei project to the thalamus to join the proprioceptive pathway of the dorsal column system, allowing conscious perception of equilibrium.

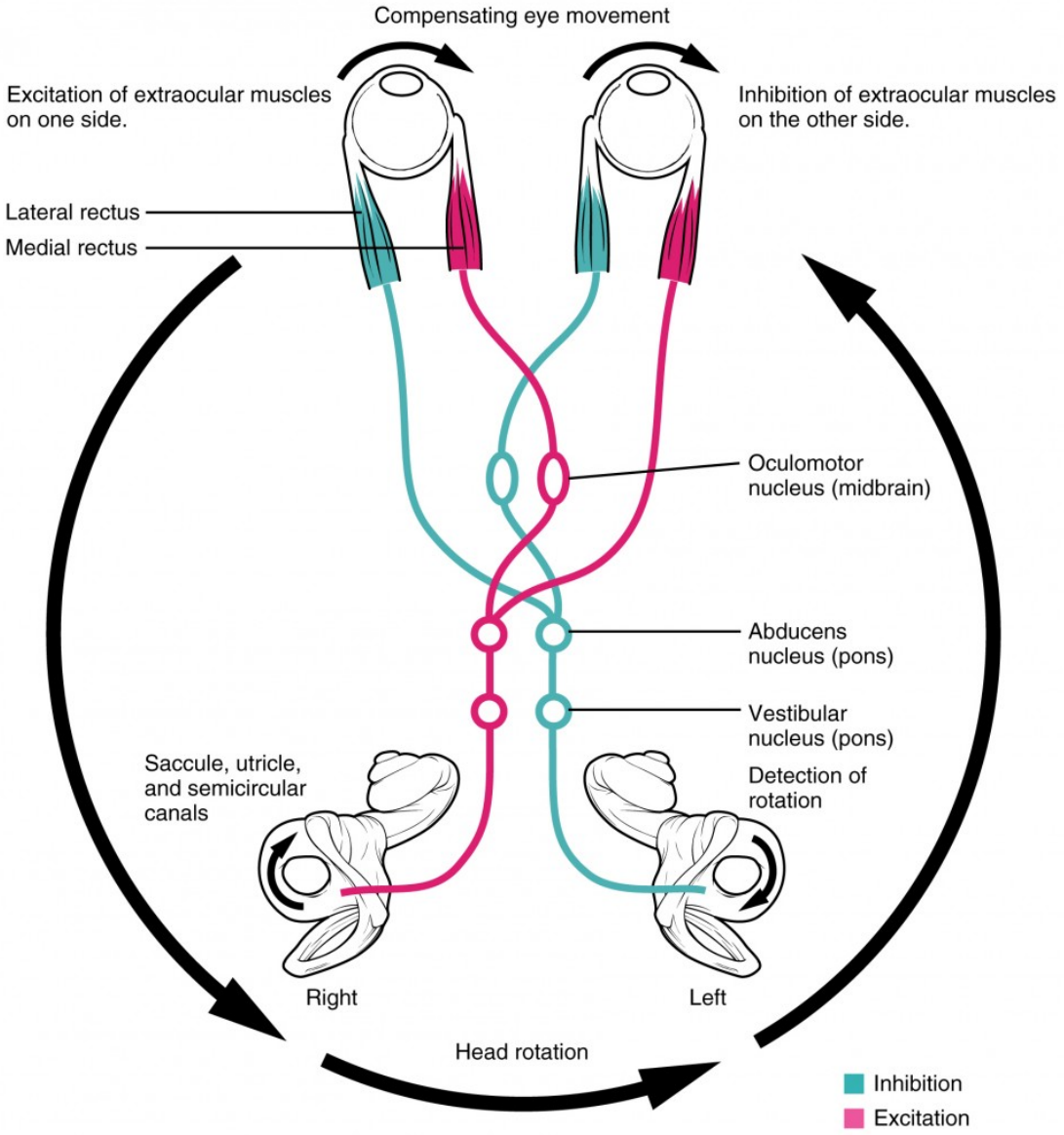


Figure 3. Vestibulo-ocular Reflex. *Connections between the vestibular system and the cranial nerves controlling eye movement keep the eyes centered on a visual stimulus, even though the head is moving. During head movement, the eye muscles move the eyes in the opposite direction as the head movement, keeping the visual stimulus centered in the field of view.*

The connections of the optic nerve are more complicated than those of other cranial nerves. Instead of the connections being between each eye and the brain, visual information is segregated between the left and right sides of the visual field. In addition, some of the information from one side of the visual field projects to the

opposite side of the brain. Within each eye, the axons projecting from the medial side of the retina decussate at the **optic chiasm**.

For example, the axons from the medial retina of the left eye cross over to the right side of the brain at the optic chiasm. However, within each eye, the axons projecting from the lateral side of the retina do not decussate. For example, the axons from the lateral retina of the right eye project back to the right side of the brain. Therefore the left field of view of each eye is processed on the right side of the brain, whereas the right field of view of each eye is processed on the left side of the brain (Figure 4).

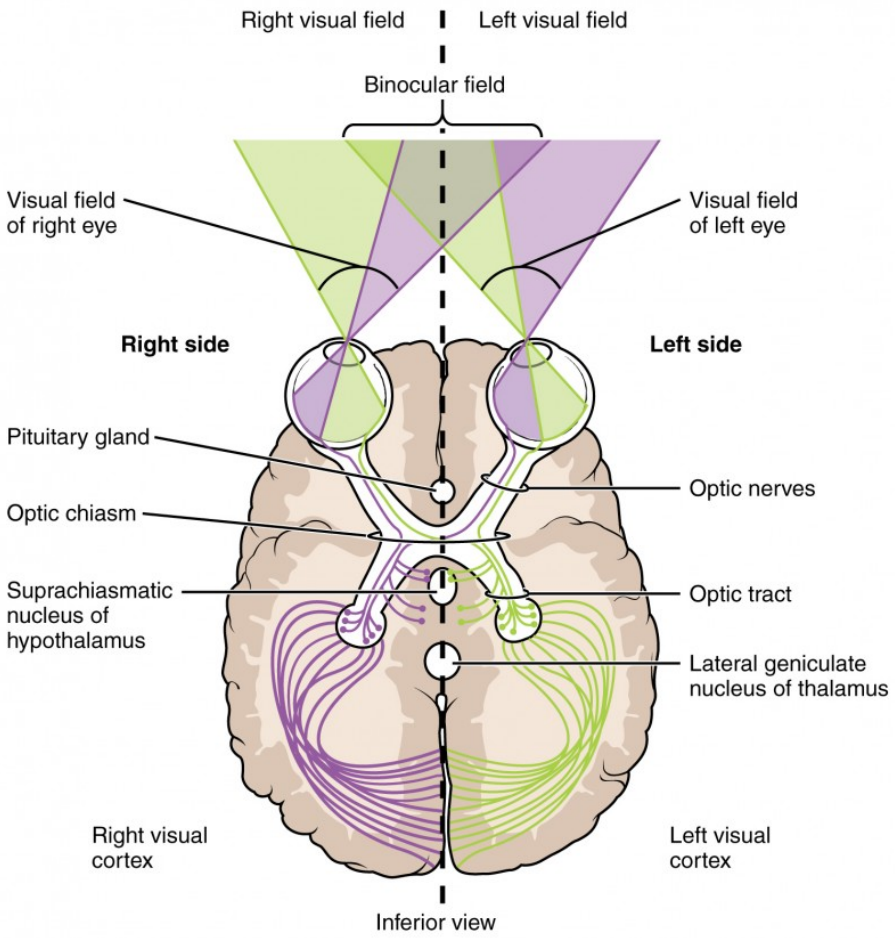


Figure 4. Segregation of Visual Field. *Information at the Optic Chiasm Contralateral visual field information from the lateral retina projects to the ipsilateral brain, whereas ipsilateral visual field information has to decussate at the optic chiasm to reach the opposite side of the brain.*

The loss of lateral peripheral vision, known as bilateral hemianopia, is a unique clinical presentation that relates to this anatomic arrangement. Bilateral hemianopia is different from "tunnel vision" because the superior and inferior peripheral fields are not lost. Visual field deficits can be disturbing for a patient, but in this case, the cause is not within the visual system itself. A growth of the pituitary gland presses against the optic chiasm and interferes with signal transmission. However, the axons projecting to the same side of the brain are unaffected. Therefore, the patient loses the outermost areas of their field of vision and cannot see objects to their right and left.

Extending from the optic chiasm, the axons of the visual system are referred to as the **optic tract** instead of the optic nerve. The optic tract has three major targets, two in the diencephalon and one in the midbrain. The connection between the eyes and diencephalon is demonstrated during development, in which the neural tissue of the retina differentiates from that of the diencephalon by the growth of the secondary vesicles. The connections of the retina into the CNS are a holdover from this developmental association. The majority of the connections of the optic tract are to the thalamus—specifically, the **lateral geniculate nucleus**. Axons from this nucleus then project to the visual cortex of the cerebrum, located in the occipital lobe.

