BIOS15: ANATOMY AND PHYSIOLOGY TEXTBOOK



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BIOS15 Anatomy and Physiology Textbook

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TABLE OF CONTENTS

Acknowledgements

Licensing

About the Author

Licensing

1: An Introduction to Anatomy and Physiology

- 1.1: Overview of Anatomy and Physiology
- 1.2: Overview of the Scientific Method
- 1.3: Structural Organization of the Human Body
- 1.4: Homeostasis
- 1.5: Anatomical Terminology
- 1.6: Review Questions

2: A Brief Overview of Chemistry

- 2.1: Elements and Atoms - The Building Blocks of Matter
- 2.2: Chemical Bonds
- 2.3: Inorganic Compounds Essential to Human Functioning
- 2.4: Review Questions

3: Cell Structure

- 3.1: The Cell Membrane
- 3.2: The Cytoplasm and Cellular Organelles
- 3.3: The Nucleus and DNA
- 3.4: Cell Transport and Osmosis
- 3.5: Review Questions

4: Tissue Organization

- 4.1: Types of Tissues
- 4.2: Epithelial Tissue
- 4.3: Connective Tissue
- 4.4: Review Questions

5: The Integumentary System

- 5.1: Introduction
- 5.2: Layers of the Skin

6: Bone Tissue and the Skeletal System

- 6.1: Functions of the Skeletal System
- 6.2: Bone Classification
- 6.3: Bone Structure
- 6.4: Bone Remodeling and Calcium Homeostasis
- 6.5: Fractures - Bone Repair

- 6.6: Review Questions

7: Joints

- 7.1: Introduction
- 7.2: Classification of Joints
- 7.3: Types of Body Movements

8: Muscle Tissue

- 8.1: Muscle Tissues
- 8.2: Skeletal Muscle Organ Structure
- 8.3: Muscle Fiber Contraction and Relaxation
- 8.4: Types of Muscle Fibers and Exercise
- 8.5: Review Questions

9: Overview of the Nervous System

- 9.1: Organization and Functions of the Nervous System
- 9.2: Anatomy of Nervous Tissue
- 9.3: Synapses
- 9.4: The Function of Nervous Tissue
- 9.5: The Central Nervous System
- 9.6: The Peripheral Nervous System
- 9.7: Review Questions

10: Sensory Perception

- 10.1: General and Special Senses
- 10.2: Special Senses - Eyes
- 10.3: Special Senses - Ears
- 10.4: Review Questions

11: The Autonomic Nervous System

- 11.1: Introduction to the Autonomic Nervous System (ANS)
- 11.2: The Sympathetic Division of the ANS
- 11.3: The Parasympathetic Division of the ANS
- 11.4: Review Questions

12: The Endocrine System

- 12.1: An Overview of the Endocrine System
- 12.2: Hormones
- 12.3: The Pituitary Gland and Hypothalamus
- 12.4: Thyroid Gland and Parathyroid Glands
- 12.5: Adrenal Glands
- 12.6: Endocrine Pancreas
- 12.7: Review Questions

13: The Cardiovascular System - Blood

- 13.1: An Overview of Blood
- 13.2: Erythrocytes
- 13.3: Leukocytes and Platelets
- 13.4: Blood Typing

- 13.5: Review Questions

14: The Cardiovascular System - Heart and Blood Vessels

- 14.1: Heart Anatomy
- 14.2: Cardiac Muscle and Electrical Activity
- 14.3: Cardiac Cycle
- 14.4: Structure and Function of Blood Vessels
- 14.5: Blood Flow, Blood Pressure, and Resistance
- 14.6: Review Questions

15: The Respiratory System

- 15.1: Organs and Structures of the Respiratory System
- 15.2: The Lungs
- 15.3: The Process of Breathing
- 15.4: Gas Exchange
- 15.5: Review Questions

16: The Digestive System

- 16.1: Overview of the Digestive System
- 16.2: Digestive System Processes and Regulation
- 16.3: The Stomach and the Upper Digestive Organs
- 16.4: Small and Large Intestines
- 16.5: Accessory Organs in Digestion- The Liver, Pancreas, and Gallbladder
- 16.6: Review Questions

17: The Urinary System

- 17.1: Introduction to the Urinary System
- 17.2: Overview of the Kidney
- 17.3: Microscopic Anatomy of the Kidney
- 17.4: Urine Formation and Glomerular Filtration Rate (GFR)
- 17.5: Tubular Reabsorption and Secretion
- 17.6: Endocrine Regulation of Kidney Function
- 17.7: Review Questions

18: The Reproductive System

- 18.1: Anatomy and Physiology of the Male Reproductive System
- 18.2: Anatomy and Physiology of the Female Reproductive System

19: Optional Reading

- 19.1: Accessory Structures of the Skin
- 19.2: Functions of the Integumentary System
- 19.3: Bone Formation and Development
- 19.4: Divisions of the Skeletal System
  - 19.4.1: The Skull
  - 19.4.2: The Vertebral Column
  - 19.4.3: The Thoracic Cage
  - 19.4.4: The Pectoral Girdle
  - 19.4.5: Bones of the Upper Limb
  - 19.4.6: The Pelvic Girdle and Pelvis

- 19.4.7: Bones of the Lower Limb
- 19.5: Introduction to the Muscular System
  - 19.5.1: Axial Muscles of the Head, Neck, and Back
  - 19.5.2: Axial Muscles of the Abdominal Wall and Thorax
  - 19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
  - 19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
- 19.6: Special Senses - Others
- 19.7: Coronary Circulation
- 19.8: Mean Arterial Pressure and Pulse Pressure

Index

Glossary

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Detailed Licensing

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CHAPTER OVERVIEW

1: An Introduction to Anatomy and Physiology

1.1: Overview of Anatomy and Physiology
1.2: Overview of the Scientific Method
1.3: Structural Organization of the Human Body
1.4: Homeostasis
1.5: Anatomical Terminology
1.6: Review Questions

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1.1: Overview of Anatomy and Physiology

Learning Objectives

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

- 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.

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 1.1.1 **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 1.1.1 **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.



Figure 1.1.1: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)

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.

Form is closely related to function in all living things. 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.

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1.2: OVERVIEW OF THE SCIENTIFIC METHOD

LEARNING OBJECTIVES

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

- Summarize the steps of the scientific method
- Understand the basic components of a scientific experiment

THE SCIENTIFIC METHOD

The scientific process typically starts with an observation (often a problem to solve) that leads to a question. Let's think about a simple problem that starts with an observation and apply the scientific method to solve the problem. One Monday morning, a student arrives at class and quickly discovers that the classroom is too warm. That is an observation that also describes a problem: the classroom is too warm. The student then asks a question: "Why is the classroom so warm?"

PROPOSING A HYPOTHESIS

Recall that a hypothesis is a suggested explanation that one can test. To solve a problem, one can propose several hypotheses. For example, one hypothesis might be, "The classroom is warm because no one turned on the air conditioning." However, there could be other responses to the question, and therefore one may propose other hypotheses. A second hypothesis might be, "The classroom is warm because there is a power failure, and so the air conditioning doesn't work."

Once one has selected a hypothesis, the student can make a prediction. A prediction is similar to a hypothesis but it typically has the format "If . . . then . . . ." For example, the prediction for the first hypothesis might be, "*If* the student turns on the air conditioning, *then* the classroom will no longer be too warm."

To test the first hypothesis, the student would find out if the air conditioning is on. If the air conditioning is turned on but does not work, there should be another reason, and the student should reject this hypothesis. To test the second hypothesis, the student could check if the lights in the classroom are functional. If so, there is no power failure and the student should reject this hypothesis. The students should test each hypothesis by carrying out appropriate experiments. Be aware that rejecting one hypothesis does not determine whether or not one can accept the other hypotheses. It simply eliminates one hypothesis that is not valid (Figure **1.2.1**). Using the scientific method, the student rejects the hypotheses that are inconsistent with experimental data.

VISUAL CONNECTION

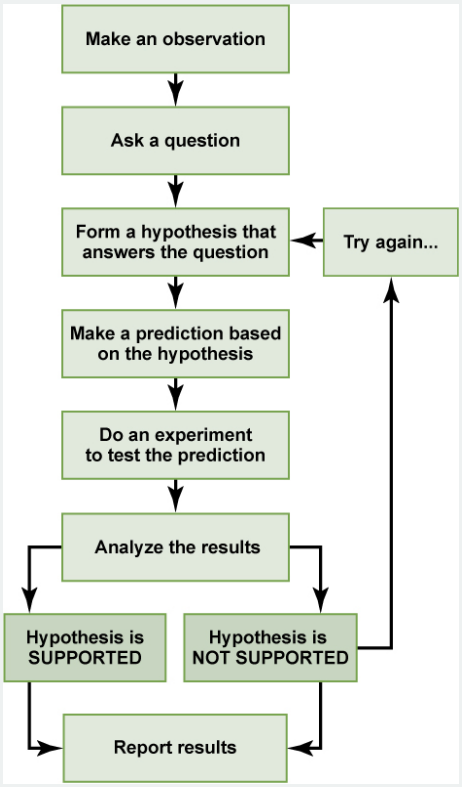


Figure 1.2.1 The scientific method consists of a series of well-defined steps. If a hypothesis is not supported by experimental data, one can propose a new hypothesis.

In the example below, the scientific method is used to solve an everyday problem. Match the scientific method steps (numbered items) with the process of solving the everyday problem (lettered items). Based on the results of the experiment, is the hypothesis correct? If it is incorrect, propose some alternative hypotheses.

1. Observation	a. There is something wrong with the electrical outlet.
2. Question	b. If something is wrong with the outlet, my coffeemaker also won't work when plugged into it.
3. Hypothesis (answer)	c. My toaster doesn't toast my bread.
4. Prediction	d. I plug my coffee maker into the outlet.
5. Experiment	e. My coffeemaker works.
6. Result	f. Why doesn't my toaster work?

EXPERIMENTAL DESIGN

A valid hypothesis must be testable. It should also be falsifiable, meaning that experimental results can disprove it. Importantly, science does not claim to "prove" anything because scientific understandings are always subject to modification with further information. This step —openness to disproving ideas—is what distinguishes sciences from non-sciences.

To test a hypothesis, a researcher will conduct one or more experiments designed to eliminate one or more of the hypotheses. Each experiment will have one or more **variables** and one or more **controls**. A **variable** is any part of the experiment that can vary or change during the experiment. The **control group** contains every feature of the experimental group except it is not given the manipulation that the researcher hypothesizes. Therefore, if the experimental group's results differ from the control group, the difference must be due to the hypothesized manipulation, rather than some outside factor. For example, you observe that there are many plants outside. You also notice that the sun is outside. Therefore, you propose that the sun makes plants grow better. You want to test this hypothesis by conducting an experiment. You decide to grow plants under different amounts of sunlight and see how much they grow. Before you can conduct your experiment, however, you need to make sure your experiment has the correct variables.

First, you need to have an **independent** variable and a **dependent** variable in your experiment. The independent variable is the variable that is being manipulated or changed. The dependent variable is the one that will be observed or measured. The observations you gather from your dependent variable "depend" on the effect of the independent variable. In your plant experiment, your independent variable is sunlight, as you will change the amount of sunlight each plant receives. Your dependent variable is plant growth, since plant growth will "depend" on how much sunlight (independent variable) it receives.

As mentioned above, your experiment needs to have a **control group**. The control group should not experience the effects of the independent variable. In your experiment, your control group will be a plant placed in the dark, receiving no sunlight.

You are now ready to conduct your plant experiment. You place Plant A outside in your backyard, receiving plenty of direct sunlight. You place Plant B inside near a window, indirectly receiving sunlight. Plant C is your control group and will be placed in a dark garage with no sunlight. See Figure 1.2.2 below for an example of the experiment.

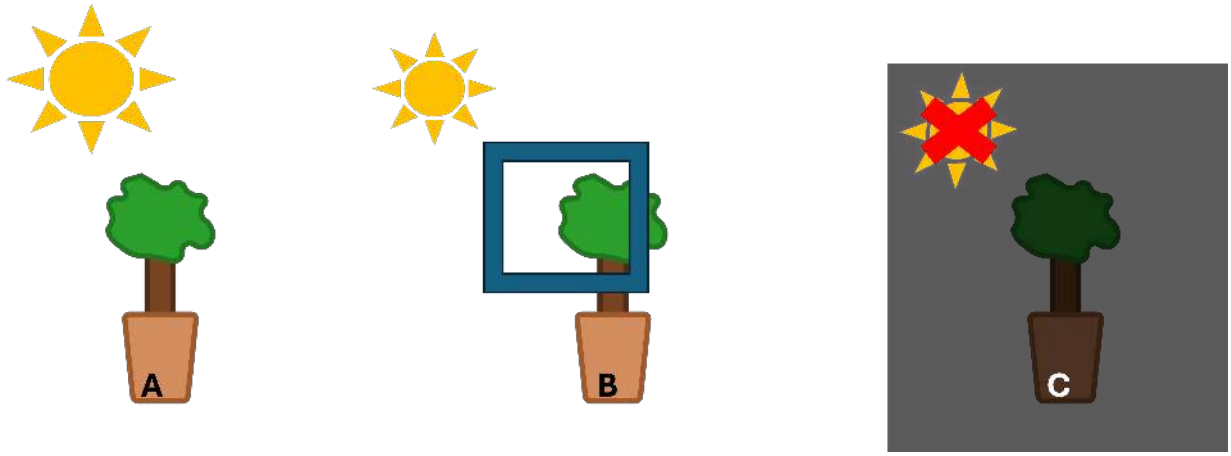


Figure 1.2.2 Plant experiment: Three plants will be tested in different sunlight conditions to observe the effects of sunlight on plant growth. *(Image by Harmony Folse is licensed under CC BY-SA 4.0, using "Vector flowerpot with smooth tree" by BoxOfNotes, CC BY-SA 4.0, via Wikimedia Commons)*

You also have to make sure that you have a set of **controlled variables**. These are variables that stay the same across each experimental group. A couple of controlled variables might be the amount of water and soil each plant receives. You will water the plants at the same time each day, with the same amount of water. You will make sure each plant has the same amount of soil and is in a pot of the same size.

You will measure my plants' growth at the same time each day. Again, you are making sure that everything is the same (controlled) among your experimental groups and that the only thing that is changing between them is the **independent variable** - the amount of sunlight they receive.

After a week of taking care of your plants and measuring them, you found that Plant A recorded the highest amount of growth, Plant B recorded just a few centimeters of growth and Plant C did not grow at all. After obtaining these results, you can conclude that your hypothesis of "the sun makes plants grow better" was supported by your experimental results. If instead you found that all your plants did not grow at all or Plant C without sunlight grew the most, then your hypothesis would have been rejected and you would have to come up with a new hypothesis.

REPORTING SCIENTIFIC WORK

Whether scientific research is basic science or applied science, scientists must share their findings in order for other researchers to expand and build upon their discoveries. Collaboration with other scientists—when planning, conducting, and analyzing results—is important for scientific research. For this reason, important aspects of a scientist's work are communicating with peers and disseminating results to peers. Scientists can share results by presenting them at a scientific meeting or conference, but this approach can reach only the select few who are present. Instead, most scientists present their results in peer-reviewed manuscripts that are published in scientific journals. Peer-reviewed manuscripts are scientific papers that a scientist's colleagues or peers review. These colleagues are qualified individuals, often experts in the same research area, who judge whether or not the scientist's work is suitable for publication. The process of peer review helps to ensure that the research in a scientific paper or grant proposal is original, significant, logical, and thorough. Grant proposals, which are requests for research funding, are also subject to peer review. Scientists publish their work so other scientists can reproduce their experiments under similar or different conditions to expand on the findings.

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1.3: Structural Organization of the Human Body

Learning Objectives

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

- 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 1.3.1).

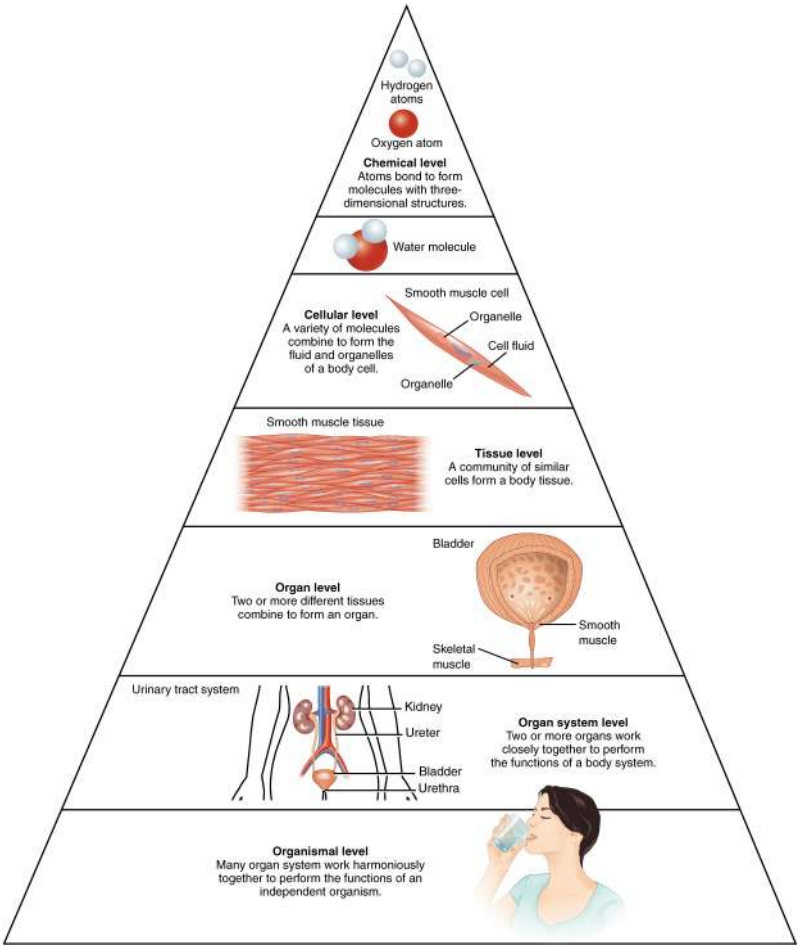


Figure 1.3.1: Levels of Structural Organization of the Human Body The organization of the body often is discussed in terms of six distinct levels of increasing complexity, from the smallest chemical building blocks to a unique human organism.

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 1.3.2and Figure 1.3.3). 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.

In this book and throughout your studies of biological sciences, you will often read descriptions related to similarities and differences among biological structures, processes, and health related to a person's biological sex. People often use the words "female" and "male" to describe two different concepts: our sense of gender identity, and our biological sex as determined by our chromosomes, hormones, organs, and other physical characteristics. For some people, gender identity is different from biological sex or their sex assigned at birth. Throughout this book, "female" and "male" refer to sex only, and the typical anatomy and physiology of XX and XY individuals is discussed.