Another target of the optic tract is the superior colliculus. In addition, a very small number of RGC axons project from the optic chiasm to the **suprachiasmatic nucleus** of the hypothalamus. These RGCs are photosensitive, in that they respond to the presence or absence of light. Unlike the photoreceptors, however, these photosensitive RGCs cannot be used to perceive images. By simply responding to the absence or presence of light, these RGCs can send information about day length. The perceived proportion of sunlight to darkness establishes the **circadian rhythm** of our bodies, allowing certain physiological events to occur at approximately the same time every day.

Diencephalon

The diencephalon is beneath the cerebrum and includes the thalamus and hypothalamus. In the somatic nervous system, the thalamus is an important relay for communication between the cerebrum and the rest of the nervous

system. The hypothalamus has both somatic and autonomic functions. In addition, the hypothalamus communicates with the limbic system, which controls emotions and memory functions.

Sensory input to the thalamus comes from most of the special senses and ascending somatosensory tracts. Each sensory system is relayed through a particular nucleus in the thalamus. The thalamus is a required transfer point for most sensory tracts that reach the cerebral cortex, where conscious sensory perception begins. The one exception to this rule is the olfactory system. The olfactory tract axons from the olfactory bulb project directly to the cerebral cortex, along with the limbic system and hypothalamus.

The thalamus is a collection of several nuclei that can be categorized into three anatomical groups. White matter running through the thalamus defines the three major regions of the thalamus, which are an anterior nucleus, a medial nucleus, and a lateral group of nuclei. The anterior nucleus serves as a relay between the hypothalamus and the emotion and memory-producing limbic system. The medial nuclei serve as a relay for information from the limbic system and basal ganglia to the cerebral cortex. This allows memory creation during learning, but also determines alertness. The special and somatic senses connect to the lateral nuclei, where their information is relayed to the appropriate sensory cortex of the cerebrum.

Cortical Processing

As described earlier, many of the sensory axons are positioned in the same way as their corresponding receptor cells in the body. This allows identification of the position of a stimulus on the basis of which receptor cells are sending information. The cerebral cortex also maintains this sensory topography in the particular areas of the cortex that correspond to the position of the receptor cells. The somatosensory cortex provides an example in which, in essence, the locations of the somatosensory receptors in the body are mapped onto the somatosensory cortex. This mapping is often depicted using a **sensory homunculus** (Figure 5). The term homunculus comes from the Latin word for “little man” and refers to a map of the human body that is laid across a portion of the cerebral cortex.

In the somatosensory cortex, the external genitals, feet, and lower legs are represented on the medial face of the gyrus within the longitudinal fissure. As the gyrus curves out of the fissure and along the surface of the parietal lobe, the body map continues through the thighs, hips, trunk, shoulders, arms, and hands. The head and face are just lateral to the fingers as the gyrus approaches the lateral sulcus.

The representation of the body in this topographical map is medial to lateral from the lower to upper body. It is a continuation of the topographical arrangement seen in the dorsal column system, where axons from the lower body are carried in the fasciculus gracilis, whereas axons from the upper body are carried in the fasciculus cuneatus. As the dorsal column system continues into the medial lemniscus, these relationships are maintained. Also, the head and neck axons running from the trigeminal nuclei to the thalamus run adjacent to the upper body fibers. The connections through the thalamus maintain topography such that the anatomic information is preserved.

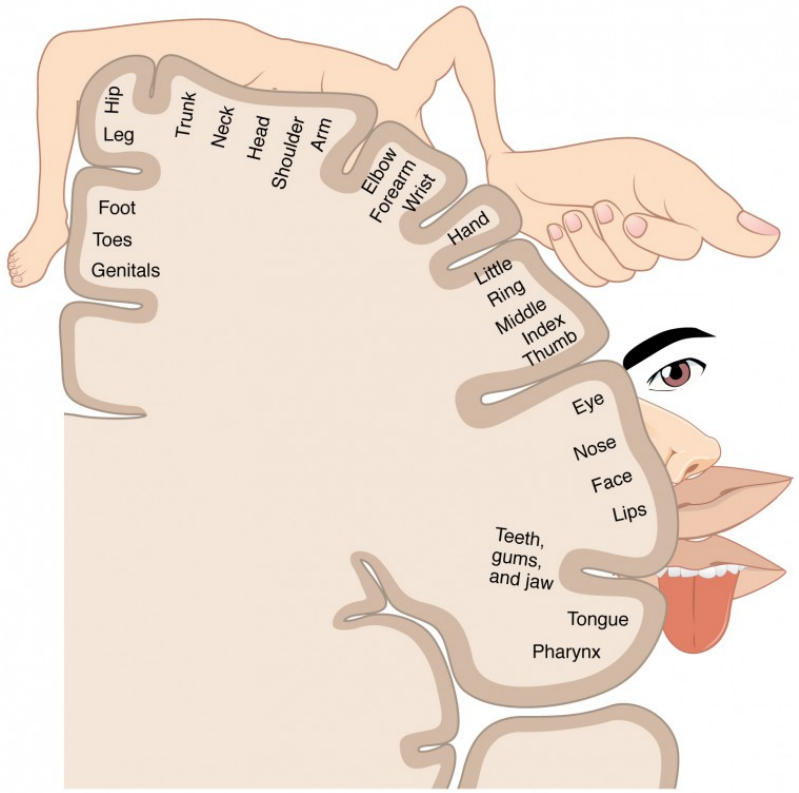


Figure 5. The Sensory Homunculus *A cartoon representation of the sensory homunculus arranged adjacent to the cortical region in which the processing takes place.*

Note that this correspondence does not result in a perfectly miniature scale version of the body, but rather exaggerates the more sensitive areas of the body, such as the fingers and lower face. Less sensitive areas of the body, such as the shoulders and back, are mapped to smaller areas on the cortex.

Likewise, the topographic relationship between the retina and the visual cortex is maintained throughout the visual pathway. The visual field is projected onto the two retinae, as described above, with sorting at the optic chiasm. The right peripheral visual field falls on the medial portion of the right retina and the lateral portion of the left retina. The right medial retina then projects across the midline through the optic chiasm. This results in the right visual field being processed in the left visual cortex. Likewise, the left visual field is processed in the right visual cortex (see Figure 4).

Though the chiasm is helping to sort right and left visual information, superior and inferior visual information is maintained topographically in the visual pathway. Light from the superior visual field falls on the inferior retina, and light from the inferior visual field falls on the superior retina. This topography is maintained such that the superior region of the visual cortex processes the inferior visual field and vice versa. Therefore, the visual field information is inverted and reversed as it enters the visual cortex—up is down, and left is right. However, the cortex processes the visual information such that the final conscious perception of the visual field is correct.

The topographic relationship is evident in that information from the foveal region of the retina is processed in the center of the primary visual cortex. Information from the peripheral regions of the retina are correspondingly processed toward the edges of the visual cortex. Similar to the exaggerations in the sensory homunculus of the somatosensory cortex, the foveal-processing area of the visual cortex is disproportionately larger than the areas processing peripheral vision. In an experiment performed in the 1960s, subjects wore prism glasses so that the visual field was inverted before reaching the eye. On the first day of the experiment, subjects would duck when walking up to a table, thinking it was suspended from the ceiling. However, after a few days of acclimation, the subjects behaved as if everything were represented correctly. Therefore, the visual cortex is somewhat flexible in adapting to the information it receives from our eyes (Figure 6).

The cortex has been described as having specific regions that are responsible for processing specific information; there is the visual cortex, somatosensory cortex, gustatory cortex, etc. However, our experience of these senses is not divided. Instead, we experience what can be referred to as a seamless percept. Our perceptions of the various sensory modalities—though distinct in their content—are integrated by the brain so that we experience the world as a continuous whole. In the cerebral cortex, sensory processing begins at the **primary sensory cortex**, then proceeds to an **association area**, and finally, into a **multimodal integration area**.

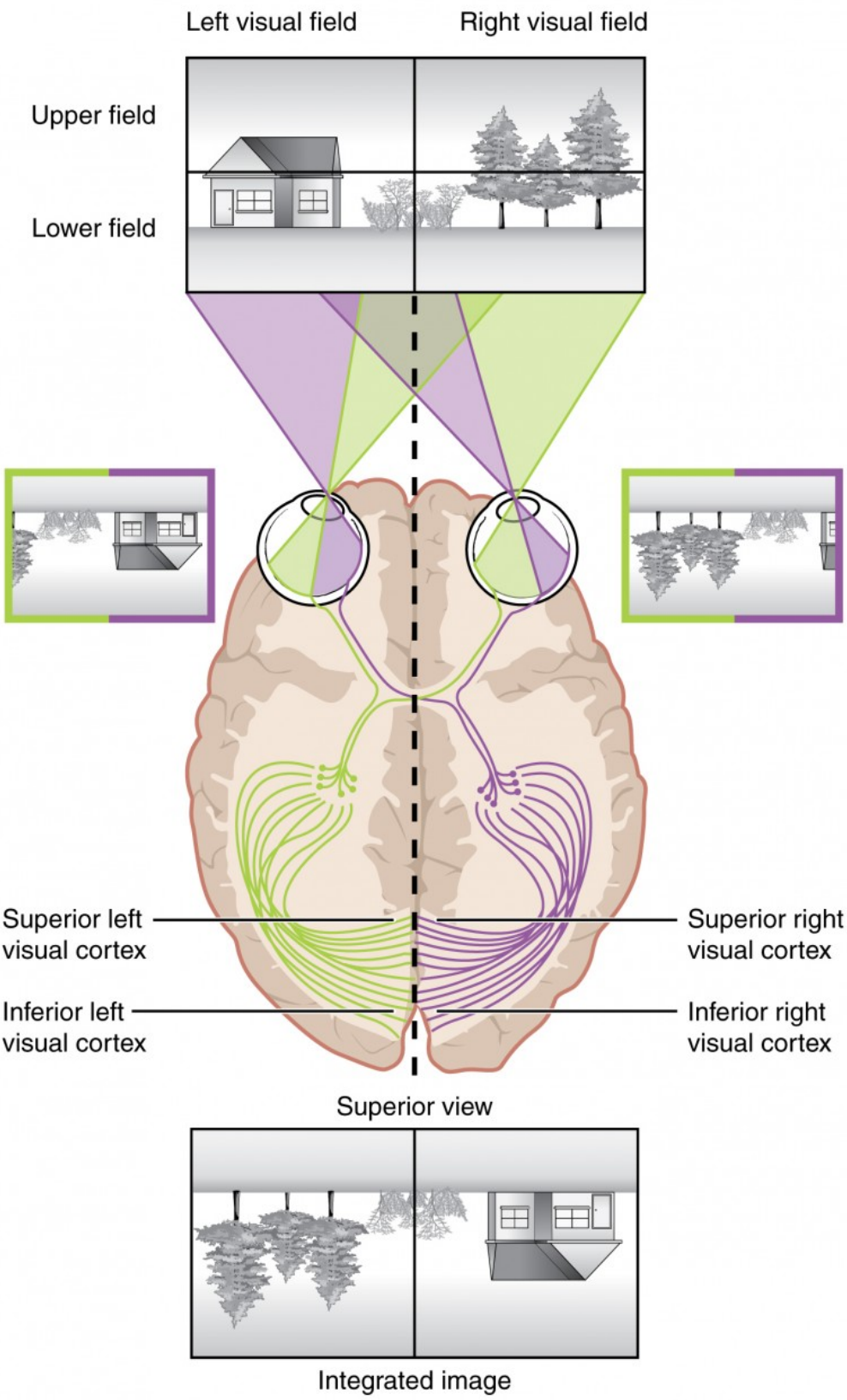


Figure 6. Topographic Mapping of the Retina onto the Visual Cortex. *The visual field projects onto the retina through the lenses and falls on the retinae as an inverted, reversed image. The topography of this image is maintained as the visual information travels through the visual pathway to the cortex.*

For example, the visual pathway projects from the retinae through the thalamus to the primary visual cortex in the occipital lobe. This area is primarily in the medial wall within the longitudinal fissure. Here, visual stimuli begin to be recognized as basic shapes. Edges of objects are recognized and built into more complex shapes. Also, inputs from both eyes are compared to extract depth information. Because of the overlapping field of view between the two eyes, the brain can begin to estimate the distance of stimuli based on **binocular depth cues**.

Watch this video to learn more about how the brain perceives 3-D motion.

Watch this video online: https://youtu.be/4VGVwOmn6bk

Similar to how retinal disparity offers 3-D moviegoers a way to extract 3-D information from the two-dimensional visual field projected onto the retina, the brain can extract information about movement in space by comparing what the two eyes see. If movement of a visual stimulus is leftward in one eye and rightward in the opposite eye, the brain interprets this as movement toward (or away) from the face along the midline. If both eyes see an object moving in the same direction, but at different rates, what would that mean for spatial movement?

Everyday Connections: Depth Perception, 3-D Movies, and Optical Illusions

The visual field is projected onto the retinal surface, where photoreceptors transduce light energy into neural signals for the brain to interpret. The retina is a two-dimensional surface, so it does not encode three-dimensional information. However, we can perceive depth. How is that accomplished?

Two ways in which we can extract depth information from the two-dimensional retinal signal are based on monocular cues and binocular cues, respectively.

Monocular depth cues are those that are the result of information within the two-dimensional visual field. One object that overlaps another object has to be in front. Relative size differences are also a cue. For example, if a basketball appears larger than the basket, then the basket must be further away. On the basis of experience, we can estimate how far away the basket is.

Binocular depth cues compare information represented in the two retinae because they do not see the visual field exactly the same. The centers of the two eyes are separated by a small distance, which is approximately 6 to 6.5 cm in most people. Because of this offset, visual stimuli do not fall on exactly the same spot on both retinae unless we are fixated directly on them and they fall on the fovea of each retina. All other objects in the visual field, either closer or farther away than the fixated object, will fall on different spots on the retina.

When vision is fixed on an object in space, closer objects will fall on the lateral retina of each eye, and more distant objects will fall on the medial retina of either eye (Figure 7). This is easily observed by holding a finger up in front of your face as you look at a more distant object.

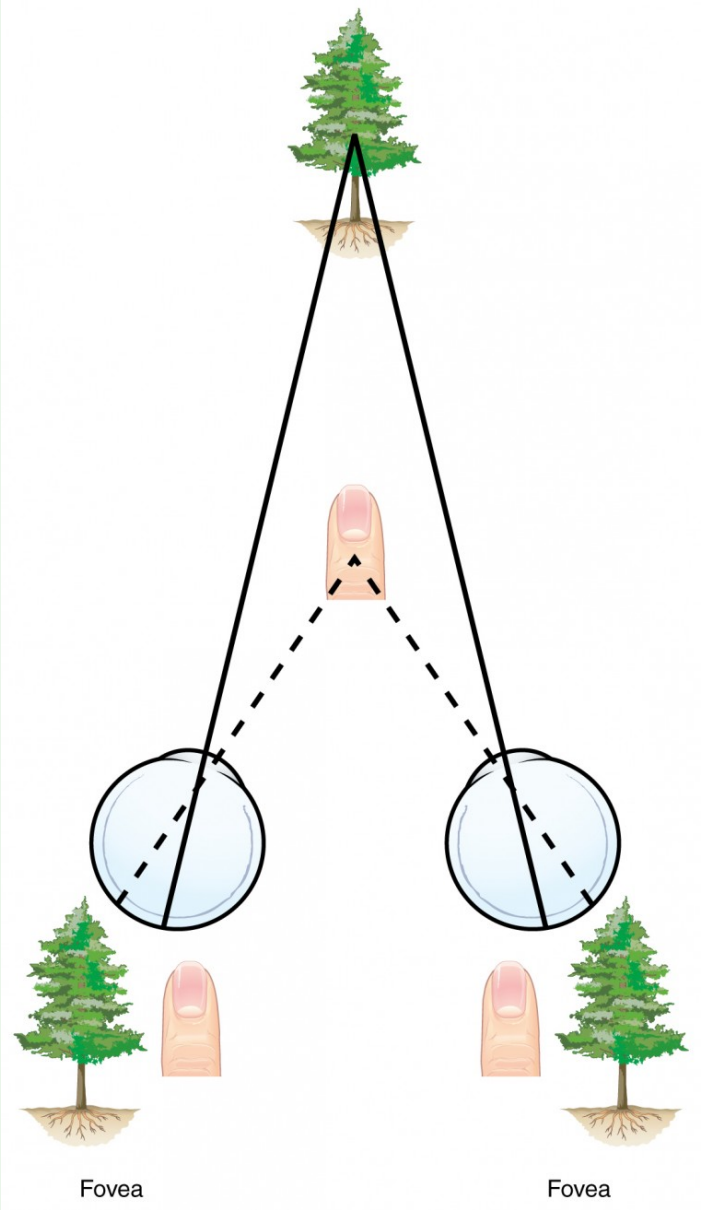


Figure 7. Retinal Disparity *Because of the interocular distance, which results in objects of different distances falling on different spots of the two retinae, the brain can extract depth perception from the two-dimensional information of the visual field.*

You will see two images of your finger that represent the two disparate images that are falling on either retina. These depth cues, both monocular and binocular, can be exploited to make the brain think there are three dimensions in two-dimensional information. This is the basis of 3-D movies. The projected image on the screen is two dimensional, but it has disparate information embedded in it. The 3-D glasses that are available at the theater filter the information so that only one eye sees one version of what is on the screen, and the other eye sees the other version. If you take the glasses off, the image on the screen will have varying amounts of blur because both eyes are seeing both layers of information, and the third dimension will not be evident.

Some optical illusions can take advantage of depth cues as well, though those are more often using monocular cues to fool the brain into seeing different parts of the scene as being at different depths.

There are two main regions that surround the primary cortex that are usually referred to as areas V2 and V3 (the primary visual cortex is area V1). These surrounding areas are the visual association cortex. The visual association regions develop more complex visual perceptions by adding color and motion information. The information processed in these areas is then sent to regions of the temporal and parietal lobes.