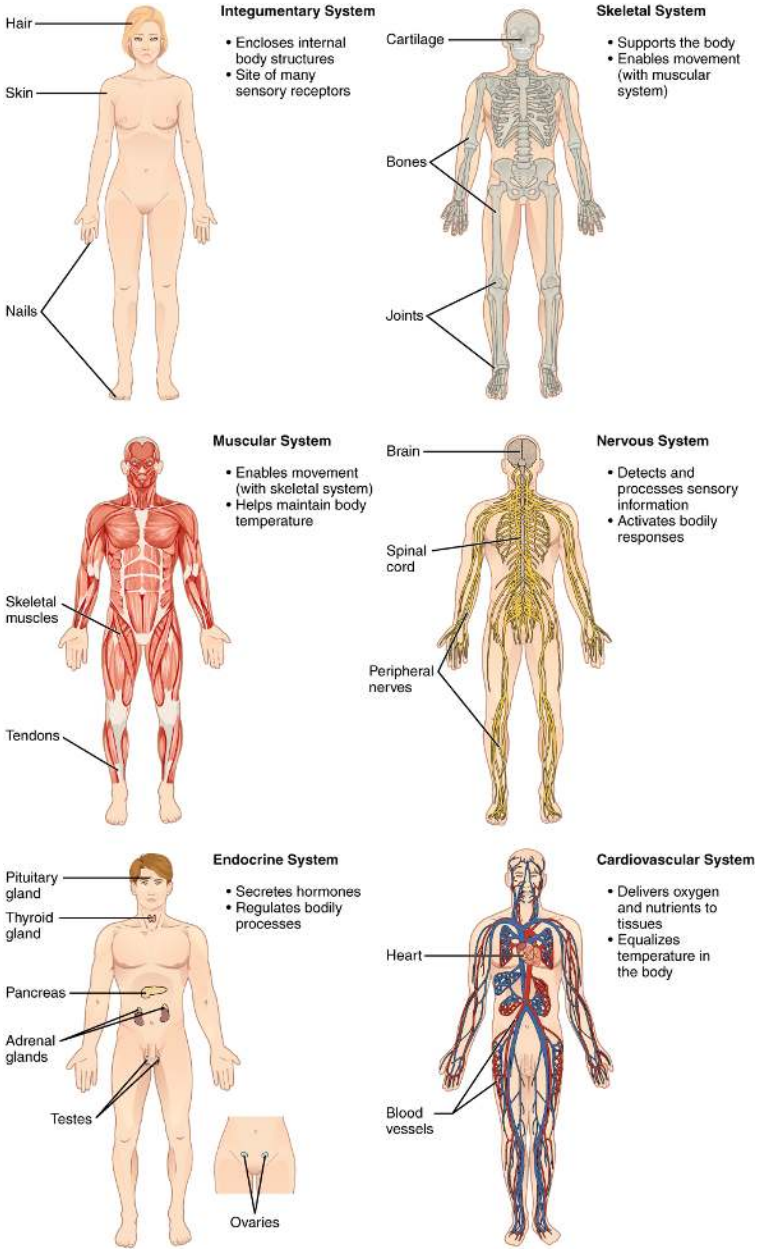
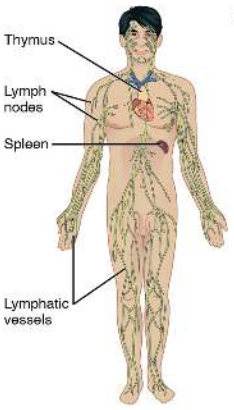
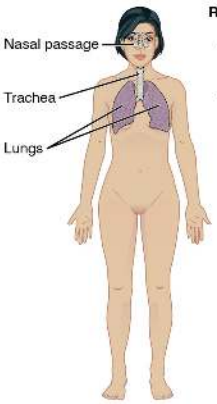

Hair
Skin
Nails
Integumentary System
• Encloses internal body structures
• Site of many sensory receptors
Cartilage
Bones
Joints
Skeletal System
• Supports the body
• Enables movement (with muscular system)
Skeletal muscles
Tendons
Muscular System
• Enables movement (with skeletal system)
• Helps maintain body temperature
Brain
Spinal cord
Peripheral nerves
Nervous System
• Detects and processes sensory information
• Activates bodily responses
Pituitary gland
Thyroid gland
Pancreas
Adrenal glands
Testes
Ovaries
Endocrine System
• Secretes hormones
• Regulates bodily processes
Heart
Blood vessels
Cardiovascular System
• Delivers oxygen and nutrients to tissues
• Equalizes temperature in the body

Figure 1.3.2:Organ Systems of the Human Body Organs that work together are grouped into organ systems.



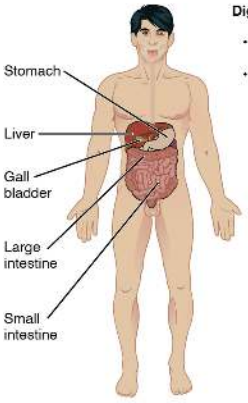
Lymphatic System

- Returns fluid to blood
- Defends against pathogens



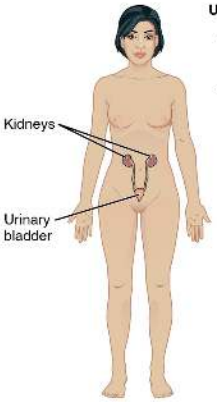
Respiratory System

- Removes carbon dioxide from the body
- Delivers oxygen to blood



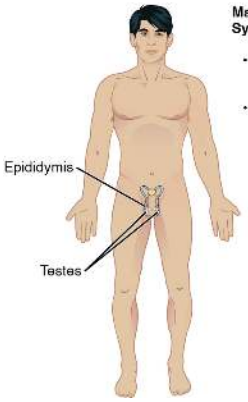
Digestive System

- Processes food for use by the body
- Removes wastes from undigested food



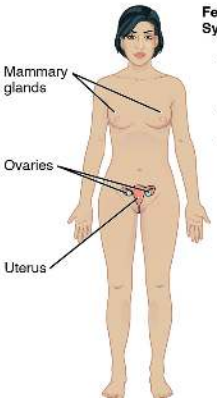
Urinary System

- Controls water balance in the body
- Removes wastes from blood and excretes them



Male Reproductive System

- Produces sex hormones and gametes
- Delivers gametes to female



Female Reproductive System

- Produces sex hormones and gametes
- Supports embryo/fetus until birth
- Produces milk for infant

Figure 1.3.3: 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.

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1.4: Homeostasis

Learning Objectives

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

- Discuss the role of homeostasis in healthy functioning
- Contrast negative and positive feedback, giving one physiologic example of each mechanism

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 and other parts of the body monitor and react to deviations from homeostasis using negative feedback. **Negative feedback** is a mechanism that reverses a deviation from the set point. Therefore, negative feedback maintains body parameters within their normal range. 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 1.4.1). 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.

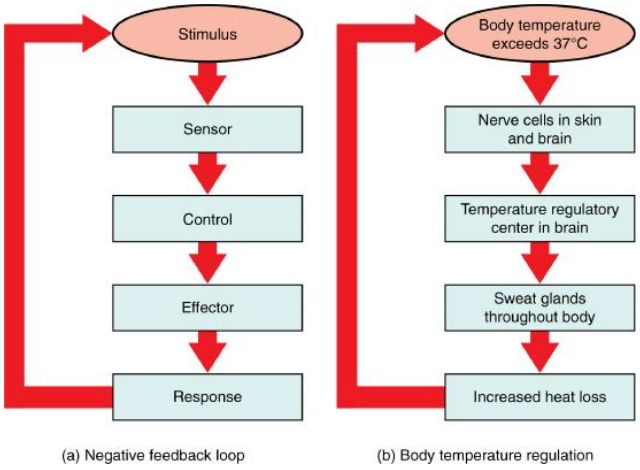


Figure 1.4.1: Negative Feedback System In a negative feedback system, a stimulus—a deviation from a set point—is resisted through a physiological process that returns the body to homeostasis. (a) A negative feedback system has five basic parts. (b) Body temperature is regulated by negative feedback.

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 1.4.1). 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.
- 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 (an energy molecule in the body). 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 (sugar), which can be used as an energy source. The breakdown of glycogen into glucose also results in increased metabolism and heat production.

Interactive Link

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. Which organ has 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 a person’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 a person giving birth and the baby are at risk. The extreme muscular work of labor and delivery are the result of a positive feedback system (Figure 1.4.2).

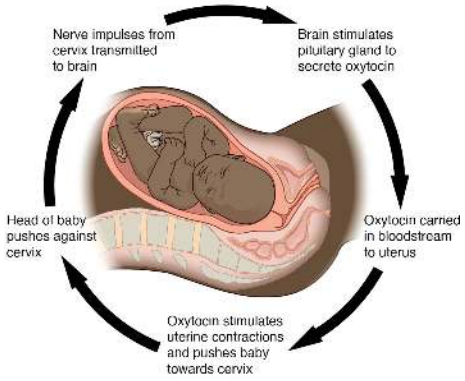


Figure 1.4.2: Positive Feedback Loop Normal childbirth is driven by a positive feedback loop. A positive feedback loop results in a change in the body’s status, rather than a return to homeostasis.

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.

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1.5: Anatomical Terminology

Learning Objectives

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

- 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 1.12. 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.

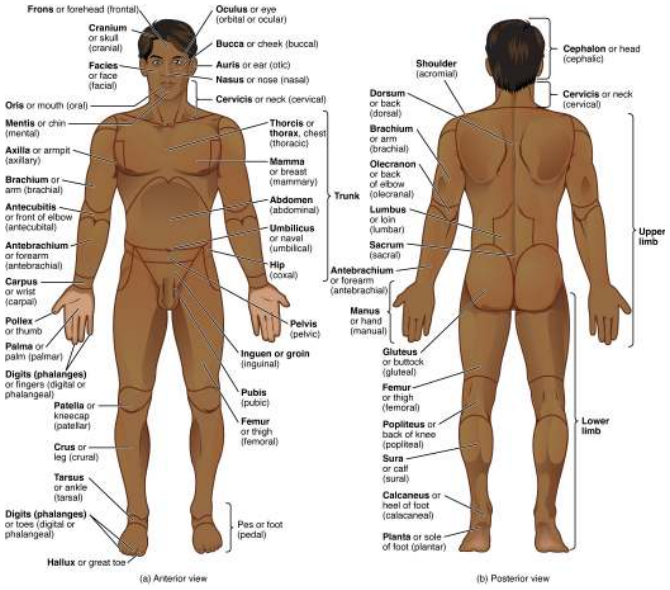


Figure 1.5.1: Regions of the Human Body The human body is shown in anatomical position in an (a) anterior view and a (b) posterior view. The regions of the body are labeled in boldface.

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 1.12). 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.

Directional Terms

Certain directional anatomical terms appear throughout this and any other anatomy textbook (Figure 1.13). 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.

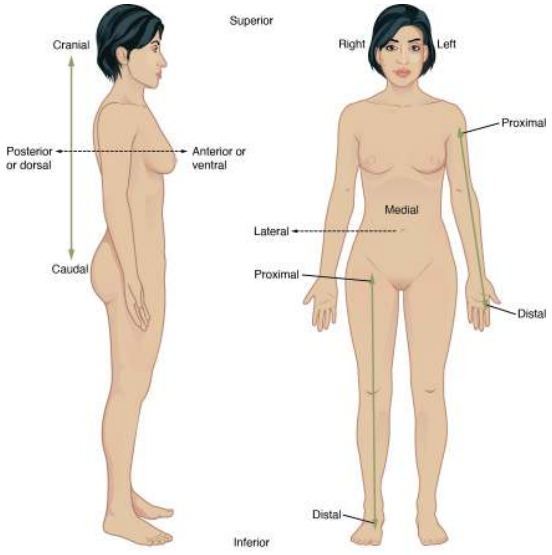


Figure 1.5.2: Directional Terms Applied to the Human Body Paired directional terms are shown as applied to the human body.

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 1.14.

- 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.

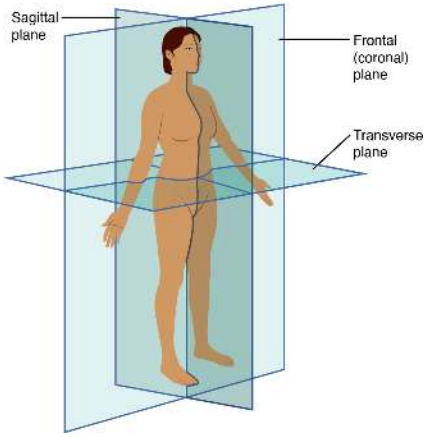


Figure 1.5.3: Planes of the Body The three planes most commonly used in anatomical and medical imaging are the sagittal, frontal (or coronal), and transverse plane.

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 1.15). 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.

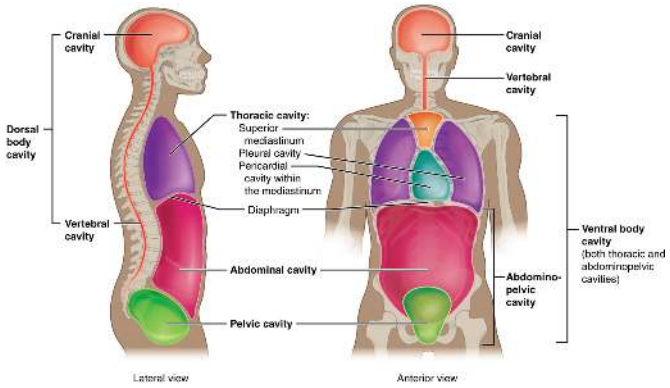


Figure 1.5.4: Dorsal and Ventral Body Cavities The ventral cavity includes the thoracic and abdominopelvic cavities and their subdivisions. The dorsal cavity includes the cranial and spinal cavities.

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1.6: Review Questions

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CHAPTER OVERVIEW

2: A Brief Overview of Chemistry

2.1: Elements and Atoms - The Building Blocks of Matter
2.2: Chemical Bonds
2.3: Inorganic Compounds Essential to Human Functioning
2.4: Review Questions

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2.1: Elements and Atoms - The Building Blocks of Matter

Learning Objectives

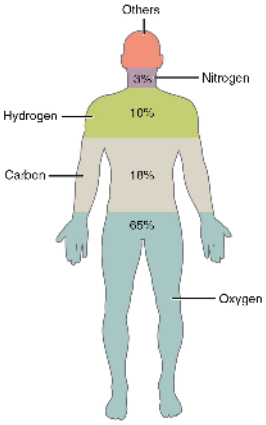
By the end of this section, you will be able to:

- Discuss the relationships between matter, mass, elements, compounds, atoms, and subatomic particles
- Distinguish between atomic number and mass number

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.

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 Figure 2.1.1, 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.



Element	Symbol	Percentage in Body
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

Figure 2.1.1: Elements of the Human Body The main elements that compose the human body are shown from most abundant to least abundant.

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.

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 protons determines 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.

Figure 2.1.2 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.

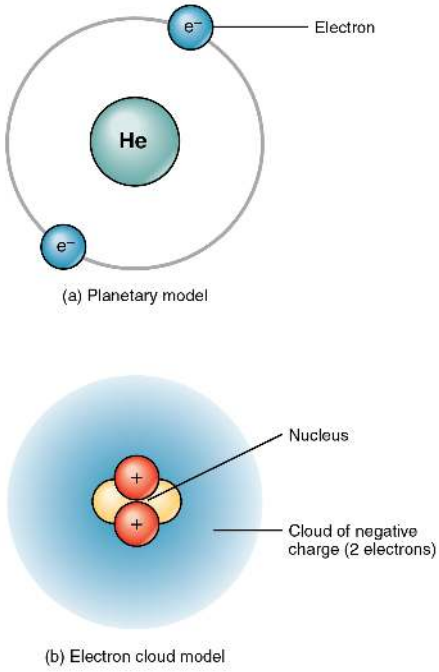


Figure 2.1.2: Two Models of Atomic Structure (a) In the planetary model, the electrons of helium are shown in fixed orbits, depicted as rings, at a precise distance from the nucleus, somewhat like planets orbiting the sun. (b) In the electron cloud model, the electrons of helium are shown in the variety 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 2.1.3, 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.

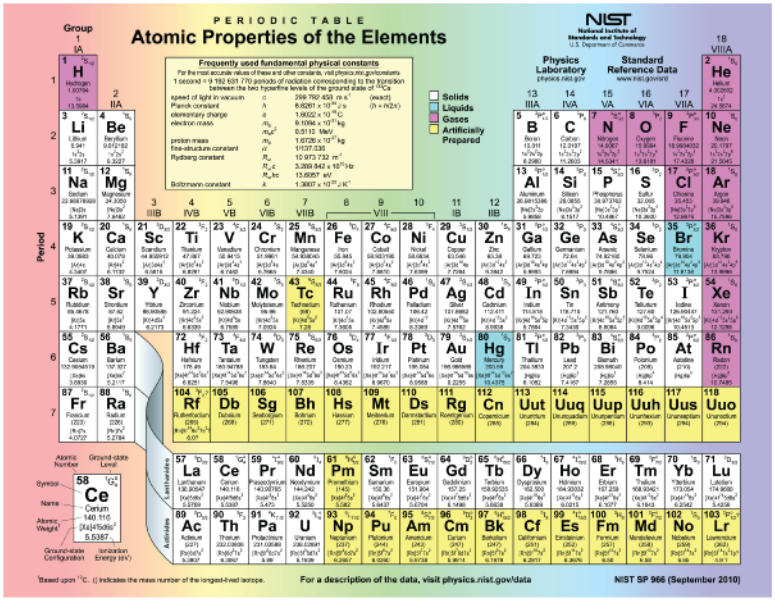


Figure 2.1.3: The Periodic Table of the Elements (credit: R.A. Dragoset, A. Musgrove, C.W. Clark, W.C. Martin)

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2.2: Chemical Bonds

Learning Objectives

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

- 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 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.

Usually atoms want to have 8 electrons orbiting around them, so chemical bonds will occur so that atoms can fulfill this requirement.

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. An atom that has an electrical charge—whether positive or negative—is an **ion**.

Interactive Link

Visit this website 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?

Potassium (K), for instance, is an important element in all body cells. Its atomic number is 19. It has just one electron. This characteristic makes potassium highly likely to participate in chemical reactions in which it donates one electron. The resulting potassium ion after donating this electron 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. 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). Fluorine will now have 8 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 2.2.1 , 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.