Visual processing has two separate streams of processing: one into the temporal lobe and one into the parietal lobe. These are the ventral and dorsal streams, respectively (Figure 8).

The **ventral stream** identifies visual stimuli and their significance. Because the ventral stream uses temporal lobe structures, it begins to interact with the non-visual cortex and may be important in visual stimuli becoming part of memories.

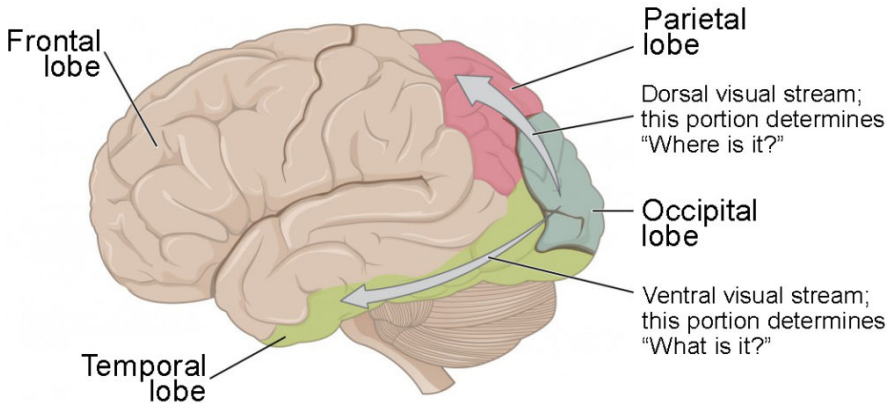


Figure 8. Ventral and Dorsal Visual Streams. *From the primary visual cortex in the occipital lobe, visual processing continues in two streams—one into the temporal lobe and one into the parietal lobe.*

The **dorsal stream** locates objects in space and helps in guiding movements of the body in response to visual inputs. The dorsal stream enters the parietal lobe, where it interacts with somatosensory cortical areas that are important for our perception of the body and its movements. The dorsal stream can then influence frontal lobe activity where motor functions originate.

Disorders of the Brain: Prosopagnosia

The failures of sensory perception can be unusual and debilitating. Prosopagnosia, or face blindness, is a particular sensory deficit that inhibits an important social function of humans. The word comes from the Greek words prosopa, that means "faces," and agnosia, that means "not knowing."

Some people may feel that they cannot recognize people easily by their faces. However, a person with prosopagnosia cannot recognize the most recognizable people in their respective cultures. They would not recognize the face of a celebrity, an important historical figure, or even a family member like their mother. They may not even recognize their own face.

Prosopagnosia can be caused by trauma to the brain, or it can be present from birth. The exact cause of proposagnosia and the reason that it happens to some people is unclear. A study of the brains of people born with the deficit found that a specific region of the brain, the anterior fusiform gyrus of the temporal lobe, is often underdeveloped. This region of the brain is concerned with the recognition of visual stimuli and its possible association with memories. Though the evidence is not yet definitive, this region is likely to be where facial recognition occurs.

Though this can be a devastating condition, people who suffer from it can get by—often by using other cues to recognize the people they see. Often, the sound of a person's voice, or the presence of unique cues such as distinct facial features (a mole, for example) or hair color can help the sufferer recognize a familiar person. In the video on prosopagnosia provided in this section, a woman is shown having trouble recognizing celebrities, family members, and herself. However, in some situations, she can use other cues to help her recognize faces.

The inability to recognize people by their faces is a troublesome problem. It can be caused by trauma, or it may be inborn. Watch this video to learn more about a person who lost the ability to recognize faces as the result of an injury.

Watch this video online: https://youtu.be/vwCrxomPbtY

She cannot recognize the faces of close family members or herself. What other information can a person suffering from prosopagnosia use to figure out whom they are seeing?

MOTOR RESPONSES

Learning Objectives

- List the components of the basic processing stream for the motor system
- Describe the pathway of descending motor commands from the cortex to the skeletal muscles
- Compare different descending pathways, both by structure and function
- Explain the initiation of movement from the neurological connections
- Describe several reflex arcs and their functional roles

The defining characteristic of the somatic nervous system is that it controls skeletal muscles. Somatic senses inform the nervous system about the external environment, but the response to that is through voluntary muscle movement. The term “voluntary” suggests that there is a conscious decision to make a movement. However, some aspects of the somatic system use voluntary muscles without conscious control. One example is the ability of our breathing to switch to unconscious control while we are focused on another task. However, the muscles that are responsible for the basic process of breathing are also utilized for speech, which is entirely voluntary.

Cortical Responses

Let’s start with sensory stimuli that have been registered through receptor cells and the information relayed to the CNS along ascending pathways. In the cerebral cortex, the initial processing of sensory perception progresses to associative processing and then integration in multimodal areas of cortex. These levels of processing can lead to the incorporation of sensory perceptions into memory, but more importantly, they lead to a response. The completion of cortical processing through the primary, associative, and integrative sensory areas initiates a similar progression of motor processing, usually in different cortical areas. While the sensory cortical areas are located in the occipital, temporal, and parietal lobes, motor functions are largely controlled by the frontal lobe.

The most anterior regions of the frontal lobe—the prefrontal areas—are important for **executive functions**, which are those cognitive functions that lead to goal-directed behaviors. These higher cognitive processes include **working memory**, which has been called a “mental scratch pad,” that can help organize and represent information that is not in the immediate environment.

The prefrontal lobe is responsible for aspects of attention, such as inhibiting distracting thoughts and actions so that a person can focus on a goal and direct behavior toward achieving that goal. The functions of the prefrontal cortex are integral to the personality of an individual, because it is largely responsible for what a person intends to do and how they accomplish those plans.

A famous case of damage to the prefrontal cortex is that of Phineas Gage, dating back to 1848. He was a railroad worker who had a metal spike impale his prefrontal cortex (Figure 1). He survived the accident, but according to second-hand accounts, his personality changed drastically.

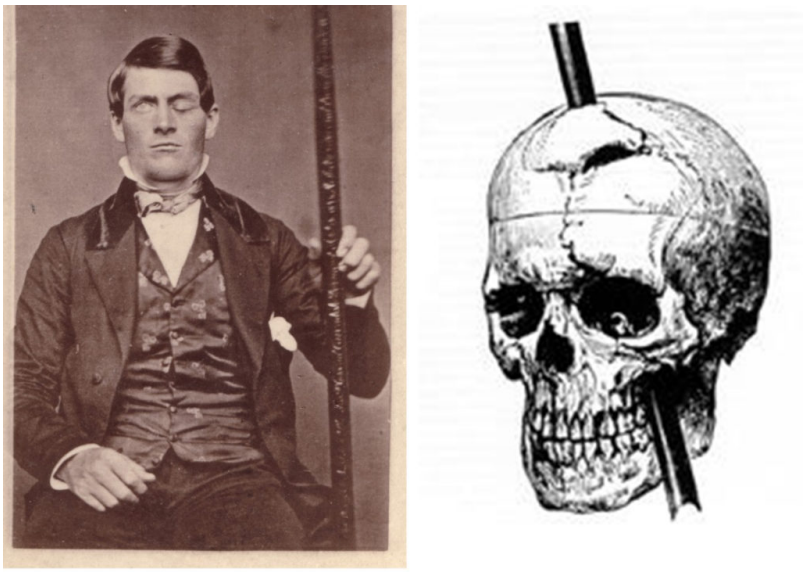


Figure 1. Phineas Gage. *The victim of an accident while working on a railroad in 1848, Phineas Gage had a large iron rod impaled through the prefrontal cortex of his frontal lobe. After the accident, his personality appeared to change, but he eventually learned to cope with the trauma and lived as a coach driver even after such a traumatic event. (credit b: John M. Harlow, MD)*

Friends described him as no longer acting like himself. Whereas he was a hardworking, amiable man before the accident, he turned into an irritable, temperamental, and lazy man after the accident. Many of the accounts of his change may have been inflated in the retelling, and some behavior was likely attributable to alcohol used as a pain medication. However, the accounts suggest that some aspects of his personality did change. There is new evidence that though his life changed dramatically, he was able to become a functioning stagecoach driver, suggesting that the brain has the ability to recover even from major trauma such as this.

Secondary Motor Cortices

In generating motor responses, the executive functions of the prefrontal cortex will need to initiate actual movements. One way to define the prefrontal area is any region of the frontal lobe that does not elicit movement when electrically stimulated. These are primarily in the anterior part of the frontal lobe. The regions of the frontal lobe that remain are the regions of the cortex that produce movement.

The prefrontal areas project into the secondary motor cortices, which include the **premotor cortex** and the **supplemental motor area**. Two important regions that assist in planning and coordinating movements are located adjacent to the primary motor cortex. The premotor cortex is more lateral, whereas the supplemental motor area is more medial and superior. The premotor area aids in controlling movements of the core muscles to maintain posture during movement, whereas the supplemental motor area is hypothesized to be responsible for planning and coordinating movement. The supplemental motor area also manages sequential movements that are based on prior experience (that is, learned movements). Neurons in these areas are most active leading up to the initiation of movement.