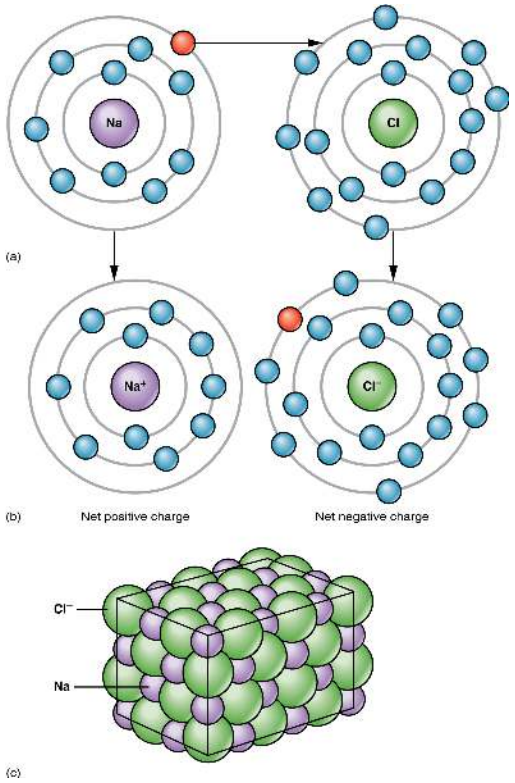


Figure 2.2.1 **Ionic Bonding:** (a) Sodium readily donates the solitary electron in its valence shell to chlorine, which needs only one electron to have a full valence shell. (b) The opposite electrical charges of the resulting sodium cation and chloride anion result in the formation of a bond of attraction 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 2.2.2: 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 two atoms' overlapping atomic orbitals are shared to satisfy the electron requirement of both atoms, ultimately stabilizing both of the atoms involved. In a single covalent bond, a single electron pair 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 electron pairs are shared between two atoms.

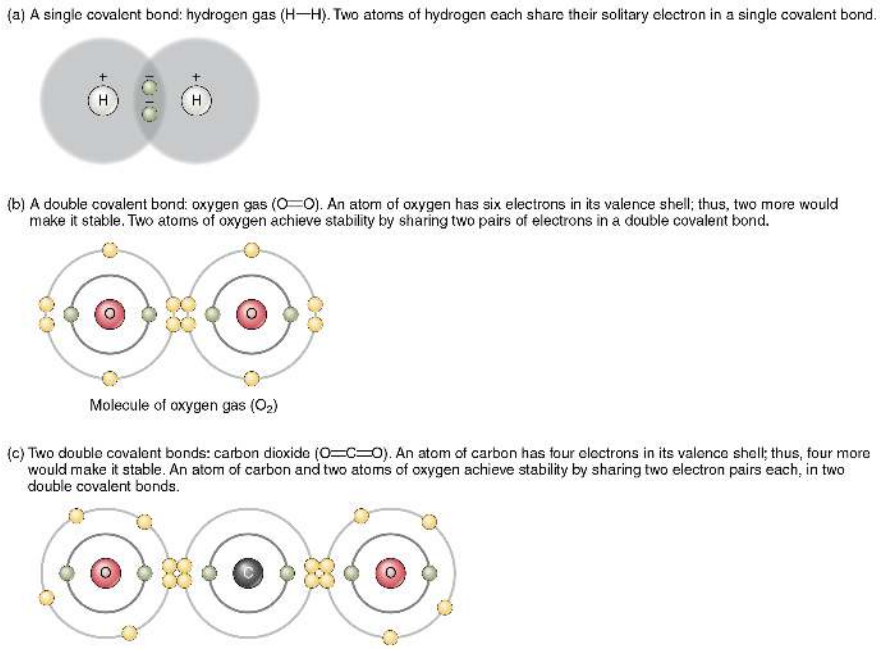


Figure 2.2.2: Covalent Bonding

You can see that the covalent bonds shown in Figure 2.2.2 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

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 2.2.3:). 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.

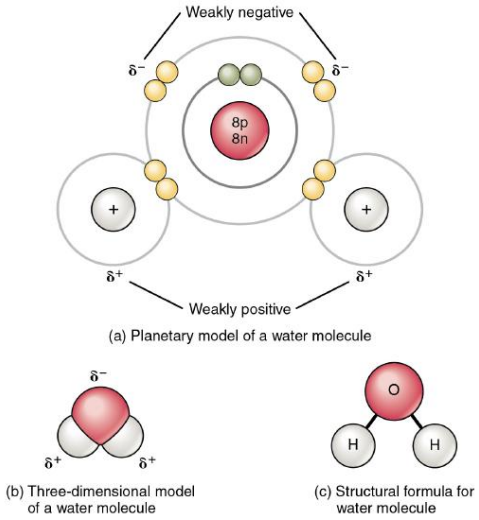


Figure 2.2.3: Polar Covalent Bonds in a Water Molecule

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 2.2.3:, regions of weak polarity are indicated with the Greek letter delta (δ) 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 (Figure 2.2.3). 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 2.2.4:).

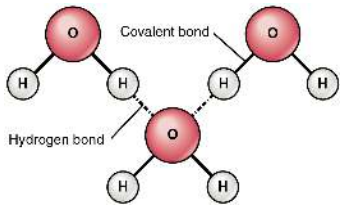


Figure 2.2.4: Hydrogen Bonds between Water Molecules Notice that the bonds occur between the weakly positive charge on the hydrogen atoms and the weakly negative charge on the oxygen atoms. Hydrogen bonds are relatively weak, and therefore are indicated with a dotted (rather than a solid) line.

Hydrogen bonds are also easily broken. When you splash around or jump into a pool, you are breaking hydrogen bonds. However, these hydrogen bonds immediately reform with the other water molecules around them.

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). The positively charged Na^+ in NaCl is attracted to the partially-negative O^- in a water molecule. The negatively charged Cl^- is attracted to the weakly partially-positive H^+ in a water molecule, forming hydrogen bonds with it. Molecules, such as ions, that easily form hydrogen bonds with water are considered **hydrophilic** molecules. They are "water loving", and this is the reason salt easily dissolves in water.

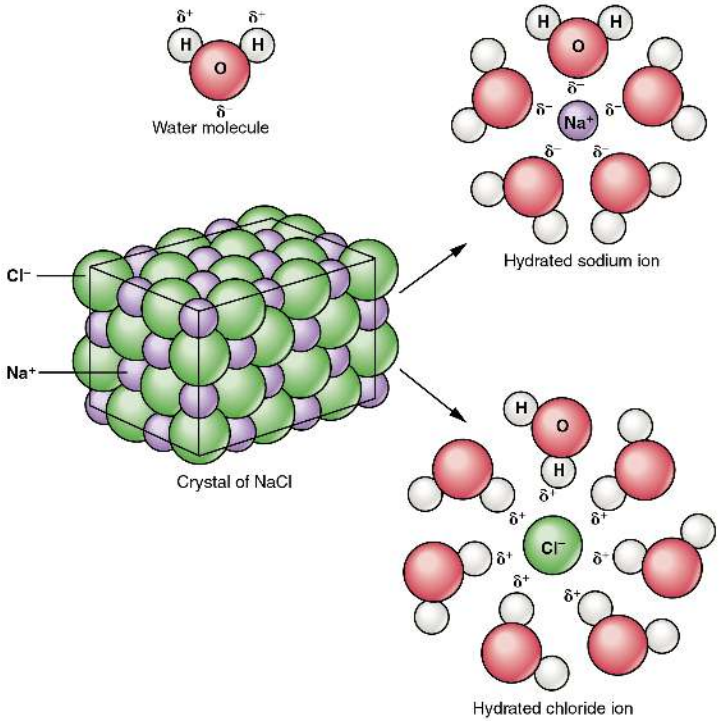


Figure 2.2.5 Hydrophilic molecules: NaCl (salt) easily dissolves in water as Na^+ is attracted to the negatively charged O^- and Cl^- is attracted to the positively charged H^+ of a water (H_2O) molecule.

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. Molecules, such as fats, are **hydrophobic** molecules. They are "water hating" or "water repelling" as they do not form hydrogen bonds with water.

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2.3: Inorganic Compounds Essential to Human Functioning

Learning Objectives

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

- Compare and contrast inorganic and organic compounds
- Identify the properties of water that make it essential to life
- 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. Carbon and hydrogen are the second and third most abundant elements in your body.

The following section examines the three groups of inorganic compounds essential to life: water, acids, and bases.

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 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.

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 2.3.1). This is also sometimes referred to as a condensation reaction.
- These reactions are reversible, and play an important role in the chemistry of organic compounds (which will be discussed shortly).

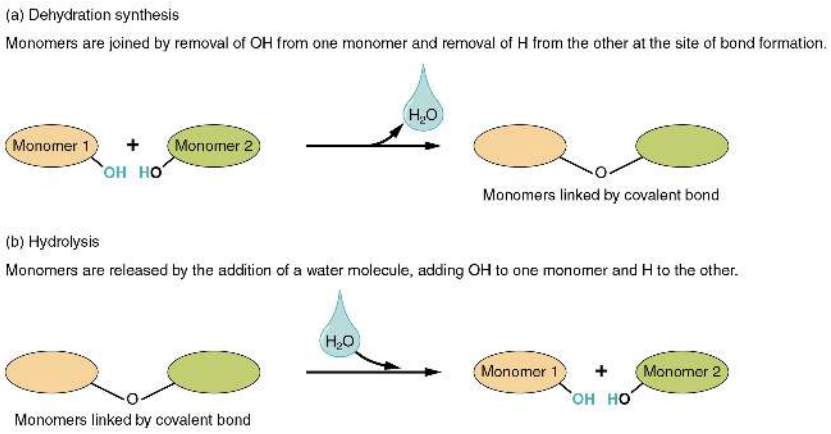


Figure 2.3.1: Dehydration Synthesis and Hydrolysis Monomers, the basic units for building larger molecules, form polymers (two or more chemically-bonded monomers). (a) In dehydration synthesis, two monomers are covalently bonded in a reaction in which one gives up a hydroxyl group and the other a hydrogen 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.

Acids and Bases

Acids and bases, like salts, dissociate in water into ions or 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 (\PageIndex{2}\)**a**). 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 hydrogen ions remain 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.

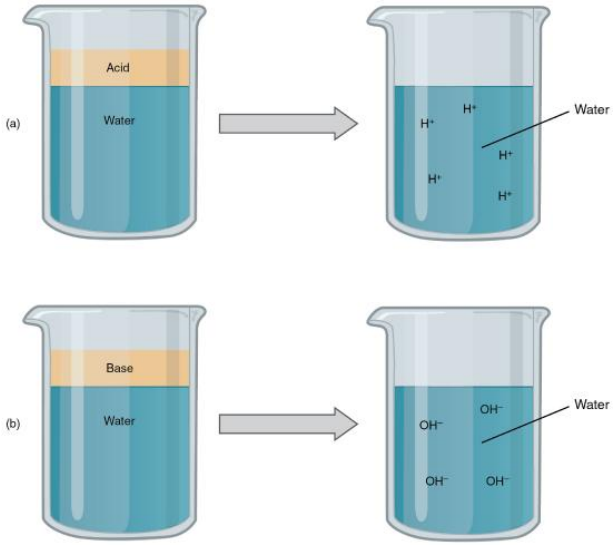


Figure 2.3.2:Acids and Bases (a) In aqueous solution, an acid dissociates into hydrogen ions (H^+) and anions. Nearly every molecule of a strong acid dissociates, producing a high concentration of H^+. (b) In aqueous solution, a base dissociates into hydroxyl ions (OH^-) and cations. Nearly every molecule 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 2.3.2**b**). The hydroxyl ions (also known as hydroxide ions) or other basic substances 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 2.3.3. 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.

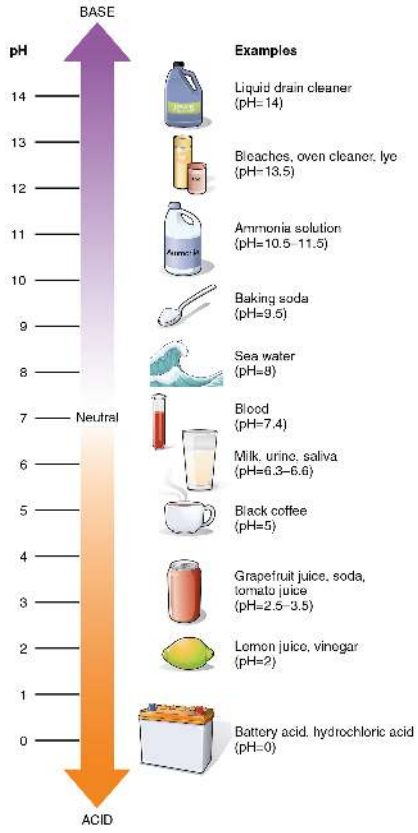


Figure 2.3.3: The pH Scale

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.

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2.4: Review Questions

Use the following questions to test your knowledge on Chemistry.

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CHAPTER OVERVIEW

3: Cell Structure

3.1: The Cell Membrane
3.2: The Cytoplasm and Cellular Organelles
3.3: The Nucleus and DNA
3.4: Cell Transport and Osmosis
3.5: Review Questions

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3.1: The Cell Membrane

Learning Objectives

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

- Describe the molecular components that make up the cell membrane
- Explain the major features and properties of the cell membrane

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 a **phospholipid bilayer** ("two layers"). 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 3.1.1). 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**. 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.

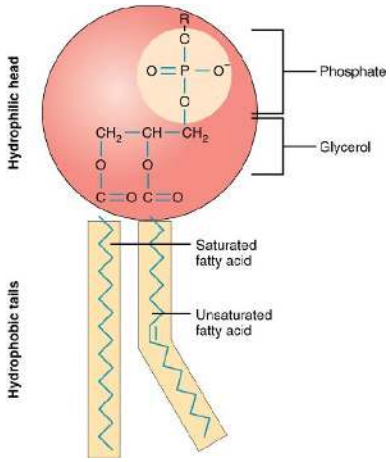


Figure 3.1.1: Phospholipid Structure A phospholipid molecule consists of a polar phosphate “head,” which is hydrophilic and a non-polar lipid “tail,” which is hydrophobic. Unsaturated fatty acids result in kinks in the hydrophobic tails.

The cell membrane consists of two adjacent layers of phospholipids (a bilayer). 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 3.1.2:). 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.

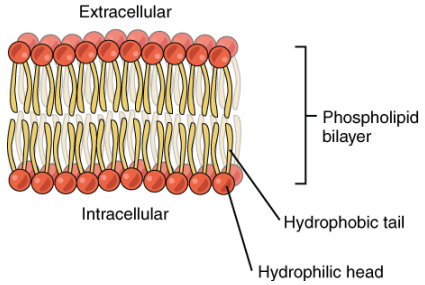


Figure 3.1.2: Phospholipid Bilayer The phospholipid bilayer consists of two adjacent sheets of phospholipids, arranged tail to tail. The hydrophobic tails associate with one another, forming the interior of the membrane. The polar heads contact the fluid inside and outside of the cell.

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 proteins** (Figure 3.1.3). 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.

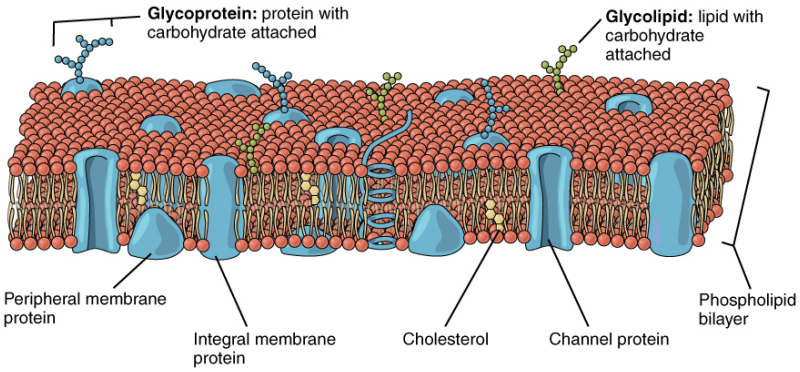


Figure 3.1.3: Cell Membrane The cell membrane of the cell is a phospholipid bilayer containing many different molecular components, including proteins and cholesterol, some with carbohydrate groups attached.

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 receptor protein opens to allow certain ions to flow into the cell.

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3.2: The Cytoplasm and Cellular Organelles

Learning Objectives

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

- 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

Now that you have learned that the cell membrane surrounds all cells, you can dive inside of a 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 3.2.1).

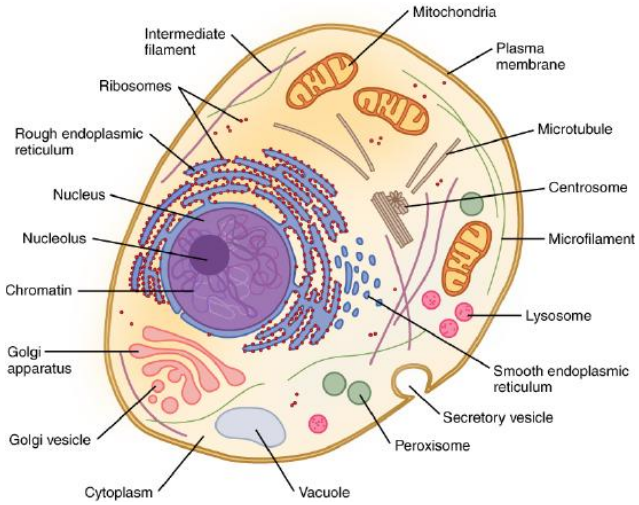


Figure 3.2.1: Prototypical Human Cell While this image is not indicative of any one particular human cell, it is an example of a cell containing the primary organelles and internal structures.

Human cells are **eukaryotic** cells. A eukaryotic cells has DNA enclosed within a nucleus and organelles that perform specialized functions for the cell. The word eukaryote comes from Greek meaning "true nucleus". This is in contrast to **prokaryotic** cells. Prokaryotic cells have DNA but do not have a nucleus that holds that DNA. Instead the DNA is usually found freely within the cytoplasm. Prokaryotic cells also do not contain organelles. An example of a prokaryotic organism is bacteria. The word prokaryote comes from Greek meaning "before (the) nucleus" as prokaryotic cells existed before eukaryotic cells arose.

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 th**e 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 3.2.2).

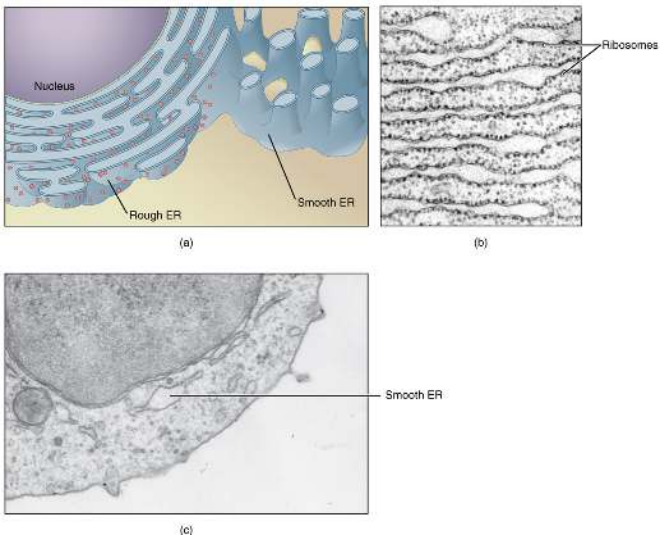


Figure 3.2.2: Endoplasmic Reticulum (ER) (a) The ER is a winding network of thin membranous sacs found in close association with the cell nucleus. The smooth and rough endoplasmic reticula are very different in appearance and function (source: mouse tissue). (b) Rough ER is studded with numerous ribosomes, 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**. 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^{2+}, a function extremely important in cells of the nervous system where Ca^{2+} 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. The Golgi apparatus has two distinct sides, each with a different role. One side of the apparatus receives products in vesicles from the RER, for example. 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 3.2.3).

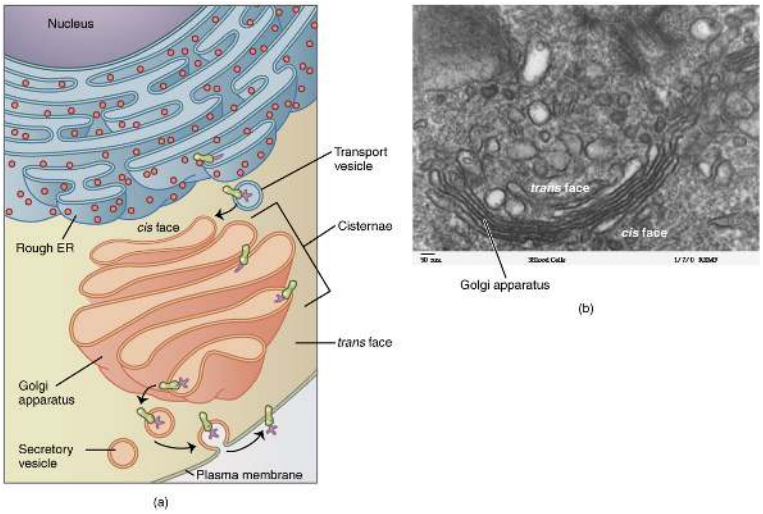


Figure 3.2.3: Golgi Apparatus (a) The Golgi apparatus manipulates products from the rough ER, and also produces new organelles called lysosomes. Proteins and other products of the ER are sent to the Golgi apparatus, which organizes, modifies, packages, and tags them. Some of these products are transported 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) eat up bacteria, the bacterial cell is transported into a lysosome and digested by the enzymes inside. As one might imagine, such certain white blood cells contain large numbers of lysosomes for this reason.

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").

Interactive Link

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?

Organelles for Energy Production

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.

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 3.2.4). 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.

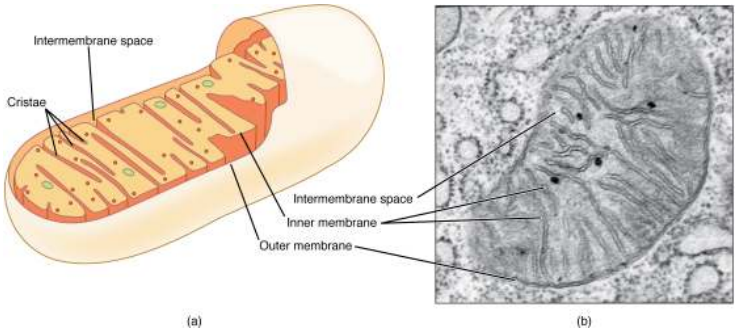


Figure 3.2.4:Mitochondrion The mitochondria are the energy-conversion factories of the cell. (a) A mitochondrion is composed of two separate lipid bilayer membranes. Along the inner membrane are various molecules that work together to produce ATP, the cell’s major energy currency. (b) An electron micrograph of mitochondria. EM × 236,000. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

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.

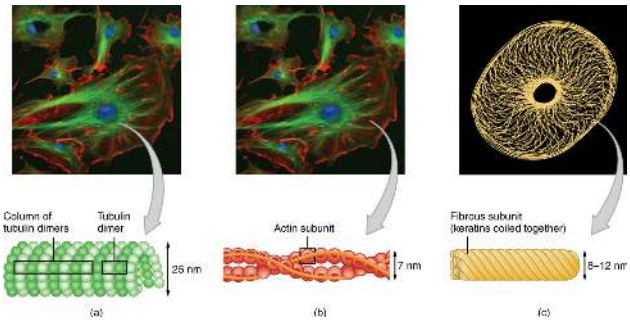


Figure 3.2.6: The Three Components of the Cytoskeleton The cytoskeleton consists of (a) microtubules, (b) microfilaments, and (c) intermediate filaments. The cytoskeleton plays an important role in maintaining cell shape and structure, promoting cellular movement, and aiding cell division.

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3.3: The Nucleus and DNA

Learning Objectives

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

- 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

The **nucleus** is the largest and most prominent of a cell's organelles (Figure 3.3.1). 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 3.3.2), making muscle cells multinucleated cells. 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 3.3.3). Without nuclei, the life span of RBCs is short, and so the body must produce new ones constantly.

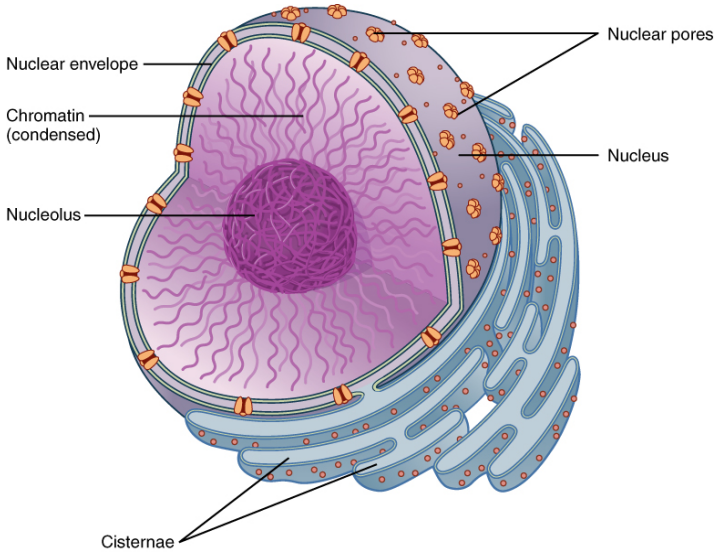


Figure 3.3.1 The Nucleus: The nucleus is the control center of the cell. The nucleus of living cells contains the genetic material that determines the entire structure and function of that cell.

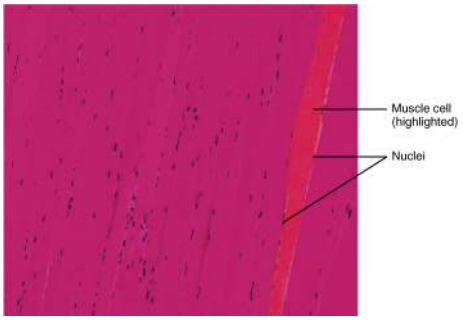


Figure 3.3.2 Multinucleate Muscle Cell: Unlike cardiac muscle cells and smooth muscle cells, which have a single nucleus, a skeletal muscle cell contains many nuclei, and is referred to as "multinucleated." These muscle cells are long and fibrous (often referred to as muscle fibers). During development, 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)

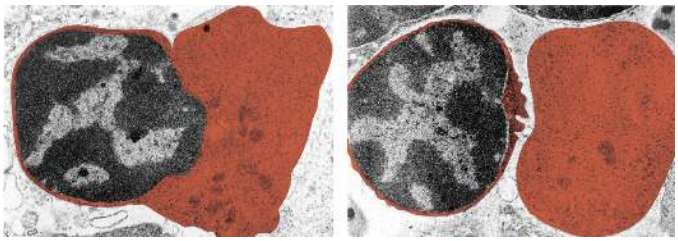


Figure 3.3.3 Red Blood Cell Extruding Its Nucleus: Mature red blood cells lack a nucleus. As they mature, erythroblasts (a precursor to a red blood cell) extrude their nucleus, making room for more hemoglobin. The two panels here show an erythroblast before and after ejecting its nucleus, respectively. (credit: modification of micrograph provided by the Regents of University of Michigan Medical School © 2012)

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.

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 3.3.4). 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.

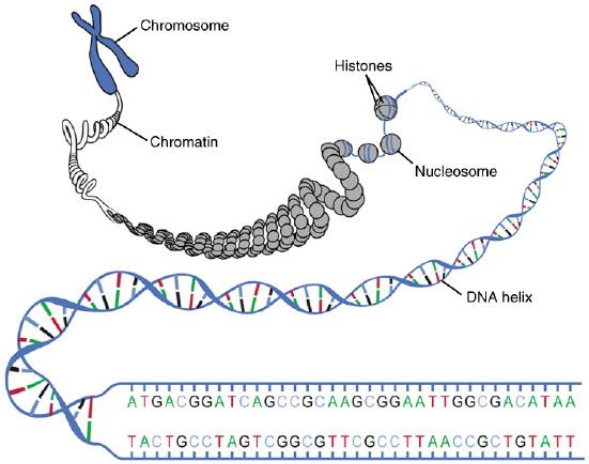


Figure 3.3.4: DNA Macrostructure Strands of DNA are wrapped around supporting histones. These proteins are increasingly bundled and condensed into chromatin, which is packed tightly into chromosomes when the cell is ready to divide.

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3.4: Cell Transport and Osmosis

Learning Objectives

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

- 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

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^{2+}, 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).** This concept of concentration gradients is a **KEY CONCEPT** across physiology and will appear again and again!

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.

Interactive Link

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 outside the cell directly through the lipid bilayer of the cell 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 inside the cell through the lipid bilayer and into the interstitial fluid outside the cell, where its concentration is lower. This mechanism of molecules moving across a cell membrane from the side where they are more concentrated to the side where they are less concentrated is a form of passive transport called **simple diffusion** (Figure 3.4.1).

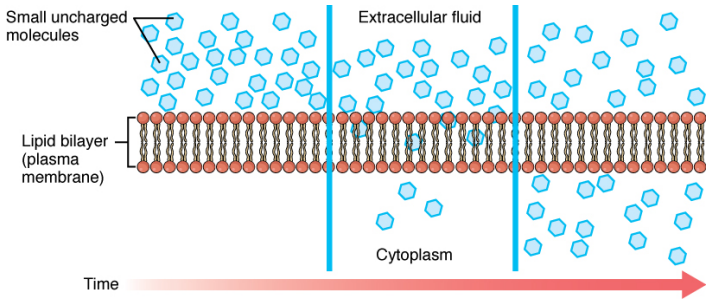


Figure 3.4.1 Simple Diffusion: across the Cell (Plasma) Membrane The structure of the lipid bilayer allows small, uncharged substances such as oxygen and carbon dioxide, and hydrophobic molecules such as lipids, to pass through the cell membrane, down their concentration gradient, by simple diffusion.

Large polar or ionic molecules, which are hydrophilic, cannot easily cross the phospholipid bilayer. Very small polar molecules, such as water, can cross via simple diffusion due to their small size. Charged atoms or molecules of any size cannot cross the cell membrane via simple diffusion as the charges are repelled by the hydrophobic tails in the interior of the phospholipid bilayer. 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, charge, and/or polarity (Figure 3.4.2). Facilitated diffusion involves the use of a **protein channel** or **carrier protein** embedded within the cell membrane to transport these substances. 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 a glucose transporter will transfer glucose molecules into the cell to facilitate its inward diffusion.

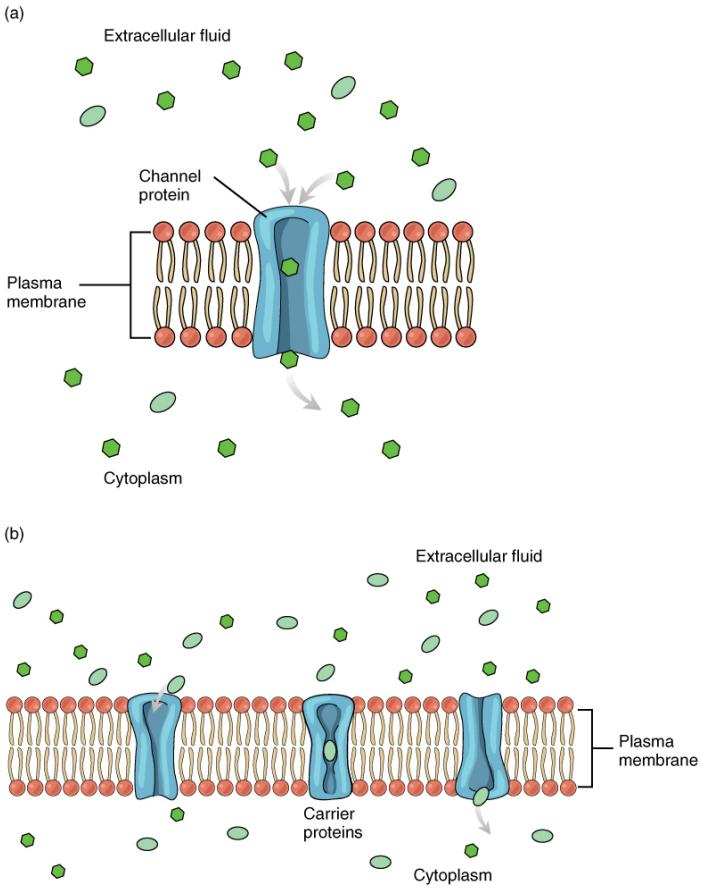


Figure 3.4.2 Facilitated Diffusion: (a) Facilitated diffusion of substances crossing the cell (plasma) membrane takes place with the help of proteins such as channel proteins and carrier proteins. Channel proteins are less selective than carrier proteins, and usually

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.

As an example, even though sodium ions (Na^+) are highly concentrated outside of cells, these ions are charged and cannot pass through the nonpolar lipid bilayer of the cell membrane. Their diffusion is facilitated by membrane proteins that form sodium channels 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 3.4.3).

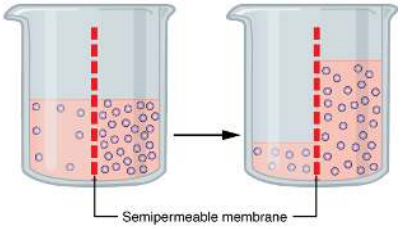


Figure 3.4.3 Osmosis: Osmosis is the diffusion of water through a semipermeable membrane down its concentration gradient. If a membrane is permeable to water, though not to a solute, water will equalize its own concentration by diffusing to the side of lower water concentration (and thus the side of 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 some cells, so it is important that these 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. **In osmosis, water will move from a solution of lower solute concentration towards the solution with the higher solute concentration**. This is another **KEY CONCEPT** of physiology that you should not forget.

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 3.4.4). For example, consider a cell that is submerged in a hypertonic solution. This means that the hypertonic solution has a higher concentration of solutes than the cell. The water inside the cell is attracted to the higher solute concentration in the hypertonic solution surrounding the cell. Water will leave the cell and move towards the hypertonic solution. 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. For example, consider a cell that is submerged in a hypotonic solution. This means that the hypotonic solution has a lower concentration of solutes than the cell. The water in the hypotonic solution surrounding the cell is attracted towards the higher solute concentration inside the cell. Water will leave the hypotonic solution and move inside the cell. 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.

> An **easy way to remember the difference between hypertonic and hypotonic** is to look at the words themselves. The "hyper" in hypertonic means "very high or excessive". The "hypo" in hypotonic means "low". Think of the "tonic" in these words as referring to the solute. So if you look at the word hypertonic, you can read it as "very high (hyper) solute (tonic)". For hypotonic, you can read it as "low (hypo) solute (tonic)".

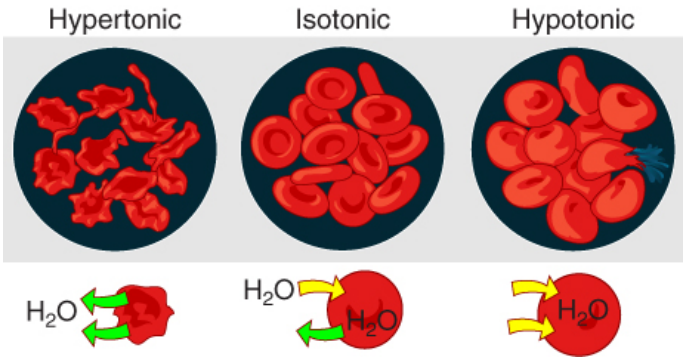


Figure 3.4.4: Concentration of Solutions A hypertonic solution has a solute concentration higher than another solution. An isotonic solution has a solute concentration equal to another solution. A hypotonic solution has a solute concentration lower than another solution.

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 Na^+/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 3.4.5). This process is so important for nerve cells that it accounts for the majority of their ATP usage.

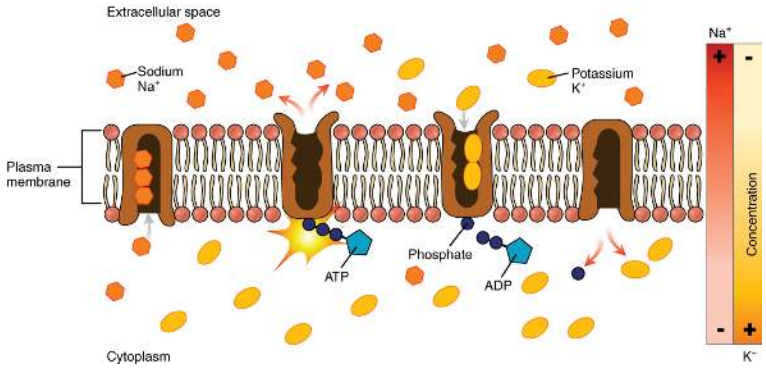


Figure 3.4.5: Sodium-Potassium Pump The sodium-potassium pump is found in many cell (plasma) membranes. Powered by ATP, the pump moves sodium and potassium ions in opposite directions, each against its concentration gradient. In a single cycle of the pump, three sodium ions are extruded from and two potassium ions are imported into the cell.

Active transport pumps can also work together with other active or passive transport systems to move substances across the membrane. For example, the sodium-potassium pump maintains a high concentration of sodium ions outside of the cell. Therefore, if the cell needs sodium ions, all it has to do is open a passive sodium channel, as the concentration gradient of the sodium ions will drive them to diffuse into the cell. In this way, the action of an active transport pump (the sodium-potassium pump) powers the passive transport of sodium ions by creating a concentration gradient. When active transport powers the transport of another substance in this way, it is called secondary active transport.

Other forms of active transport do not involve membrane carriers. **Endocytosis** (endo = into/inside, cyto = cell, "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 3.4.6). 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 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.