For example, these areas might prepare the body for the movements necessary to drive a car in anticipation of a traffic light changing. Adjacent to these two regions are two specialized motor planning centers. The **frontal eye fields** are responsible for moving the eyes in response to visual stimuli. There are direct connections between the frontal eye fields and the superior colliculus. Also, anterior to the premotor cortex and primary motor cortex is **Broca's area**. This area is responsible for controlling movements of the structures of speech production. The area is named after a French surgeon and anatomist who studied patients who could not produce speech. They did not have impairments to understanding speech, only to producing speech sounds, suggesting a damaged or underdeveloped Broca's area.

Primary Motor Cortex

The primary motor cortex is located in the precentral gyrus of the frontal lobe. Walter Penfield, a neurosurgeon, described much of the basic understanding of the primary motor cortex by electrically stimulating the surface of the cerebrum. Penfield would probe the surface of the cortex while the patient was only under local anesthesia so that he could observe responses to the stimulation. This led to the belief that the precentral gyrus directly stimulated muscle movement. We now know that the primary motor cortex receives input from several areas that aid in planning movement, and its principle output stimulates spinal cord neurons to stimulate skeletal muscle contraction.

The primary motor cortex is arranged in a similar fashion to the primary somatosensory cortex, in that it has a topographical map of the body, creating a motor homunculus. The neurons responsible for musculature in the feet and lower legs are in the medial wall of the precentral gyrus, with the thighs, trunk, and shoulder at the crest of the longitudinal fissure. The hand and face are in the lateral face of the gyrus.

Additionally, the relative space allotted for the different regions is exaggerated in muscles that have greater enervation. The greatest amount of cortical space is given to muscles that perform fine, agile movements, such as the muscles of the fingers and the lower face. The “power muscles” that perform coarser movements, such as the buttock and back muscles, occupy much less space on the motor cortex.

Descending Pathways

The motor output from the cortex descends into the brain stem and to the spinal cord to control the musculature through motor neurons. Neurons located in the primary motor cortex, named **Betz cells**, are large cortical neurons that synapse with lower motor neurons in the spinal cord or the brain stem. The two descending pathways travelled by the axons of Betz cells are the **corticospinal tract** and the **corticobulbar tract**. Both tracts are named for their origin in the cortex and their targets—either the spinal cord or the brain stem (the term “bulbar” refers to the brain stem as the bulb, or enlargement, at the top of the spinal cord).

These two descending pathways are responsible for the conscious or voluntary movements of skeletal muscles. Any motor command from the primary motor cortex is sent down the axons of the Betz cells to activate upper motor neurons in either the cranial motor nuclei or in the ventral horn of the spinal cord. The axons of the corticobulbar tract are ipsilateral, meaning they project from the cortex to the motor nucleus on the same side of the nervous system. Conversely, the axons of the corticospinal tract are largely contralateral, meaning that they cross the midline of the brain stem or spinal cord and synapse on the opposite side of the body. Therefore, the right motor cortex of the cerebrum controls muscles on the left side of the body, and vice versa.

The corticospinal tract descends from the cortex through the deep white matter of the cerebrum. It then passes between the caudate nucleus and putamen of the basal nuclei as a bundle called the **internal capsule**. The tract then passes through the midbrain as the **cerebral peduncles**, after which it burrows through the pons. Upon entering the medulla, the tracts make up the large white matter tract referred to as the **pyramids** (Figure 2). The defining landmark of the medullary-spinal border is the **pyramidal decussation**, which is where most of the fibers in the corticospinal tract cross over to the opposite side of the brain. At this point, the tract separates into two parts, which have control over different domains of the musculature.

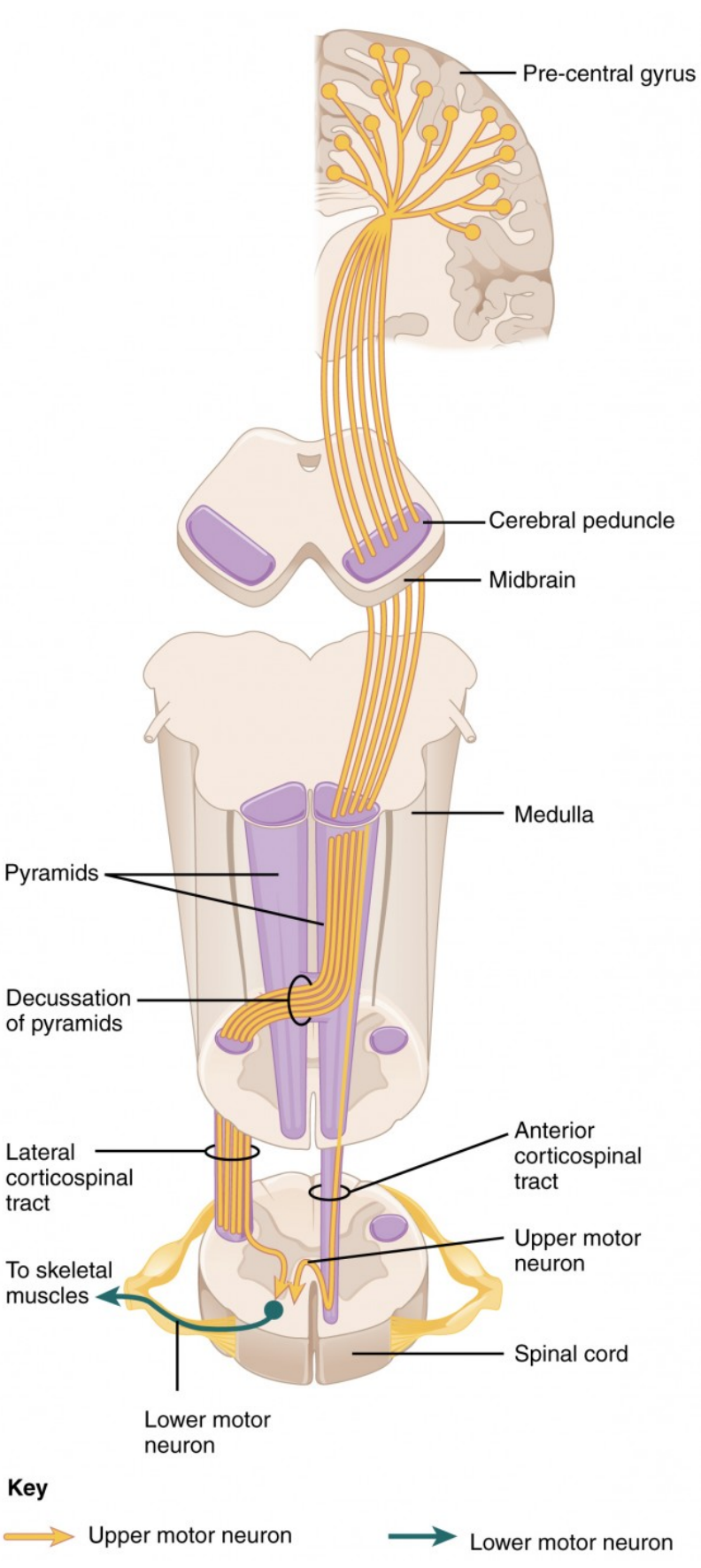
Appendicular Control

The **lateral corticospinal tract** is composed of the fibers that cross the midline at the pyramidal decussation (see Figure 2). The axons cross over from the anterior position of the pyramids in the medulla to the lateral column of the spinal cord. These axons are responsible for controlling appendicular muscles. This influence over the appendicular muscles means that the lateral corticospinal tract is responsible for moving the muscles of the arms and legs.

The ventral horn in both the lower cervical spinal cord and the lumbar spinal cord both have wider ventral horns, representing the greater number of muscles controlled by these motor neurons. The **cervical enlargement** is particularly large because there is greater control over the fine musculature of the upper limbs, particularly of the fingers. The **lumbar enlargement** is not as significant in appearance because there is less fine motor control of the lower limbs.

Axial Control

The **anterior corticospinal tract** is responsible for controlling the muscles of the body trunk (see Figure 2). These axons do not decussate in the medulla. Instead, they remain in an anterior position as they descend the brain stem



and enter the spinal cord. These axons then travel to the spinal cord level at which they synapse with a lower motor neuron. Upon reaching the appropriate level, the axons decussate, entering the ventral horn on the opposite side of the spinal cord from which they entered.

Figure 2. Corticospinal Tract. *The major descending tract that controls skeletal muscle movements is the corticospinal tract. It is composed of two neurons, the upper motor neuron and the lower motor neuron. The upper motor neuron has its cell body in the primary motor cortex of the frontal lobe and synapses on the lower motor neuron, which is in the ventral horn of the spinal cord and projects to the skeletal muscle in the periphery.*

In the ventral horn, these axons synapse with their corresponding lower motor neurons. The lower motor neurons are located in the medial regions of the ventral horn, because they control the axial muscles of the trunk. Because movements of the body trunk involve both sides of the body, the anterior corticospinal tract is not entirely contralateral. Some collateral branches of the tract will project into the ipsilateral ventral horn to control synergistic muscles on that side of the body, or to inhibit antagonistic muscles through interneurons within the ventral horn.