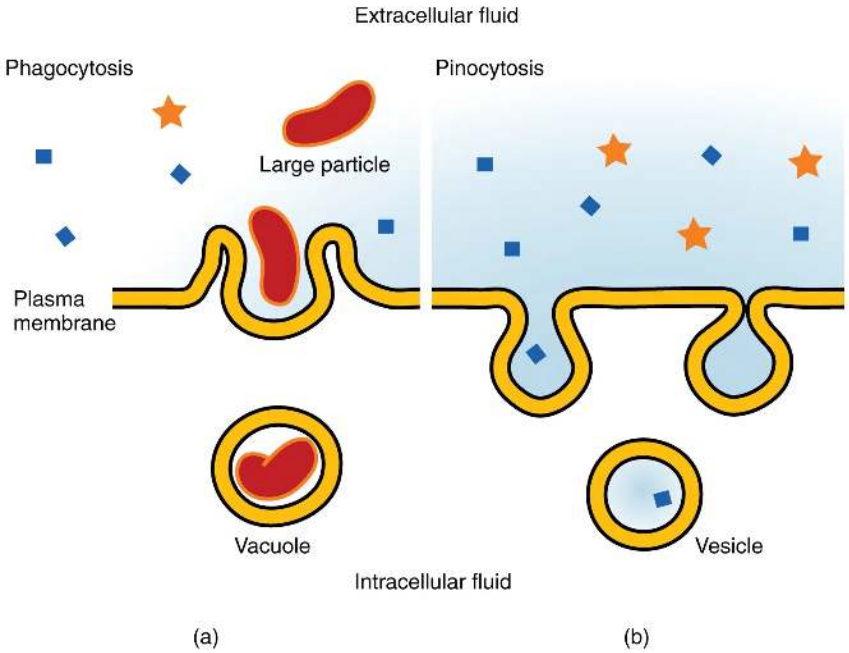


Figure 3.4.6 Three Forms of Endocytosis: Endocytosis is a form of active transport in which a cell envelopes extracellular materials using its cell membrane. (a) In phagocytosis, which is relatively nonselective, the cell takes in a large particle. (b) In pinocytosis, the cell takes in small particles in fluid. / Cropped from original

In contrast with endocytosis, **exocytosis** (exo = out/outside, cyto = cell, taking "out of the cell") is the process of a cell exporting material using vesicular transport (Figure 3.4.7). 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 outside of the cell. The vesicle membrane then becomes part of the cell membrane. Cells of the stomach and pancreas produce and secrete digestive enzymes through exocytosis (Figure 3.4.8). 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.

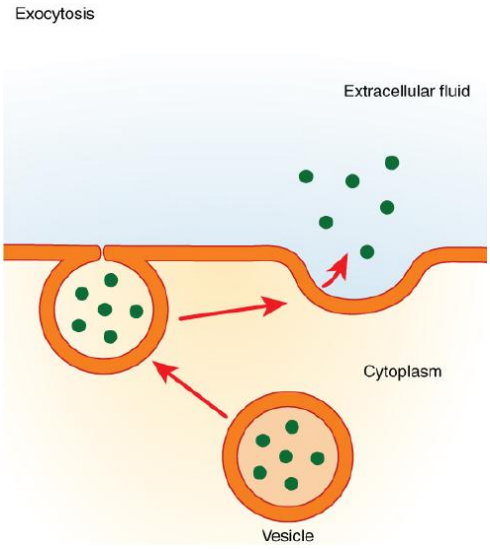


Figure 3.4.7 Exocytosis: Exocytosis is much like endocytosis in reverse. Material destined for export is packaged into a vesicle inside the cell. The membrane of the vesicle fuses with the cell membrane, and the contents are released into the extracellular space.

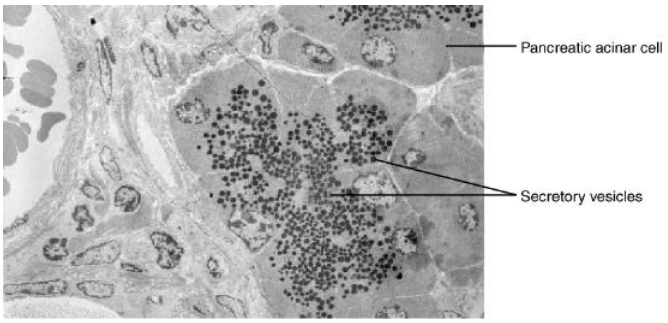


Figure 3.4.8*u* Pancreatic Cells' Enzyme Products: The pancreatic acinar cells produce and secrete many enzymes that digest food. The tiny black granules in this electron micrograph are secretory vesicles filled with enzymes that will be exported from the cells via exocytosis. LM × 2900. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

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.

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3.5: Review Questions

Use the following questions to test your knowledge on Cell Structure.

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CHAPTER OVERVIEW

4: Tissue Organization

4.1: Types of Tissues
4.2: Epithelial Tissue
4.3: Connective Tissue
4.4: Review Questions

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4.1: Types of Tissues

Learning Objectives

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

- Identify the four main tissue types
- Discuss the functions of each tissue type
- Relate the structure of each tissue type to their function

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

The four types of tissues are:

1. **Epithelial tissue**: Also referred to as epithelium. Epithelial tissue corresponds to the sheets of cells that cover exterior surfaces of the body, line internal cavities and passageways, and form certain glands.
2. **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.
3. **Muscle tissue:** Responds to nervous system stimulation and contracts to provide movement. There are three types of muscle tissue: skeletal, smooth, and cardiac. These will be explored in a future chapter.
4. **Nervous tissue:** Propagates electrochemical signals in the form of nerve impulses that communicate between different regions of the body (Figure 4.1.1).

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.

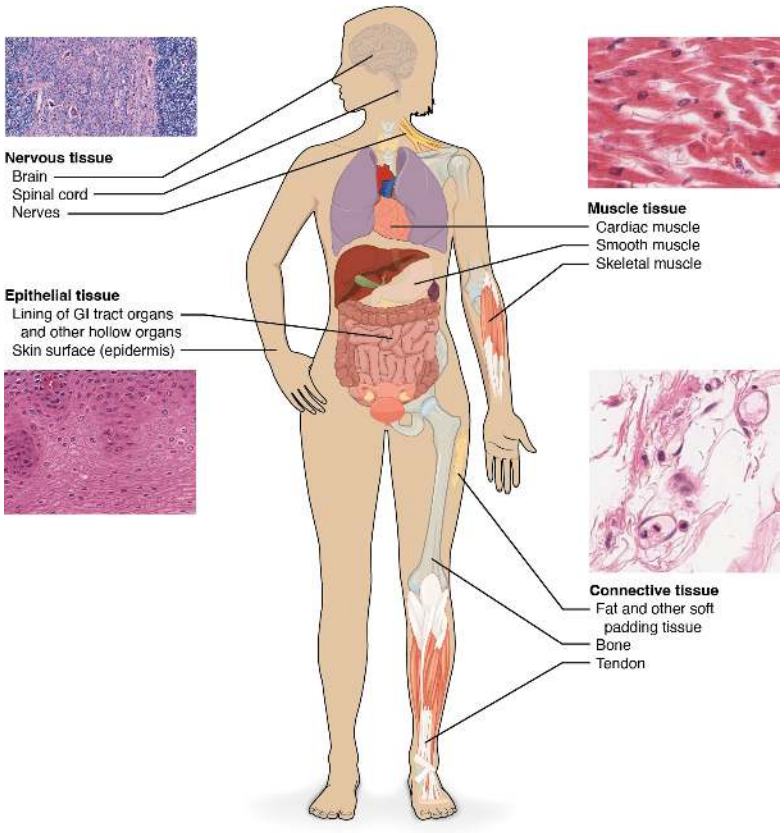


Figure 4.1.1: Four Types of Tissue: Body The four types of tissues are exemplified in nervous tissue, stratified squamous epithelial tissue, cardiac muscle tissue, and connective tissue. (Micrographs provided by the Regents of University of Michigan Medical School © 2012)

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, the pericardium that surrounds the heart), internal passageways that lead to the exterior of the body (for example, mucosa of

stomach), and the lining of the moveable joint cavities. There are two basic types of tissue membranes: connective tissue and epithelial membranes (Figure 4.1.3).

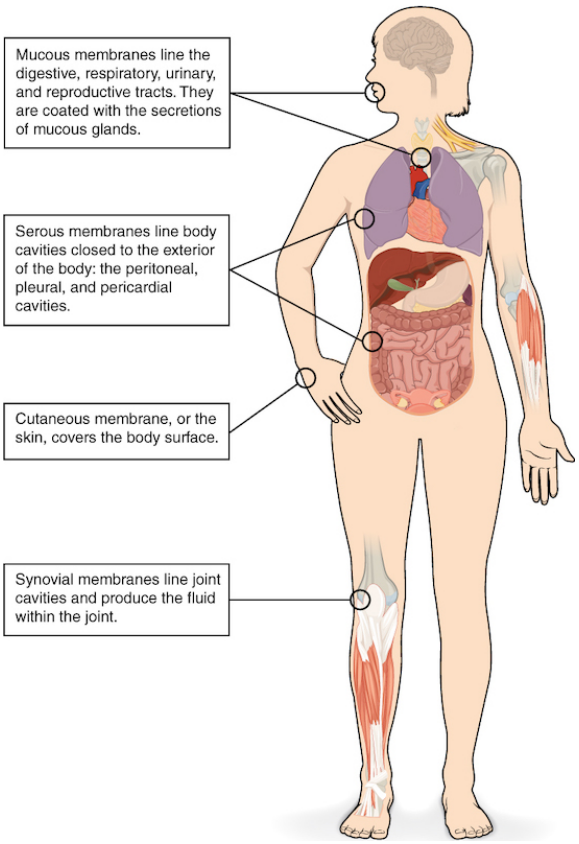


Figure 4.1.3: Tissue Membranes The two broad categories of tissue membranes in the body are (1) connective tissue membranes, which include synovial membranes, and (2) epithelial membranes, which include mucous membranes, serous membranes, and the cutaneous membrane, in other words, the skin.

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. Mucus, 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 with a layer called the mesothelium on the surface and supported by connective tissue. These membranes line body 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 based on their 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 c**utaneous 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.

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 (cells found within connective tissue) 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.

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4.2: Epithelial Tissue

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

- 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 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 the heart, are lined by endothelium (plural = endothelia), which is a type of epithelium.

Generalized Functions of Epithelial Tissue

- **Physical Protection:** Epithelial tissues provide the body's first line of protection from physical, chemical, and biological wear and tear.
- **Selective Permeability:** The cells of an epithelium can 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.
- **Secretion:** Many epithelial cells are capable of producing substances and releasing (secreting) them 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 may contain many secretory cells, such as the alpha and beta cells of the pancreas that produce hormones.
- **Sensation:** Some epithelial tissues also provide sensation. Nerve supply to epithelial tissues can alert the body to pressure, pain, and temperature from external or internal stimuli. This can help the body to maintain homeostasis or avoid harmful situations in the environment.

Epithelium Structure

Since epithelia are located at all free surfaces, they separate the outside of the body from the inside of the body and have distinct structural specializations that allow them to fulfill this unique role. Both the individual cells and the sheet of cells exhibit a characteristic polarity: they have an **apical surface** that is exposed and is in contact with the outside as well as a **basal surface** that is attached to an underlying proteinaceous layer called the **basement membrane**. This membrane allows the epithelial cells to hook onto one side of it and the underlying connective tissue, called the **lamina propria**, to attach to the other (Figure 4.2.1). This keeps the epithelium firmly anchored in place and helps prevent distortions and tearing.

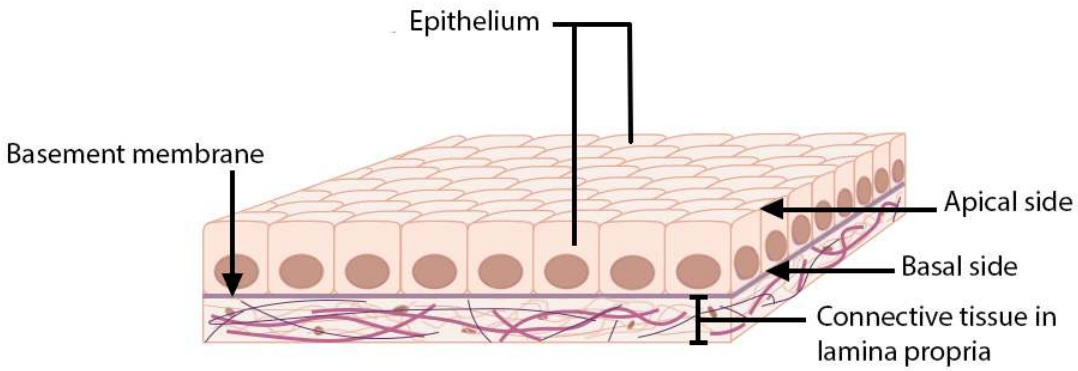


Figure 4.2.1: ABC's of an Epithelium. From the exterior toward the interior the structures of an epithelium are: **A**pical surface, **B**asal surface and **B**asement membrane, **C**onnective Tissue of the lamina propria. *(Image credit: "ABC's of an Epithelium" by Jennifer Lange is licensed under CC-BY-NC-SA 4.0, modified from original by Cancer Research UK via Wikimedia Commons.)*

Epithelial cells also have a 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. The transport channels within the cell membranes also differ between the two sides. For example, if you want to absorb a glucose molecule you need two transporters - one to bring the molecule into the cell on the apical side and another to kick it out of the cell so it can enter into the bloodstream. If both transporters were exactly the same you could only move sugar into the cell but not transport it to the rest of the body.

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 4.2.2).

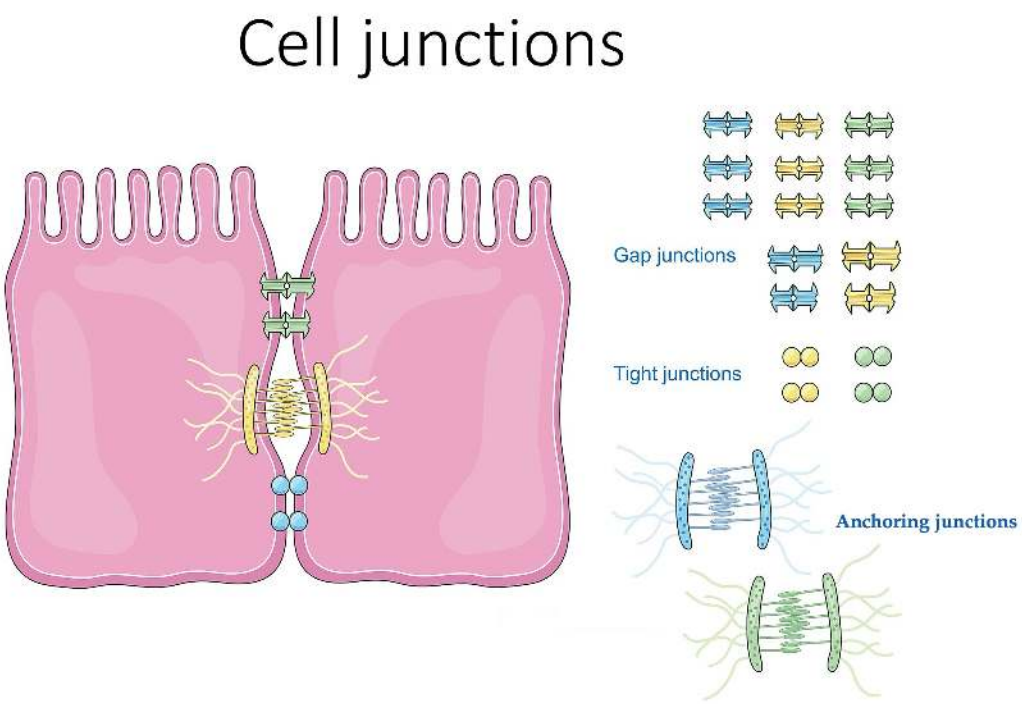


Figure 4.2.2 Types of Celll Junctions: The three types of cell junctions are gap junctions, tight junctions and anchoring junctions. *(Image credit: "*Cell junctions*" by Servier Medical Art, licensed under CC BY 4.0. via Wikimedia Commons) / Label modified by Harmony Folse*

- At one end of the spectrum is the **tight junction**, which separates the cells into apical and basal compartments. Tight junctions essentially "stitch" adjacent cell together, forming an impermeable barrier.
- 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.
- 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 4.2.3). 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 layer—where every cell rests on the basal lamina—called a **simple** epithelium, or more than one layer, called 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.

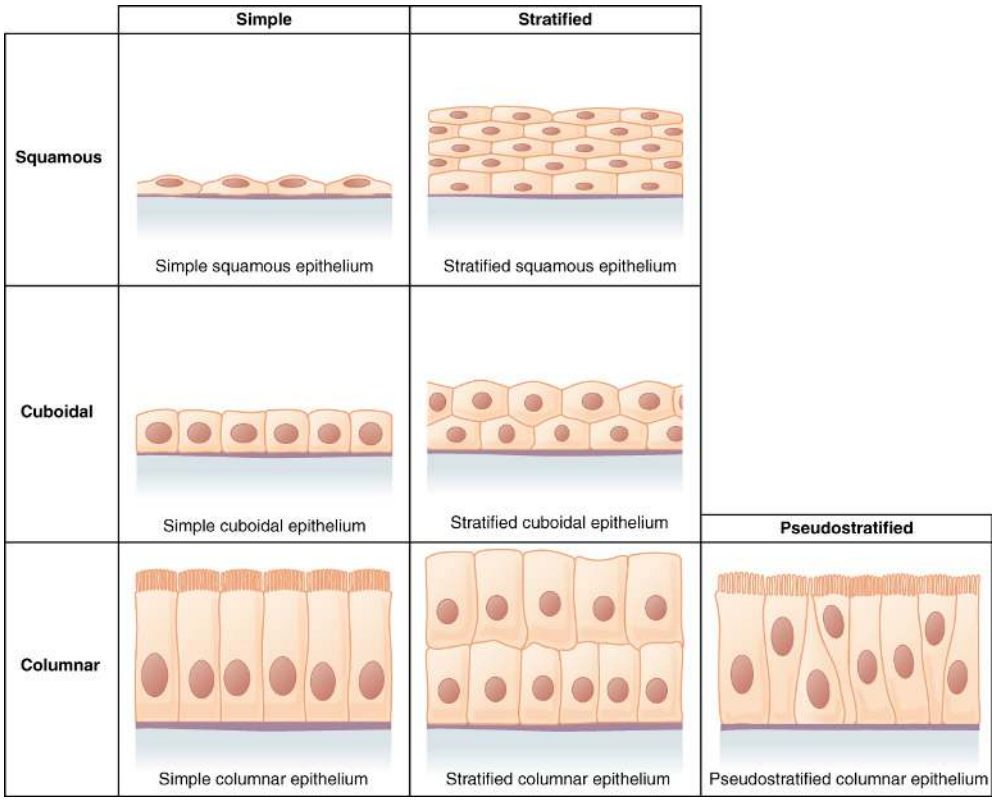


Figure 4.2.3: Epithelial Tissues. Simple epithelial tissue is organized as a single layer of cells and stratified epithelial tissue is formed by several layers of cells. *(Image credit: "Epithelial Tissue" by OpenStax is licensed under CC BY 3.0.)*

Simple Epithelia

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** (Figure 4.2.3 and Figure 4.2.4) 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.

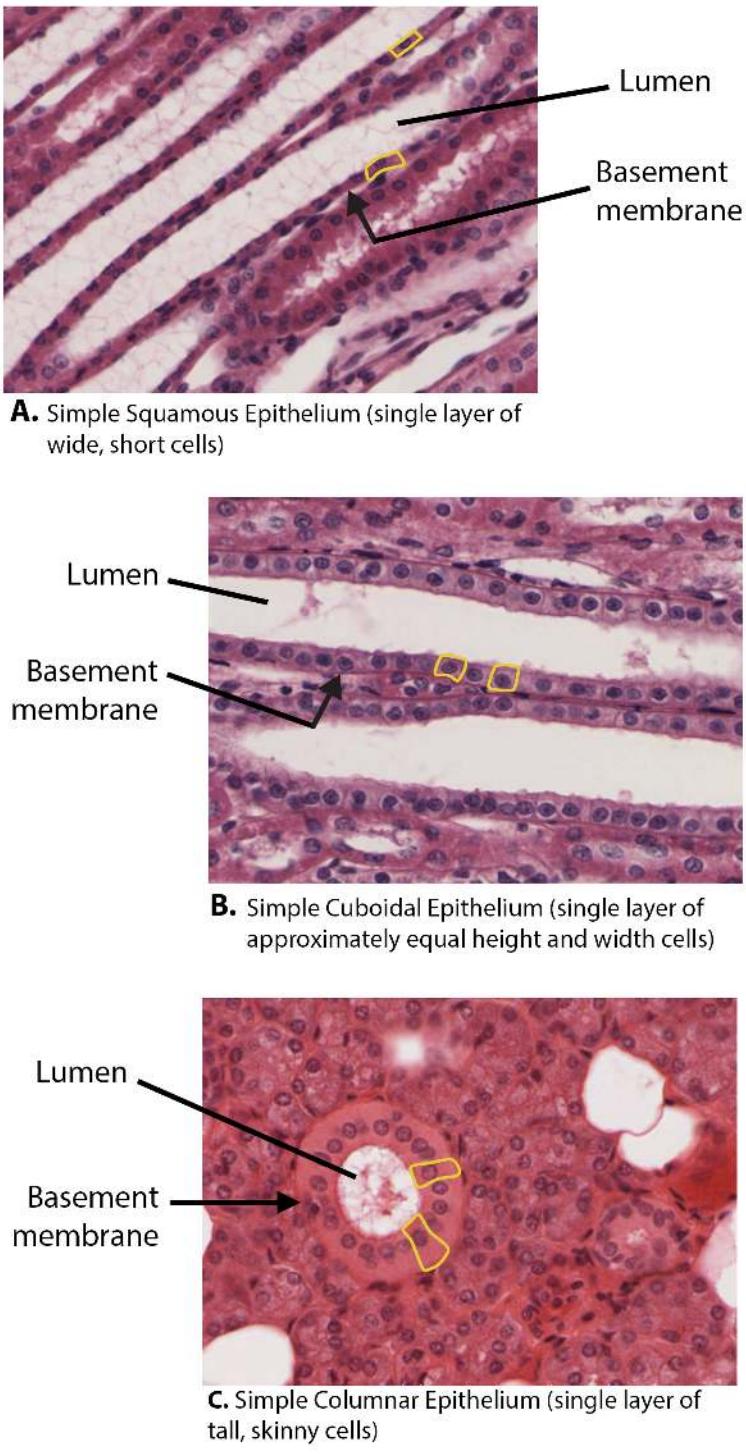


Figure 4.2.4: Histology of Simple Epithelia @ 400x. All simple epithelia have a single layer of cells between the lumen and the basal side and all cells attach to the basement membrane. Individual cells are outlined in yellow to illustrate their characteristic shape: A. simple squamous epithelium in the kidney, B. simple cuboidal epithelium in the kidney, C. simple columnar epithelium in the salivary glands. *(Image credit: "Histology of Simple Epithelia" by Jennifer Lange is licensed under CC-BY-NC-SA 4.0, images provided by the Regents of the University of Michigan Medical School under CC-BY-NC-SA 4.0 © 2022.)*

In **simple cuboidal epithelium** (Figure 4.2.3 and Figure 4.2.4), 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 absorption of molecules. Simple cuboidal epithelia are observed in the lining of the kidney tubules and in the ducts of glands.

In **simple columnar epithelium** (Figure 4.2.3 and Figure 4.2.4), 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 (Figure 4.2.3 and Figure 4.2.5) 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 toward the basal side. The arrangement gives the appearance of stratification; but in fact all the cells are in contact with the basement membrane, although some do not reach the apical surface. Pseudostratified columnar epithelium is found in the respiratory tract, where some of these cells have cilia.

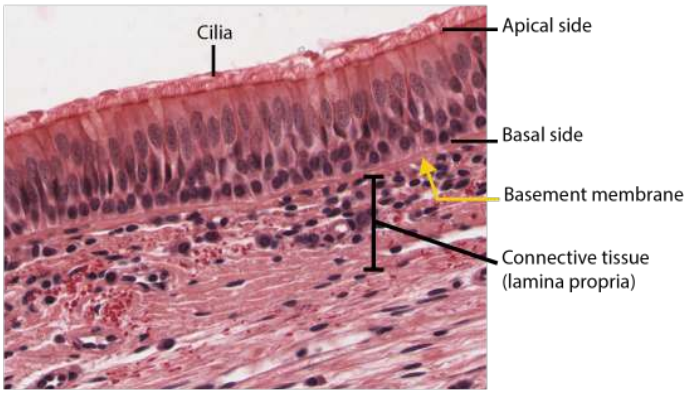


Figure 4.2.5: Histology of Pseudostratified Columnar Epithelium @ 400x. Although it appears to have multiple layers because of the postion of the nuclei, all cells attach to the basement membrane. *(Image credit: "Histology of Pseudostratified Columnar Epithelium" by Jennifer Lange, is licensed under CC-BY-NC-SA 4.0, image provided by the Regents of the University of Michigan Medical School under CC-BY-NC-SA 4.0 © 2022).*

Both simple and pseudostratified columnar epithelia can 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 4.2.6).

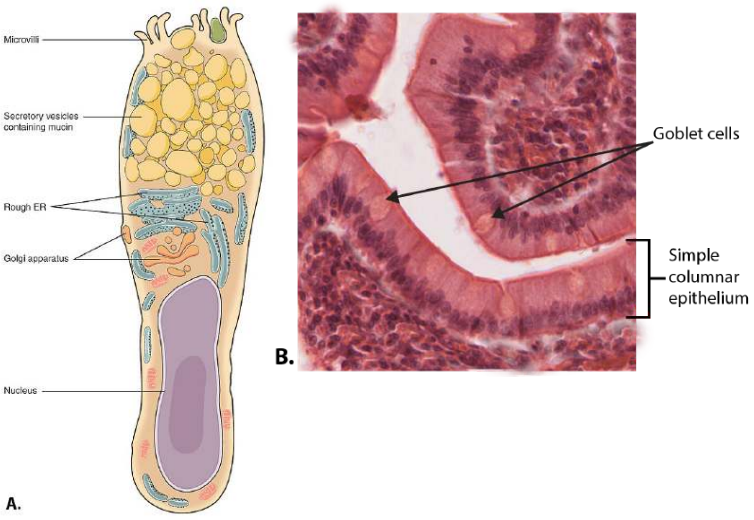


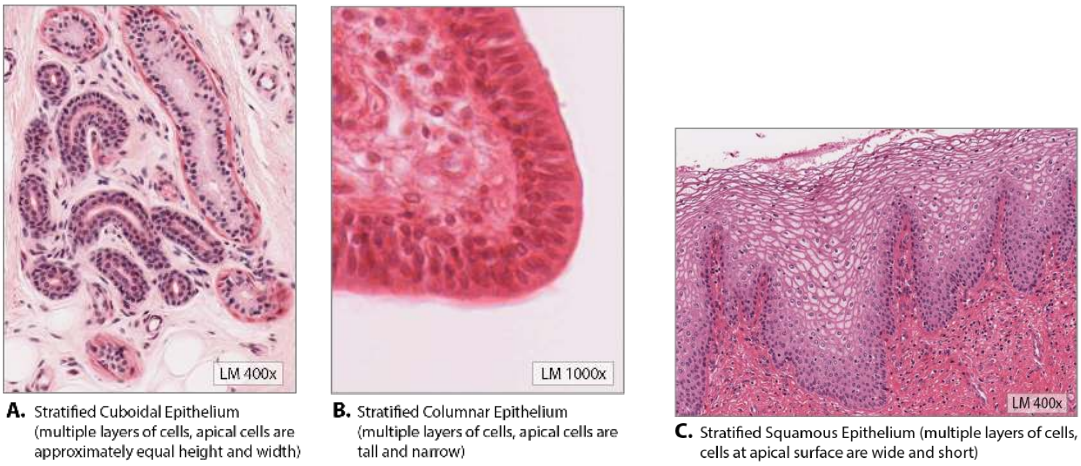
Figure 4.2.6: Goblet Cells. A. Goblet cells are specialized for the production and secretion of the protein mucin that becomes mucous when it is mixed with water. B. In the lining of the small intestine, goblet cells are scattered amoungst the columnar cells. LM × 1000. *(Image credits: A. "Goblet Cell" by OpenStax is licensed under CC BY 3.0; B. "Goblet Cell Histology" by Jennifer Lange is licensed under CC-BY-NC-SA 4.0, micrograph provided by the Regents of the University of Michigan Medical School under CC-BY-NC-SA 4.0 © 2022.)*

Stratified Epithelia

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 (Figure 4.2.7*C*) is the most common type of stratified epithelium in the human body. The apical cells are squamous, whereas the basal layer appears either columnar or cuboidal. The top layer may be covered with dead cells filled with the protein keratin. The epidermis of mammalian skin is an example of this dry, keratinized, stratified squamous epithelium. The lining of the oral cavity is an example of an non-keratinized, stratified squamous epithelium.

Stratified cuboidal epithelium and **stratified columnar epithelium** (Figure 4.2.7.*A*.*B*) can be found in certain glands and ducts. Both are uncommon in the human body.



A. Stratified Cuboidal Epithelium (multiple layers of cells, apical cells are approximately equal height and width)

B. Stratified Columnar Epithelium (multiple layers of cells, apical cells are tall and narrow)

C. Stratified Squamous Epithelium (multiple layers of cells, cells at apical surface are wide and short)

Figure 4.2.7: Stratified Epithelia Histology. All stratified epithelia have multiple layers of cells between the apical surface and basal surface, with the superficial cells attaching to the deeper cells instead of to the basement membrane. A. stratified cuboidal epithelium of a sweat gland, B. stratified columnar epithelium of the male urethra, C. stratified squamous epithelium of the vagina. *(Image credit: "Histology of Stratified Epithelia" by Jennifer Lange is licensed under CC-BY-NC-SA 4.0, images provided by the Regents of the University of Michigan Medical School under CC-BY-NC-SA 4.0 © 2022.)*

Another kind of stratified epithelium is **transitional epithelium** (Figure 4.2.8), 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.

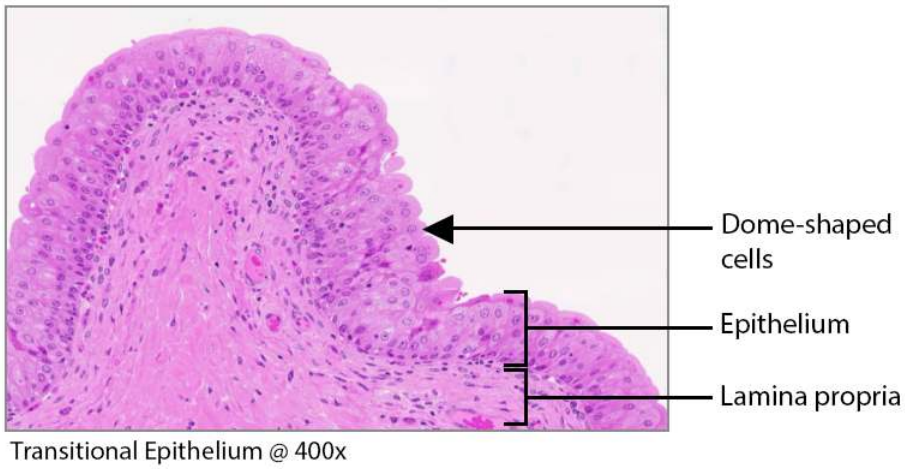
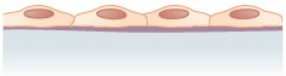
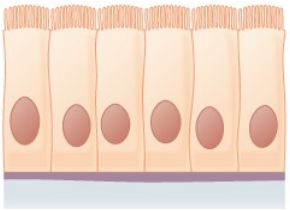
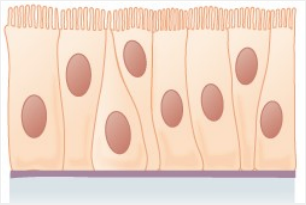
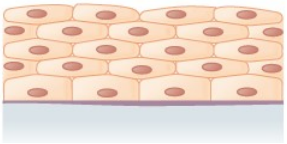
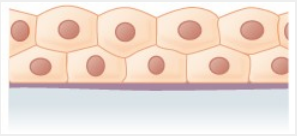
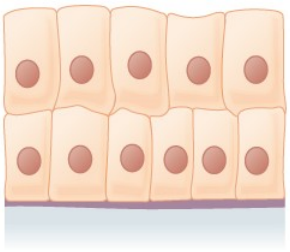
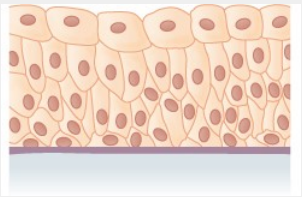


Figure 4.2.8: Transitional Epithelium. Transitional epithelium is found lining organs of the urinary system. These organs are able to stretch because the rounded epithelial cells will flatten out. *(Image credit: "Histology of Transitional Epithelium" by Jennifer Lange is licensed under, image provided by the Regents of the University of Michigan Medical School under CC-BY-NC-SA 4.0 © 2022.)*

Table 4.2.1: Summary of Epithelial Tissues. The cell shape and number of layers determines an epithelial tissue's location and function.

Tissue	Location	Function
Simple Squamous Epithelium 	Air sacs of lungs, tubules of the kidneys, and lining of the heart, blood vessels, and lymphatic vessels.	Allows material to pass through by diffusion and filtration, and secretes lubricating substance
Simple Cuboidal Epithelium 	In ducts and secretory portions of small glands and in the kidney tubules	Secretes and absorbs
Simple Columnar Epithelium 	Ciliated tissues are in bronchi, uterine tubes, and uterus Smooth (nonciliated tissues) are in the digestive tract, gallbladder	Absorbs; it also secretes mucous and enzymes May have goblet cells
Pseudostratified Columnar Epithelium 	Ciliated tissue lines the trachea and much of the upper respiratory tract Nonciliated tissue is found in the middle regions of the male urethra	Secretes mucus, ciliated tissue moves mucus Has goblet cells
Stratified Squamous Epithelium 	Lines the esophagus, mouth, anus, vagina, and distal urethra; forms epidermis of the skin	Protects against abrasion

Tissue	Location	Function
Stratified Cuboidal Epithelium 	Sweat glands, salivary glands, and the mammary glands	Secretory tissue
Stratified Columnar Epithelium 	The ducts of some glands	Secretes and protects
Transitional Epithelium 	Lines the urinary bladder, proximal urethra, and the ureters	Allows the urinary organs to expand and stretch

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 such as blood (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 (ovaries and testes).

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.

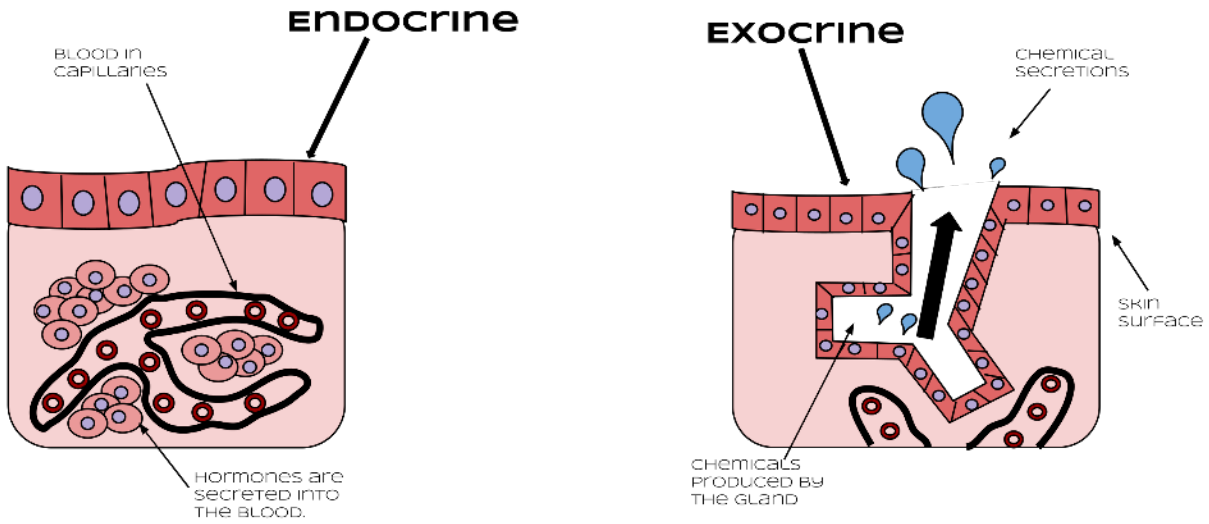


Figure 4.2.9 Types of Glands: Endocrine glands secrete their products into the bloodstream, while exocrine glands secrete their products into ducts. *(Image credit: "Endocrine vs exocrine" by* Mntrue15, *licensed under CC BY-SA 4.0, via Wikimedia Commons)*

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4.3: Connective Tissue

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

- Explain how connective tissues are classified.
- Identify and distinguish between the individual types of connective tissue within each category: proper, supportive, and fluid
- Identify the cellular and extracellular matrix features of each connective tissue type
- Explain the functions of each type of connective tissue relate to their structure

As may be obvious from its name, one of the major functions of connective tissue is to connect tissues together to form an organ. 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 **extracellular matrix** plays a major role in the functioning of this tissue. The two components of the matrix are a **ground substance** and **protein fibers**. This ground substance is usually a liquid of varying viscosity, 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: scattered 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, phagocytic cells that engulf pathogens and also rid tissue of cellular debris are common in many connective tissues.

Functions of Connective Tissues

Connective tissues perform many functions in the body, but most importantly, they support and connect other tissues. Connective tissue is found in many places of the body: 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. 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.

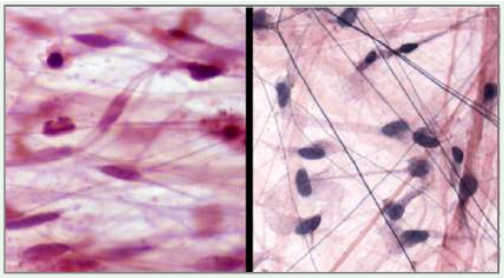
Connective Tissue Fibers and Ground Substance

Three main types of fibers in the extracellular matrix are: collagen fibers, elastic fibers, and reticular fibers (see Figure 4.3.1 and Figure 4.3.2).