Through the influence of both sides of the body, the anterior corticospinal tract can coordinate postural muscles in broad movements of the body. These coordinating axons in the anterior corticospinal tract are often considered bilateral, as they are both ipsilateral and contralateral.

Watch this video to learn more about the descending motor pathway for the somatic nervous system.

Watch this video online: https://youtu.be/I4HPqjDcq5I

The autonomic connections are mentioned, which are covered in another chapter. From this brief video, only some of the descending motor pathway of the somatic nervous system is described. Which division of the pathway is described and which division is left out?

Extrapyramidal Controls

Other descending connections between the brain and the spinal cord are called the **extrapyramidal system**. The name comes from the fact that this system is outside the corticospinal pathway, which includes the pyramids in the medulla. A few pathways originating from the brain stem contribute to this system.

- The **tectospinal tract** projects from the midbrain to the spinal cord and is important for postural movements that are driven by the superior colliculus. The name of the tract comes from an alternate name for the superior colliculus, which is the tectum.
- The **reticulospinal tract** connects the reticular system, a diffuse region of gray matter in the brain stem, with the spinal cord. This tract influences trunk and proximal limb muscles related to posture and locomotion. The reticulospinal tract also contributes to muscle tone and influences autonomic functions.
- The **vestibulospinal tract** connects the brain stem nuclei of the vestibular system with the spinal cord. This allows posture, movement, and balance to be modulated on the basis of equilibrium information provided by the vestibular system.

The pathways of the extrapyramidal system are influenced by subcortical structures. For example, connections between the secondary motor cortices and the extrapyramidal system modulate spine and cranium movements. The basal nuclei, which are important for regulating movement initiated by the CNS, influence the extrapyramidal system as well as its thalamic feedback to the motor cortex. The conscious movement of our muscles is more complicated than simply sending a single command from the precentral gyrus down to the proper motor neurons. During the movement of any body part, our muscles relay information back to the brain, and the brain is constantly sending “revised” instructions back to the muscles.

The cerebellum is important in contributing to the motor system because it compares cerebral motor commands with proprioceptive feedback. The corticospinal fibers that project to the ventral horn of the spinal cord have branches that also synapse in the pons, which project to the cerebellum. Also, the proprioceptive sensations of the dorsal column system have a collateral projection to the medulla that projects to the cerebellum. These two streams of information are compared in the cerebellar cortex. Conflicts between the motor commands sent by the cerebrum and body position information provided by the proprioceptors cause the cerebellum to stimulate the **red nucleus** of the midbrain. The red nucleus then sends corrective commands to the spinal cord along the **rubrospinal tract**. The name of this tract comes from the word for red that is seen in the English word “ruby.”

A good example of how the cerebellum corrects cerebral motor commands can be illustrated by walking in water. An original motor command from the cerebrum to walk will result in a highly coordinated set of learned movements. However, in water, the body cannot actually perform a typical walking movement as instructed. The cerebellum can alter the motor command, stimulating the leg muscles to take larger steps to overcome the water resistance. The cerebellum can make the necessary changes through the rubrospinal tract. Modulating the basic command to walk also relies on spinal reflexes, but the cerebellum is responsible for calculating the appropriate response.

When the cerebellum does not work properly, coordination and balance are severely affected. The most dramatic example of this is during the overconsumption of alcohol. Alcohol inhibits the ability of the cerebellum to interpret proprioceptive feedback, making it more difficult to coordinate body movements, such as walking a straight line, or guide the movement of the hand to touch the tip of the nose.

Visit this site to read about an elderly woman who starts to lose the ability to control fine movements, such as speech and the movement of limbs. Many of the usual causes were ruled out. It was not a stroke, Parkinson's disease, diabetes, or thyroid dysfunction. The next most obvious cause was medication, so her pharmacist had to be consulted. The side effect of a drug meant to help her sleep had resulted in changes in motor control. What regions of the nervous system are likely to be the focus of haloperidol side effects?

Ventral Horn Output

The somatic nervous system provides output strictly to skeletal muscles. The lower motor neurons, which are responsible for the contraction of these muscles, are found in the ventral horn of the spinal cord. These large, multipolar neurons have a corona of dendrites surrounding the cell body and an axon that extends out of the ventral horn. This axon travels through the ventral nerve root to join the emerging spinal nerve. The axon is relatively long because it needs to reach muscles in the periphery of the body. The diameters of cell bodies may be on the order of hundreds of micrometers to support the long axon; some axons are a meter in length, such as the lumbar motor neurons that innervate muscles in the first digits of the feet. The axons will also branch to innervate multiple muscle fibers.

Together, the motor neuron and all the muscle fibers that it controls make up a motor unit. Motor units vary in size. Some may contain up to 1000 muscle fibers, such as in the quadriceps, or they may only have 10 fibers, such as in an extraocular muscle. The number of muscle fibers that are part of a motor unit corresponds to the precision of control of that muscle. Also, muscles that have finer motor control have more motor units connecting to them, and this requires a larger topographical field in the primary motor cortex.

Motor neuron axons connect to muscle fibers at a neuromuscular junction. This is a specialized synaptic structure at which multiple axon terminals synapse with the muscle fiber sarcolemma. The synaptic end bulbs of the motor neurons secrete acetylcholine, which binds to receptors on the sarcolemma. The binding of acetylcholine opens ligand-gated ion channels, increasing the movement of cations across the sarcolemma. This depolarizes the sarcolemma, initiating muscle contraction. Whereas other synapses result in graded potentials that must reach a threshold in the postsynaptic target, activity at the neuromuscular junction reliably leads to muscle fiber contraction with every nerve impulse received from a motor neuron. However, the strength of contraction and the number of fibers that contract can be affected by the frequency of the motor neuron impulses.

Reflexes

This chapter began by introducing reflexes as an example of the basic elements of the somatic nervous system. Simple somatic reflexes do not include the higher centers discussed for conscious or voluntary aspects of movement. Reflexes can be spinal or cranial, depending on the nerves and central components that are involved.

The Withdrawal Reflex

At the beginning of this chapter, we discussed the heat and pain sensations from a hot stove causing withdrawal of the arm through a connection in the spinal cord that leads to contraction of the biceps brachii. The description

of this withdrawal reflex was simplified, for the sake of the introduction, to emphasize the parts of the somatic nervous system.

In order to consider reflexes fully, let's revisit this example with more attention to the details. As you withdraw your hand from the stove, you do not want to slow that reflex down. As the biceps brachii contracts, the antagonistic triceps brachii needs to relax. Because the neuromuscular junction is strictly excitatory, the biceps will contract when the motor nerve is active. Skeletal muscles do not actively relax. Instead the motor neuron needs to "quiet down," or be inhibited. In the hot-stove withdrawal reflex, this occurs through an interneuron in the spinal cord. The interneuron's cell body is located in the dorsal horn of the spinal cord. The interneuron receives a synapse from the axon of the sensory neuron that detects that the hand is being burned. In response to this stimulation from the sensory neuron, the interneuron then inhibits the motor neuron that controls the triceps brachii. This is done by releasing a neurotransmitter or other signal that hyperpolarizes the motor neuron connected to the triceps brachii, making it less likely to initiate an action potential. With this motor neuron being inhibited, the triceps brachii relaxes. Without the antagonistic contraction, withdrawal from the hot stove is faster and keeps further tissue damage from occurring.

Another example of a withdrawal reflex occurs when you step on a painful stimulus, like a tack or a sharp rock. The nociceptors that are activated by the painful stimulus activate the motor neurons responsible for contraction of the tibialis anterior muscle. This causes dorsiflexion of the foot. An inhibitory interneuron, activated by a collateral branch of the nociceptor fiber, will inhibit the motor neurons of the gastrocnemius and soleus muscles to cancel plantar flexion. An important difference in this reflex is that plantar flexion is most likely in progress as the foot is pressing down onto the tack. Contraction of the tibialis anterior is not the most important aspect of the reflex, as continuation of plantar flexion will result in further damage from stepping onto the tack.

The Stretch Reflex

Another type of reflex is a **stretch reflex**. In this reflex, when a skeletal muscle is stretched, a muscle spindle receptor is activated. The axon from this receptor structure will cause direct contraction of the muscle. A collateral of the muscle spindle fiber will also inhibit the motor neuron of the antagonist muscles. The reflex helps to maintain muscles at a constant length. A common example of this reflex is the knee jerk that is elicited by a rubber hammer struck against the patellar ligament in a physical exam.

The Corneal Reflex

A specialized reflex to protect the surface of the eye is the **corneal reflex**, or the eye blink reflex. When the cornea is stimulated by a tactile stimulus, or even by bright light in a related reflex, blinking is initiated. The sensory component travels through the trigeminal nerve, which carries somatosensory information from the face, or through the optic nerve, if the stimulus is bright light. The motor response travels through the facial nerve and innervates the orbicularis oculi on the same side. This reflex is commonly tested during a physical exam using an air puff or a gentle touch of a cotton-tipped applicator.