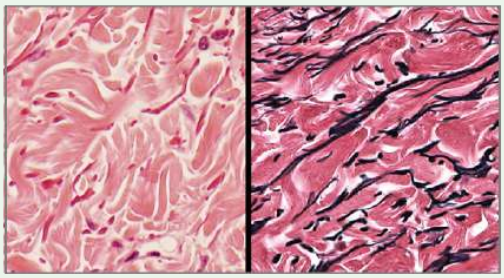
- **Collagen fibers** are made from fibrous protein subunits linked together to form a long and straight fiber. Collagen fibers, while flexible, have great tensile strength, resist stretching, and give ligaments and tendons their characteristic resilience and strength. These fibers hold connective tissues together, even during the movement of the body.
- **Elastic fibers** contain 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 fibers** are 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 the functional cells, blood vessels, and nerves of the organ.

Visualizing Protein Fibers in Connective Tissue

In order to see the protein fibers on a slide they needed to be stained. Which fibers you can see depends on which staining technique is used, but you will not see all three types with any one stain.

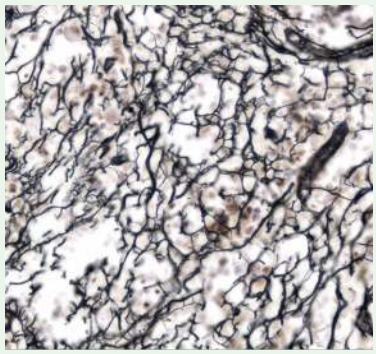


A. Areolar tissue @ 1000x - collagen and elastin



B. Dense irregular tissue @ 400x - collagen and elastin

(Figure 4.3.1): The most common stain seen in introductory anatomy courses is hematoxylin and eosin (H&E) that shows both collagen and elastin, but the elastin is harder to distinguish (both left-hand images). Both elastin and collagen can be visualized using the Verhoeff method in which collagen appears pink/red and elastin is dark purple/black. *(Image credit: "Collagen and Elastin Staining" by Jennifer Lange is licensed under CC-BY-NC-SA 4.0. Micrographs provided by Virginia Commonwealth University.)*



Reticular tissue - reticular fibers

(Figure 4.3.2): Reticular fibers need a different stain to show on the slide - either silver or Periodic Acid Schiff (PAS). Both techniques show the branching nature of the fibers. *(Image credit: "Reticulin Staining" by Jennifer Lange is licensed under CC-BY-NC-SA 4.0. Micrograph provided by Virginia Commonwealth University.)*

All of these fiber types are embedded in ground substance. Secreted by the connective tissue cells, ground substance is made of polysaccharides and proteins. These combine and the resultant structure attracts and traps available moisture. This forms the clear, viscous, colorless matrix you now know as ground substance.

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 (Figure 4.3.3).

- **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 solid and described as

calcified because of the deposited calcium salts. In cartilage the matrix is semi-solid, with abundant collagen and proteoglycans and lesser amounts of water, other proteins, and glycoproteins.

- In **fluid connective tissue**, lymph and blood, various specialized cells circulate in a watery fluid containing salts, nutrients, and dissolved proteins. This group of connective tissues do not have protein fibers in their matrix.

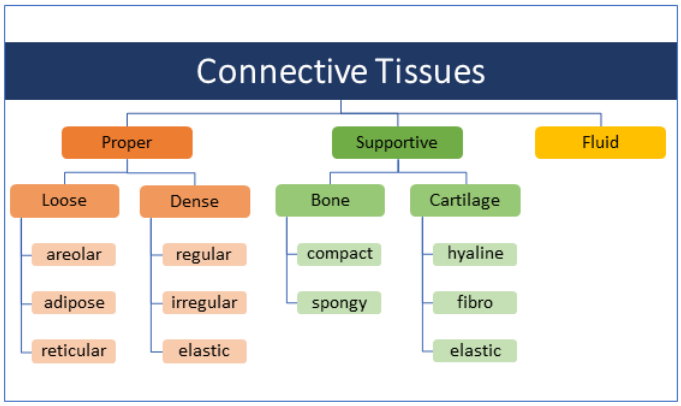


Figure 4.3.3: Classification of Connective Tissues. Connective tissues are divided into groups based on the viscosity (thickness) of their ground substance and then into sub-groups based on their fiber types and arrangement. *(Image Credit: "Classification of Connective Tissues" by Jennifer Lange, licensed under CC-BY-NC-SA 4.0)*

Connective Tissue Proper

Connective tissue proper include the types of connective tissues that have a mixture of the possible cell types, varying amounts and types of protein fibers, and a ground substance that has a gel-like consistency. Because of their variety in structure, they can perform a variety of functions.

Cell Types

The most abundant cell in connective tissue proper is the **fibroblast**. Polysaccharides and proteins such as collagen secreted by fibroblasts combine with extra-cellular fluids to produce a viscous ground substance that 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.

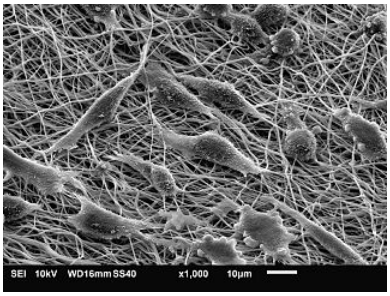


Figure 4.3.4: Cells of Connective Tissue Proper: Fibroblasts. Fibroblasts produce materials in the extracellular matrix of proper connective tissues. C SEM × 1000. *(Image credit: "SEM of fibroblasts" by Judyta Dulnik is licensed under CC-BY-SA 4.0)*

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 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 white 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.

The **mast cell**, another type of white blood cell found in proper connective tissues, releases inflammatory chemicals.

Loose Connective Tissues

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 embedded cells and tissues.

- **Adipose tissue** consists mostly of fat storage cells, with little extracellular matrix (Figure 4.3.5). 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.

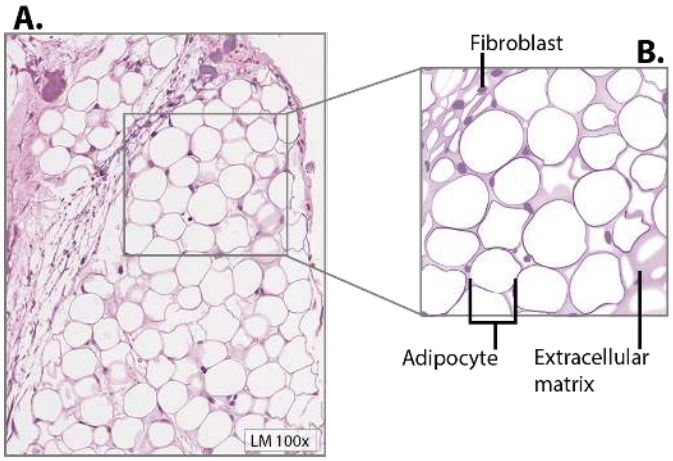


Figure 4.3.5: Adipose Tissue. This is a loose connective tissue that consists of adipocytes and limited extracellular matrix. Adipocytes store fat for energy and provides insulation. The number of adipocytes stays constant after adolescence, the cells just change in size. *(Image credit: "Adipose Tissue" by Jennifer Lange, illustration by Claire McGuire, is licensed under CC-BY-NC-SA 4.0. Micrograph provided by Berkshire Community College Bioscience Image Library is in the Public Domain.)*

- **Areolar tissue** shows little specialization, yet is it found almost everywhere in the body. It is like an all purpose glue. It contains all the cell types and fibers previously described. The fibers are distributed in a random, web-like fashion (Figure 4.3.6). 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.

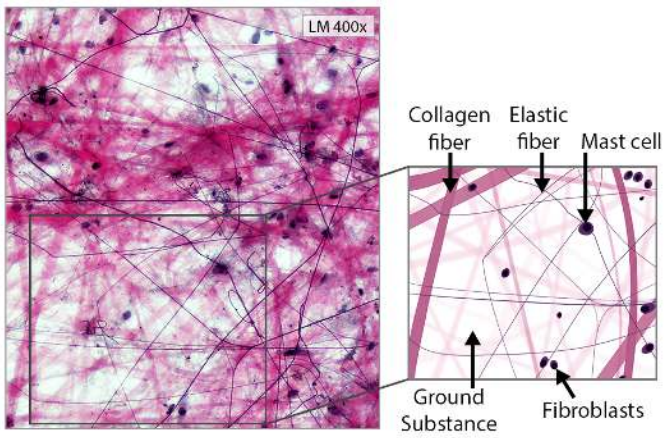


Figure 4.3.6: Areolar Connective Tissue. This is a loose connective tissue containing all components found in connective tissue proper, though not all are visible at the same time on a slide. Reticulin fibers are visualized using a different staining technique than in this image. *(Image credit: “Areolar Connective Tissue" by Jennifer Lange, illustration by Claire McGuire, is licensed under CC BY-NC-SA 4.0. Micrograph provided by Berkshire Community College Bioscience Image Library is in the Public Domain.)*

- **Reticular tissue** is a mesh-like, supportive framework for soft organs such as lymphatic tissue, the spleen, and the liver (Figure 4.3.7). Fibroblasts (and a specialized subtype cell called 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.”

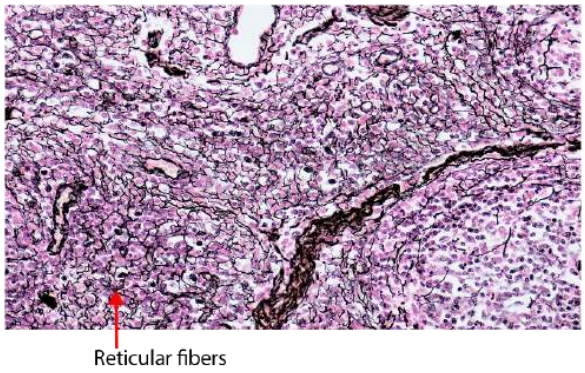


Figure 4.3.6: Reticular Tissue. This is a loose connective tissue made up of a network of reticular fibers that provides a supportive framework for soft organs. LM × 200x. *(Image credit: "Reticular Tissue" by Jennifer Lange is licensed under CC BY-NC-SA 4.0. Micrograph provided by Berkshire Community College Bioscience Image Library is in the Public Domain.)*

Dense Connective Tissue

Dense connective tissues contain more protein fibers than do loose connective tissues. As a consequence, visually they have little "white space" filled with ground substance and the fibers are more densely packed. There are three major categories of dense connective tissue: elastic, regular and irregular.

- **Dense regular connective tissue**'s abundant collagen fibers are parallel to each other, enhancing tensile strength and resistance to stretching in the direction of the fiber orientation (Figure 4.3.7). Ligaments and tendons are made of dense regular connective tissue.

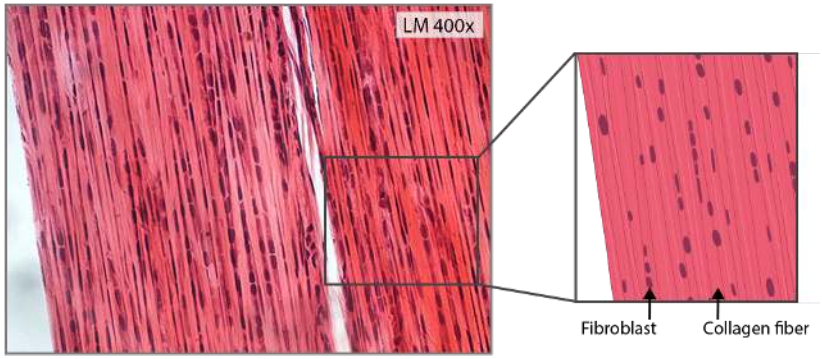


Figure 4.3.7: Dense Regular Connective Tissue. Dense connective tissues have small amounts of ground substance; dense regular has almost none that is visible on a slide using a light microscope. The collagen fibers are arranged in thick, parallel bundles and the fibroblasts are often oval as they are compressed between the fibers. *(Image credit: "Dense Regular Connective Tissue" by Jennifer Lange, illustration by Claire McGuire, is licensed under CC BY-NC-SA 4.0. Micrograph by J Jana, CC BY-SA 4.0, via Wikimedia Commons.)*

- In **dense irregular connective tissue**, the direction of fiber bundles is random (Figure 4.3.8*A*). This arrangement gives the tissue greater strength in all directions and less strength than dense regular connective tissue in one particular direction. The majority of the fibers are collagen, with a smaller quantity of elastin also present. The dermis of the skin is an example of dense irregular connective tissue rich in collagen fibers.
- Some applications require a balance between tensile strength and elasticity, and thus contain **elastic connective tissue** with abundant elastin fibers in addition to collagen fibers (Figure 4.3.8*B*). The ligaments in the vocal folds and between the vertebrae in the cervical vertebral column are composed of elastic connective tissue. This type of tissue also gives the walls of large arteries both strength and the ability to regain original shape after stretching.

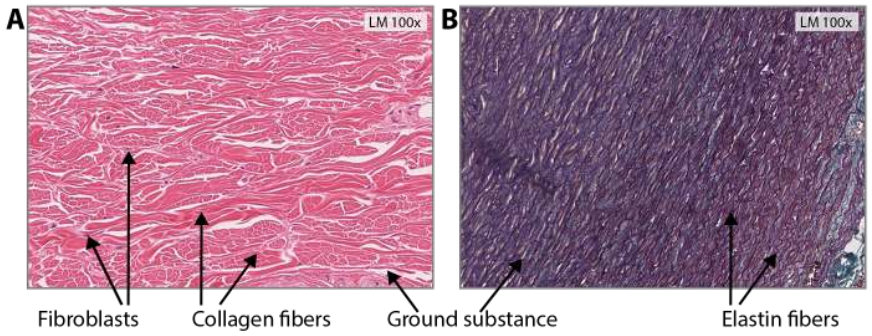
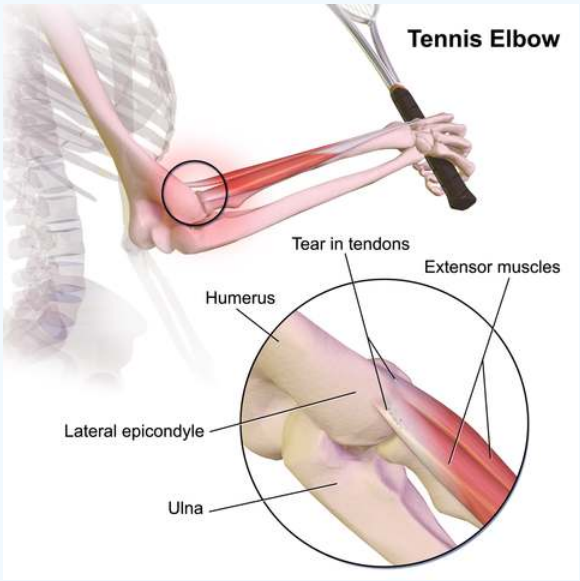


Figure 4.3.8: Dense Connective Tissues: Dense Irregular and Elastic. (A) Dense irregular connective tissue consists of collagenous fibers interwoven into a mesh-like network. Of the dense connective tissues, this one has the most ground substance. (B) Elastin fibers are visualized here using a different dye, appearing as wavy, parallel dark lines. (*Image credit: "Dense Connective Tissues: Irregular and Elastic" by Jennifer Lange is licensed under CC BY-NC-SA 4.0. Micrographs provided by the Regents of the University of Michigan Medical School* © 2022.)

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 arm and you drop the tennis racket. That dull ache in the elbow that you ignored through the summer is now an unbearable pain. The game is over for now.



After examining your painful elbow, the doctor in the emergency room announces that you have developed extensor tendinitis, commonly called tennis elbow. She recommends icing the tender area, taking non-steroidal anti-inflammatory medication to ease the pain and to reduce swelling, and completely 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 dense regular 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, dynamic 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.

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 extracellular matrix composition 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 spaces they occupy are called **lacunae** (singular = lacuna). 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 are hyaline cartilage, fibrocartilage, and elastic cartilage (Figure 4.3.9).

- **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 it 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, which allows it to resist compression and absorb shock. The knee and jaw joints and 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.

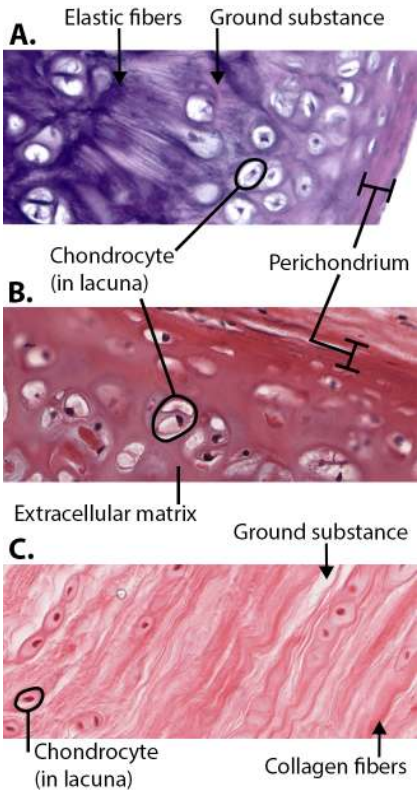


Figure 4.3.9: Types of Cartilage @ 600x. Cartilage is a supportive connective tissue with a semi-solid ground substance. A. Elastic cartilage has elastin fibers oriented in multiple directions that are densest near the cells. B. Hyaline cartilage does not have visible protein fibers. C. Fibrocartilage has fewer cells and thin, wavy collagen fibers. *(Image credit: "Types of Cartilage" by Jennifer Lange is licensed under CC-BY-NC-SA 4.0.; micrographs provided by the Regents of University of Michigan Medical School © 2022, under CC-BY-NC-SA 4.0.)*

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 organic collagen, bones would be brittle and shatter easily. Without inorganic mineral crystals, bones would flex and provide little support. **Osteocytes**, bone cells like chondrocytes, are located within lacunae. Bone is a highly vascularized tissue. Unlike cartilage, bone tissue can recover from injuries in a relatively short time.

The histology of transverse tissue from long bone (Figure 4.3.10*A*) shows a typical arrangement of osteocytes in concentric circles around a central canal. This compact bone arrangement is solid and has great structural strength. Spongy bone looks like a sponge under the microscope (Figure 4.3.10*B*) and contains empty spaces between trabeculae, or arches of bone tissue. 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. The specific arrangement of cells and extracellular matrix within each bone tissue type will be further discussed in the skeletal system chapter.