Watch this video to learn more about the reflex arc of the corneal reflex.

Watch this video online: https://youtu.be/x4UrvhaetdE

When the right cornea senses a tactile stimulus, what happens to the left eye? Explain your answer.

Watch this video to learn more about newborn reflexes.

Watch this video online: https://youtu.be/OUV_XfSk1RM

Newborns have a set of reflexes that are expected to have been crucial to survival before the modern age. These reflexes disappear as the baby grows, as some of them may be unnecessary as they age. The video demonstrates a reflex called the Babinski reflex, in which the foot flexes dorsally and the toes splay out when the sole of the foot is lightly scratched. This is normal for newborns, but it is a sign of reduced myelination of the spinal tract in adults. Why would this reflex be a problem for an adult?

VIDEO: SENSORY RECEPTORS

Watch this video online: https://youtu.be/2pJnrPmzNds

ADDITIONAL LINKS

Interactive Links

The Brain from Top to Bottom:

- http://thebrain.mcgill.ca/index.php

View Brain Anatomy on the free 3D Brain App:

- https://itunes.apple.com/us/app/3d-brain/id331399332?mt=8

Brain Anatomy Games:

- http://www.anatomyarcade.com/games/gamesNervous.html

GLOSSARY: THE BRAIN AND CRANIAL NERVES

alkaloid: substance, usually from a plant source, that is chemically basic with respect to pH and will stimulate bitter receptors

amacrine cell: type of cell in the retina that connects to the bipolar cells near the outer synaptic layer and provides the basis for early image processing within the retina

ampulla: in the ear, the structure at the base of a semicircular canal that contains the hair cells and cupula for transduction of rotational movement of the head

anosmia: loss of the sense of smell; usually the result of physical disruption of the first cranial nerve

anterior corticospinal tract: division of the corticospinal pathway that travels through the ventral (anterior) column of the spinal cord and controls axial musculature through the medial motor neurons in the ventral (anterior) horn

aqueous humor: watery fluid that fills the anterior chamber containing the cornea, iris, ciliary body, and lens of the eye

ascending pathway: fiber structure that relays sensory information from the periphery through the spinal cord and brain stem to other structures of the brain

association area: region of cortex connected to a primary sensory cortical area that further processes the information to generate more complex sensory perceptions

audition: sense of hearing

auricle: fleshy external structure of the ear

Betz cells: output cells of the primary motor cortex that cause musculature to move through synapses on cranial and spinal motor neurons

Broca's area: region of the frontal lobe associated with the motor commands necessary for speech production

basilar membrane: in the ear, the floor of the cochlear duct on which the organ of Corti sits

binocular depth cues: indications of the distance of visual stimuli on the basis of slight differences in the images projected onto either retina

bipolar cell: cell type in the retina that connects the photoreceptors to the RGCs

capsaicin: molecule that activates nociceptors by interacting with a temperature-sensitive ion channel and is the basis for "hot" sensations in spicy food

cerebral peduncles: segments of the descending motor pathway that make up the white matter of the ventral midbrain

cervical enlargement: region of the ventral (anterior) horn of the spinal cord that has a larger population of motor neurons for the greater number of and finer control of muscles of the upper limb

chemoreceptor: sensory receptor cell that is sensitive to chemical stimuli, such as in taste, smell, or pain

chief sensory nucleus: component of the trigeminal nuclei that is found in the pons

choroid: highly vascular tissue in the wall of the eye that supplies the outer retina with blood

ciliary body: smooth muscle structure on the interior surface of the iris that controls the shape of the lens through the zonule fibers

circadian rhythm: internal perception of the daily cycle of light and dark based on retinal activity related to sunlight

cochlea: auditory portion of the inner ear containing structures to transduce sound stimuli

cochlear duct: space within the auditory portion of the inner ear that contains the organ of Corti and is adjacent to the scala tympani and scala vestibuli on either side

cone photoreceptor: one of the two types of retinal receptor cell that is specialized for color vision through the use of three photopigments distributed through three separate populations of cells

contralateral: word meaning "on the opposite side," as in axons that cross the midline in a fiber tract

cornea: fibrous covering of the anterior region of the eye that is transparent so that light can pass through it

corneal reflex: protective response to stimulation of the cornea causing contraction of the orbicularis oculi muscle resulting in blinking of the eye

corticobulbar tract: connection between the cortex and the brain stem responsible for generating movement

corticospinal tract: connection between the cortex and the spinal cord responsible for generating movement

cupula: specialized structure within the base of a semicircular canal that bends the stereocilia of hair cells when the head rotates by way of the relative movement of the enclosed fluid

decussate: to cross the midline, as in fibers that project from one side of the body to the other

dorsal column system: ascending tract of the spinal cord associated with fine touch and proprioceptive sensations

dorsal stream: connections between cortical areas from the occipital to parietal lobes that are responsible for the perception of visual motion and guiding movement of the body in relation to that motion

encapsulated ending: configuration of a sensory receptor neuron with dendrites surrounded by specialized structures to aid in transduction of a particular type of sensation, such as the lamellated corpuscles in the deep dermis and subcutaneous tissue

equilibrium: sense of balance that includes sensations of position and movement of the head

executive functions: cognitive processes of the prefrontal cortex that lead to directing goal-directed behavior, which is a precursor to executing motor commands

external ear: structures on the lateral surface of the head, including the auricle and the ear canal back to the tympanic membrane

exteroceptor: sensory receptor that is positioned to interpret stimuli from the external environment, such as photoreceptors in the eye or somatosensory receptors in the skin

extraocular muscle: one of six muscles originating out of the bones of the orbit and inserting into the surface of the eye which are responsible for moving the eye

extrapyramidal system: pathways between the brain and spinal cord that are separate from the corticospinal tract and are responsible for modulating the movements generated through that primary pathway

fasciculus cuneatus: lateral division of the dorsal column system composed of fibers from sensory neurons in the upper body

fasciculus gracilis: medial division of the dorsal column system composed of fibers from sensory neurons in the lower body

fibrous tunic: outer layer of the eye primarily composed of connective tissue known as the sclera and cornea

fovea: exact center of the retina at which visual stimuli are focused for maximal acuity, where the retina is thinnest, at which there is nothing but photoreceptors

free nerve ending: configuration of a sensory receptor neuron with dendrites in the connective tissue of the organ, such as in the dermis of the skin, that are most often sensitive to chemical, thermal, and mechanical stimuli

frontal eye fields: area of the prefrontal cortex responsible for moving the eyes to attend to visual stimuli

general sense: any sensory system that is distributed throughout the body and incorporated into organs of multiple other systems, such as the walls of the digestive organs or the skin

gustation: sense of taste

gustatory receptor cells: sensory cells in the taste bud that transduce the chemical stimuli of gustation

hair cells: mechanoreceptor cells found in the inner ear that transduce stimuli for the senses of hearing and balance

incus: (also, anvil) ossicle of the middle ear that connects the malleus to the stapes

inferior colliculus: last structure in the auditory brainstem pathway that projects to the thalamus and superior colliculus

inferior oblique: extraocular muscle responsible for lateral rotation of the eye

inferior rectus: extraocular muscle responsible for looking down

inner ear: structure within the temporal bone that contains the sensory apparati of hearing and balance

inner segment: in the eye, the section of a photoreceptor that contains the nucleus and other major organelles for normal cellular functions

inner synaptic layer: layer in the retina where bipolar cells connect to RGCs

interaural intensity difference: cue used to aid sound localization in the horizontal plane that compares the relative loudness of sounds at the two ears, because the ear closer to the sound source will hear a slightly more intense sound

interaural time difference: cue used to help with sound localization in the horizontal plane that compares the relative time of arrival of sounds at the two ears, because the ear closer to the sound source will receive the stimulus microseconds before the other ear

internal capsule: segment of the descending motor pathway that passes between the caudate nucleus and the putamen

interoceptor: sensory receptor that is positioned to interpret stimuli from internal organs, such as stretch receptors in the wall of blood vessels

ipsilateral: word meaning on the same side, as in axons that do not cross the midline in a fiber tract

iris: colored portion of the anterior eye that surrounds the pupil

kinesthesia: sense of body movement based on sensations in skeletal muscles, tendons, joints, and the skin

lacrimal duct: duct in the medial corner of the orbit that drains tears into the nasal cavity

lacrimal gland: gland lateral to the orbit that produces tears to wash across the surface of the eye

lateral corticospinal tract: division of the corticospinal pathway that travels through the lateral column of the spinal cord and controls appendicular musculature through the lateral motor neurons in the ventral (anterior) horn

lateral geniculate nucleus: thalamic target of the RGCs that projects to the visual cortex

lateral rectus: extraocular muscle responsible for abduction of the eye

lens: component of the eye that focuses light on the retina

levator palpebrae superioris: muscle that causes elevation of the upper eyelid, controlled by fibers in the oculomotor nerve

lumbar enlargement: region of the ventral (anterior) horn of the spinal cord that has a larger population of motor neurons for the greater number of muscles of the lower limb

macula: enlargement at the base of a semicircular canal at which transduction of equilibrium stimuli takes place within the ampulla

malleus: (also, hammer) ossicle that is directly attached to the tympanic membrane

mechanoreceptor: receptor cell that transduces mechanical stimuli into an electrochemical signal

medial geniculate nucleus: thalamic target of the auditory brain stem that projects to the auditory cortex

medial lemniscus: fiber tract of the dorsal column system that extends from the nuclei gracilis and cuneatus to the thalamus, and decussates

medial rectus: extraocular muscle responsible for adduction of the eye

mesencephalic nucleus: component of the trigeminal nuclei that is found in the midbrain

middle ear: space within the temporal bone between the ear canal and bony labyrinth where the ossicles amplify sound waves from the tympanic membrane to the oval window

multimodal integration area: region of the cerebral cortex in which information from more than one sensory modality is processed to arrive at higher level cortical functions such as memory, learning, or cognition

neural tunic: layer of the eye that contains nervous tissue, namely the retina

nociceptor: receptor cell that senses pain stimuli

nucleus cuneatus: medullary nucleus at which first-order neurons of the dorsal column system synapse specifically from the upper body and arms

nucleus gracilis: medullary nucleus at which first-order neurons of the dorsal column system synapse specifically from the lower body and legs

odorant molecules: volatile chemicals that bind to receptor proteins in olfactory neurons to stimulate the sense of smell

olfaction: sense of smell

olfactory bulb: central target of the first cranial nerve; located on the ventral surface of the frontal lobe in the cerebrum

olfactory epithelium: region of the nasal epithelium where olfactory neurons are located

olfactory sensory neuron: receptor cell of the olfactory system, sensitive to the chemical stimuli of smell, the axons of which compose the first cranial nerve

opsin: protein that contains the photosensitive cofactor retinal for phototransduction

optic chiasm: decussation point in the visual system at which medial retina fibers cross to the other side of the brain

optic disc: spot on the retina at which RGC axons leave the eye and blood vessels of the inner retina pass

optic nerve: second cranial nerve, which is responsible visual sensation

optic tract: name for the fiber structure containing axons from the retina posterior to the optic chiasm representing their CNS location

organ of Corti: structure in the cochlea in which hair cells transduce movements from sound waves into electrochemical signals

osmoreceptor: receptor cell that senses differences in the concentrations of bodily fluids on the basis of osmotic pressure

ossicles: three small bones in the middle ear

otolith: gelatinous substance in the utricle and saccule of the inner ear that contains calcium carbonate crystals and into which the stereocilia of hair cells are embedded

outer segment: in the eye, the section of a photoreceptor that contains opsin molecules that transduce light stimuli

outer synaptic layer: layer in the retina at which photoreceptors connect to bipolar cells

oval window: membrane at the base of the cochlea where the stapes attaches, marking the beginning of the scala vestibuli

palpebral conjunctiva: membrane attached to the inner surface of the eyelids that covers the anterior surface of the cornea

papilla: for gustation, a bump-like projection on the surface of the tongue that contains taste buds

photoisomerization: chemical change in the retinal molecule that alters the bonding so that it switches from the 11-*cis*-retinal isomer to the all-*trans*-retinal isomer

photon: individual “packet” of light

photoreceptor: receptor cell specialized to respond to light stimuli

premotor cortex: cortical area anterior to the primary motor cortex that is responsible for planning movements

primary sensory cortex: region of the cerebral cortex that initially receives sensory input from an ascending pathway from the thalamus and begins the processing that will result in conscious perception of that modality

proprioception: sense of position and movement of the body

proprioceptor: receptor cell that senses changes in the position and kinesthetic aspects of the body

pupil: open hole at the center of the iris that light passes through into the eye

pyramidal decussation: location at which corticospinal tract fibers cross the midline and segregate into the anterior and lateral divisions of the pathway

pyramids: segment of the descending motor pathway that travels in the anterior position of the medulla

receptor cell: cell that transduces environmental stimuli into neural signals

red nucleus: midbrain nucleus that sends corrective commands to the spinal cord along the rubrospinal tract, based on disparity between an original command and the sensory feedback from movement

reticulospinal tract: extrapyramidal connections between the brain stem and spinal cord that modulate movement, contribute to posture, and regulate muscle tone

retinal ganglion cell (RGC): neuron of the retina that projects along the second cranial nerve

retinal: cofactor in an opsin molecule that undergoes a biochemical change when struck by a photon (pronounced with a stress on the last syllable)

retina: nervous tissue of the eye at which phototransduction takes place

rhodopsin: photopigment molecule found in the rod photoreceptors

rod photoreceptor: one of the two types of retinal receptor cell that is specialized for low-light vision

round window: membrane that marks the end of the scala tympani

rubrospinal tract: descending motor control pathway, originating in the red nucleus, that mediates control of the limbs on the basis of cerebellar processing

saccule: structure of the inner ear responsible for transducing linear acceleration in the vertical plane

scala tympani: portion of the cochlea that extends from the apex to the round window

scala vestibuli: portion of the cochlea that extends from the oval window to the apex

sclera: white of the eye

semicircular canals: structures within the inner ear responsible for transducing rotational movement information

sensory homunculus: topographic representation of the body within the somatosensory cortex demonstrating the correspondence between neurons processing stimuli and sensitivity

sensory modality: a particular system for interpreting and perceiving environmental stimuli by the nervous system

solitary nucleus: medullar nucleus that receives taste information from the facial and glossopharyngeal nerves

somatosensation: general sense associated with modalities lumped together as touch

special sense: any sensory system associated with a specific organ structure, namely smell, taste, sight, hearing, and balance

spinal trigeminal nucleus: component of the trigeminal nuclei that is found in the medulla

spinothalamic tract: ascending tract of the spinal cord associated with pain and temperature sensations

spiral ganglion: location of neuronal cell bodies that transmit auditory information along the eighth cranial nerve

stapes: (also, stirrup) ossicle of the middle ear that is attached to the inner ear

stereocilia: array of apical membrane extensions in a hair cell that transduce movements when they are bent

stretch reflex: response to activation of the muscle spindle stretch receptor that causes contraction of the muscle to maintain a constant length

submodality: specific sense within a broader major sense such as sweet as a part of the sense of taste, or color as a part of vision

superior colliculus: structure in the midbrain that combines visual, auditory, and somatosensory input to coordinate spatial and topographic representations of the three sensory systems

superior oblique: extraocular muscle responsible for medial rotation of the eye

superior rectus: extraocular muscle responsible for looking up

supplemental motor area: cortical area anterior to the primary motor cortex that is responsible for planning movements

suprachiasmatic nucleus: hypothalamic target of the retina that helps to establish the circadian rhythm of the body on the basis of the presence or absence of daylight

taste buds: structures within a papilla on the tongue that contain gustatory receptor cells

tectorial membrane: component of the organ of Corti that lays over the hair cells, into which the stereocilia are embedded

tectospinal tract: extrapyramidal connections between the superior colliculus and spinal cord

thermoreceptor: sensory receptor specialized for temperature stimuli

topographical: relating to positional information

transduction: process of changing an environmental stimulus into the electrochemical signals of the nervous system

trochlea: cartilaginous structure that acts like a pulley for the superior oblique muscle

tympanic membrane: ear drum

umami: taste submodality for sensitivity to the concentration of amino acids; also called the savory sense

utricle: structure of the inner ear responsible for transducing linear acceleration in the horizontal plane

vascular tunic: middle layer of the eye primarily composed of connective tissue with a rich blood supply

ventral posterior nucleus: nucleus in the thalamus that is the target of gustatory sensations and projects to the cerebral cortex

ventral stream: connections between cortical areas from the occipital lobe to the temporal lobe that are responsible for identification of visual stimuli

vestibular ganglion: location of neuronal cell bodies that transmit equilibrium information along the eighth cranial nerve

vestibular nuclei: targets of the vestibular component of the eighth cranial nerve

vestibule: in the ear, the portion of the inner ear responsible for the sense of equilibrium

vestibulo-ocular reflex (VOR): reflex based on connections between the vestibular system and the cranial nerves of eye movements that ensures images are stabilized on the retina as the head and body move

vestibulospinal tract: extrapyramidal connections between the vestibular nuclei in the brain stem and spinal cord that modulate movement and contribute to balance on the basis of the sense of equilibrium

visceral sense: sense associated with the internal organs

vision: special sense of sight based on transduction of light stimuli

visual acuity: property of vision related to the sharpness of focus, which varies in relation to retinal position

vitreous humor: viscous fluid that fills the posterior chamber of the eye

working memory: function of the prefrontal cortex to maintain a representation of information that is not in the immediate environment

zonule fibers: fibrous connections between the ciliary body and the lens

PRACTICE TEST: THE BRAIN AND CRANIAL NERVES

Review the material from this module by completing the practice in course online.