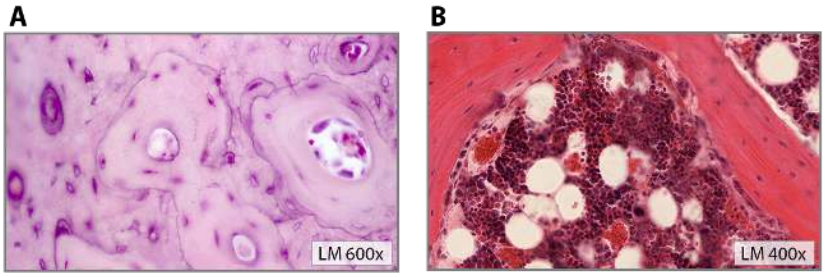


Figure 4.3.10: Bone Tissue. (A) Compact bone only has spaces for the passage of nerves and blood vessels. (B) Spongy bone has large spaces filled with bone marrow. (*Image credit: "Bone Tissue Arrangements" by Jennifer Lange is licensed under CC-BY-NC-SA 4.0; micrographs provided by Virginia Commonwealth University under CC-BY-NC-SA 4.0.*)

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 stem cells located in bone marrow (Figure 4.3.11). These formed elements include erythrocytes, called red blood cells, leukocytes, called white blood cells, and cell fragments called platelets involved in blood clotting. Nutrients, salts, and wastes are dissolved in the liquid ground substance and transported through the body. The details of the both the formed elements and the ground substance of blood will be discussed in future chapters.

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.

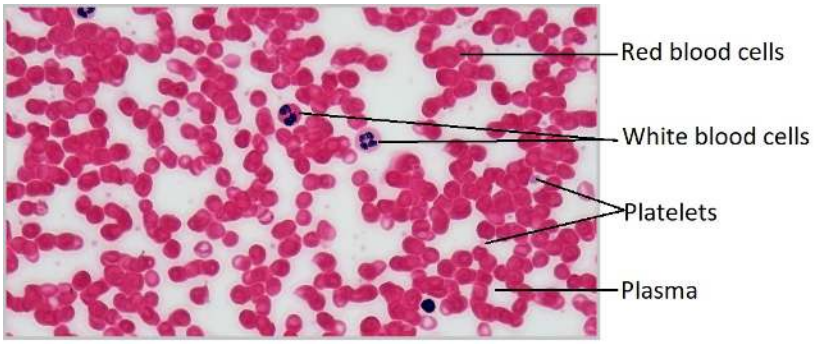


Figure 4.3.11: Fluid Connective Tissue: Blood. Blood is a fluid connective tissue containing various types of blood cells that circulate in a liquid extracellular matrix. LM × 400. *(Image credit: "Fluid Connective Tissue" by Jennifer Lange is licensed under CC-BY-NC-SA 4.0. Micrograph provided by Berkshire Community College Bioscience Image Library is in the Public Domain.)*

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4.4: Review Questions

Use the following questions to test your knowledge on Tissue Organization.

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CHAPTER OVERVIEW

5: The Integumentary System

5.1: Introduction
5.2: Layers of the Skin

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5.1: Introduction



Figure 5.1.1: Your skin is a vital part of your life and appearance (a–b). Some people choose to embellish it with tattoos (a) or makeup (b). (credit a: Steve Teo; credit b: “spaceodissey”/flickr)

Chapter Objectives

After studying the chapter, you will be able to:

- Describe the integumentary system and the role it plays in homeostasis
- Describe the layers of the skin and the functions of each layer

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.

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5.2: Layers of the Skin

Learning Objectives

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

- Identify the components of the integumentary system
- Describe the layers of the skin and the functions of each layer
- Identify and describe the hypodermis
- Describe the role of keratinocytes
- 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 5.2.1). 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.

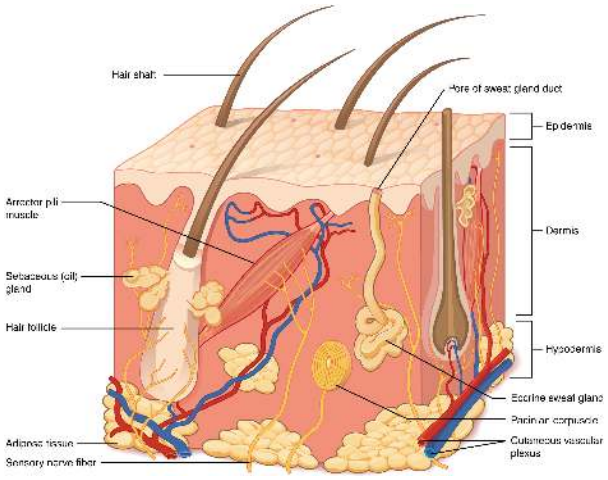


Figure 5.2.1: Layers of Skin The skin is composed of two main layers: the epidermis, made of closely packed epithelial cells, and the dermis, made of dense, irregular connective tissue that houses blood vessels, hair follicles, sweat glands, and other structures. Beneath the dermis lies the hypodermis, which is composed mainly of loose connective and fatty tissues.

Interactive Link

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 5.2.2).

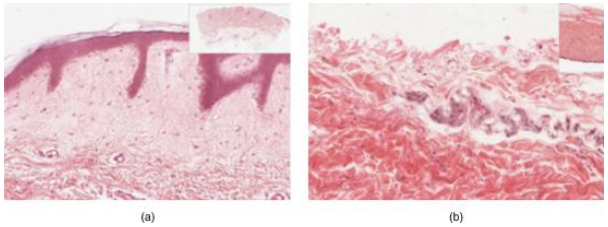


Figure 5.2.2: Thin Skin versus Thick Skin These slides show cross-sections of the epidermis and dermis of (a) thin and (b) thick skin. Note the significant difference in the thickness of the epithelial layer of the thick skin. From top, LM × 40, LM × 40. (Micrographs provided by the Regents of University 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 5.2.3).

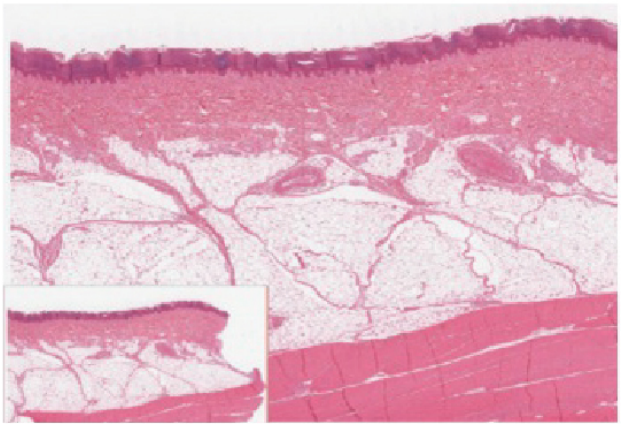


Figure 5.2.3: Epidermis The epidermis is epithelium composed of multiple layers of cells. The basal layer consists of cuboidal cells, whereas the outer layers are squamous, keratinized cells, so the whole epithelium is often described as being keratinized stratified squamous epithelium. LM × 40. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

Interactive Link

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?

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 5.2.6). It consists of the papillary layer and recticular layer.



Figure 5.2.6: 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)

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. Males tend to accumulate fat in different areas (neck, arms, lower back, and abdomen) than do females (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. 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 5.2.7).

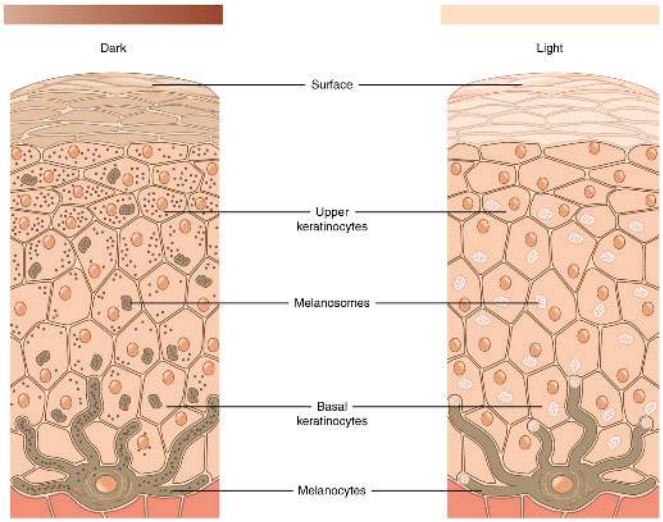


Figure 5.2.7: Skin Pigmentation The relative coloration of the skin depends of the amount of melanin produced by melanocytes in the stratum basale and taken up by keratinocytes.

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.

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 5.2.8).



Figure 5.2.8: Moles Moles range from benign accumulations of melanocytes to melanomas. These structures populate the landscape of our skin. (credit: the National Cancer Institute)

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 5.2.9). Neither albinism nor vitiligo directly affects the lifespan of an individual.



Figure 5.2.9: Vitiligo Individuals with vitiligo experience depigmentation that results in lighter colored patches of skin. The condition is especially noticeable

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.

Interactive Link

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?

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CHAPTER OVERVIEW

6: Bone Tissue and the Skeletal System

6.1: Functions of the Skeletal System
6.2: Bone Classification
6.3: Bone Structure
6.4: Bone Remodeling and Calcium Homeostasis
6.5: Fractures - Bone Repair
6.6: Review Questions

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6.1: Functions of the Skeletal System

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

- Define bone, cartilage, and the skeletal system
- List and describe the functions of the skeletal system

Bone, or **osseous tissue**, is a hardened 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.

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 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 articulations (where two bones come together, also known as joints) serve as fulcrums. Unless a muscle spans an articulation and contracts, a bone is not going to move. Information on the interactions of the skeletal and muscular systems, that is the musculoskeletal system, will be covered in the upcoming chapters of this book.

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 6.1.1).



Figure 6.1.1: Bones Protecting the Spinal Cord . Bone of the vertebral column surround the spinal cord, protecting it from traumatic injury. *(Image credit: by Amada44, CC BY-SA 3.0, via Wikimedia Commons)*

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 6.1.2).



Figure 6.1.2: Applying a posterior upper-extremity plaster splint. Plaster splints are often used immediately following an injury due to the swelling in the area. *(Image credit: "Orthopedic Clinic Keeps Patients Happy and Active [Image 3 of 3], by CPO Brannon Deugan, identified by DVIDS, is in the Public Domain.)*

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.

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.

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 6.1.3). There are two types of bone marrow: yellow marrow (deep) and red marrow (superficial). **Yellow marrow** contains adipose tissue; the triglycerides (lipids) 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.

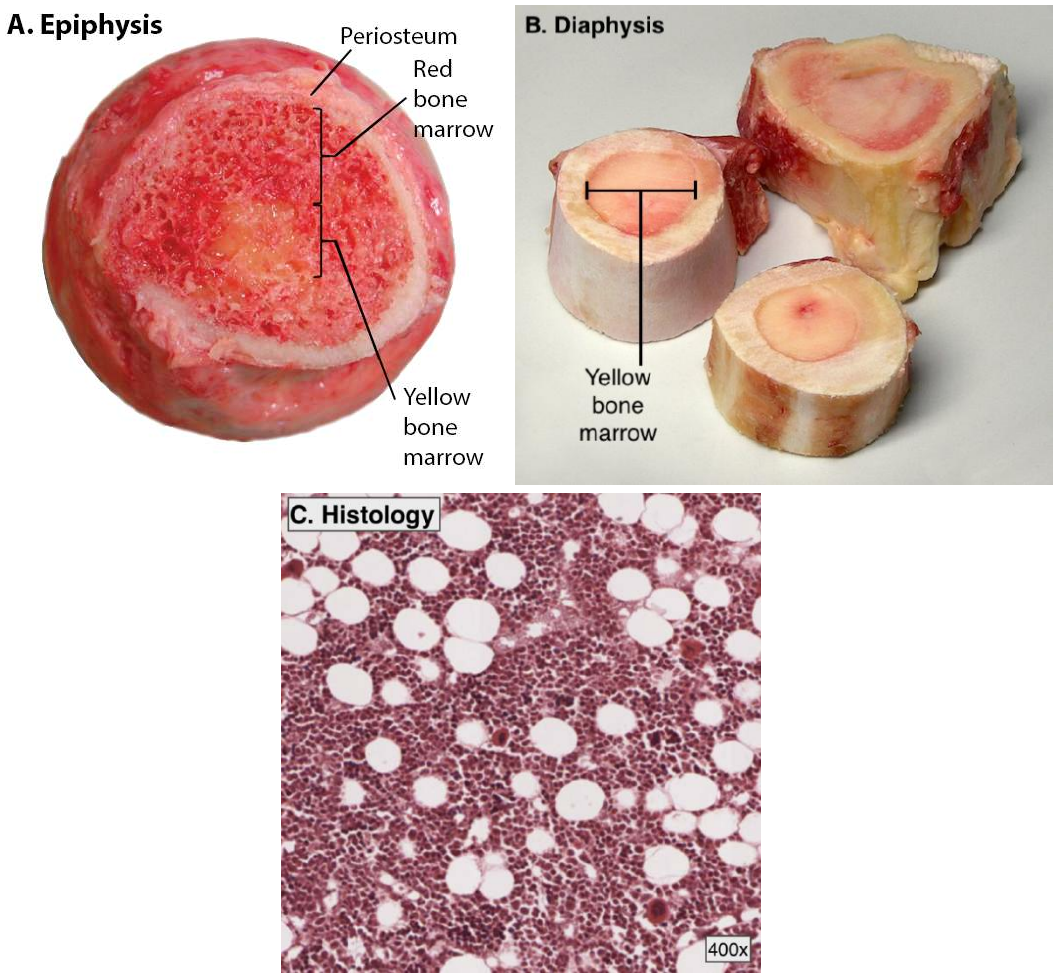


Figure 6.1.3: Red and Yellow Bone Marrow. (A) The epiphysis of the femur contains both yellow marrow (stores fat) and red marrow (responsible for hematopoiesis. (B) The diaphysis of the bone contains only yellow bone marrow. (C) Histologically, we can see that red bone marrow contains numerous developing blood cells as well as scattered adipocytes. *(Image credits: (A) "Bone Marrow - Epiphysis" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original by OpenStax; (B) "Bone Marrow - Diaphysis" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original by by Rainer Zenz assumed (based on copyright claims), via Wikimedia Commons; (C) "Red Bone Marrow Histology" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, slide provided by the Regents of the University of Michigan Medical School under CC BY-NC-SA 4.0 © 2022)*

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6.2: Bone Classification

Learning Objectives

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

- 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 6.2.1). Their shapes and their functions are related such that each categorical shape of bone has a distinct function.

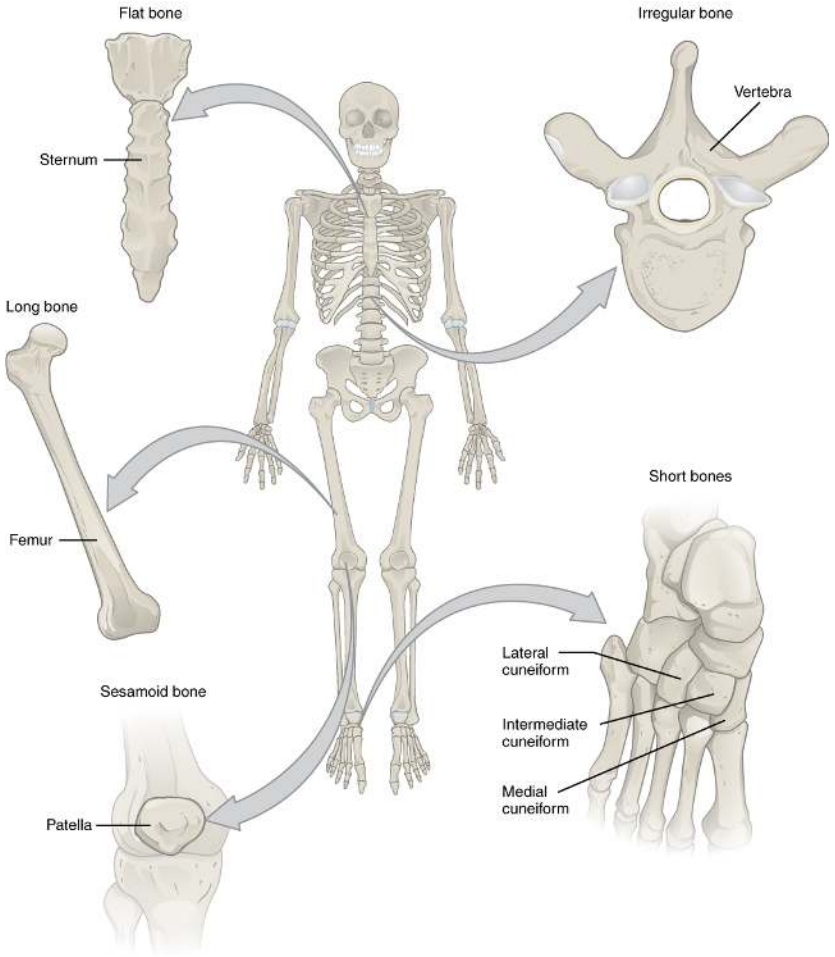


Figure 6.2.1: Classifications of Bones Bones are classified according to their shape.

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 6.2.1 reviews bone classifications with their associated features, functions, and examples.

Table 6.2.1: 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

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6.3: Bone Structure

Learning Objectives

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

- 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 6.3.1). 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.

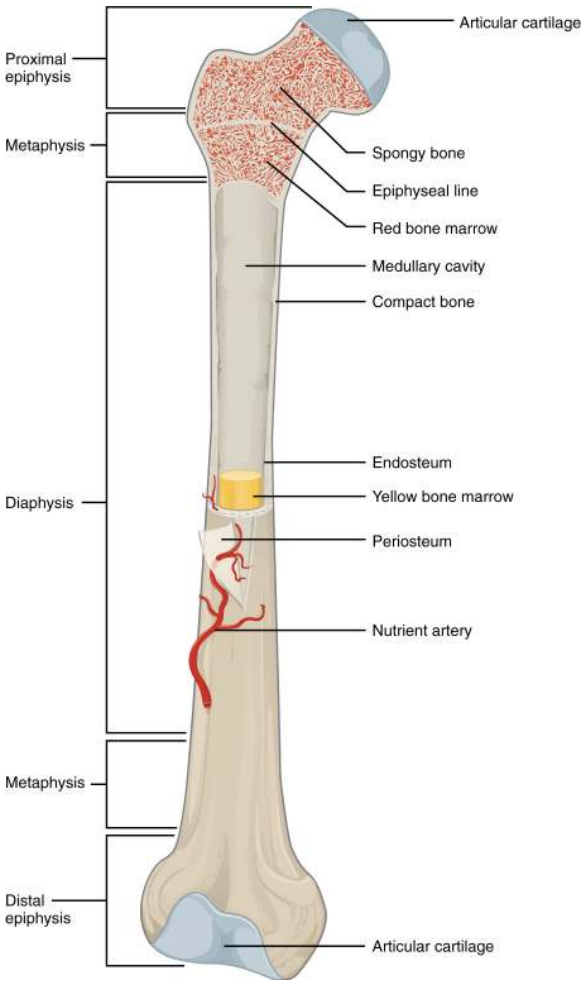


Figure 6.3.1: \ Anatomy of a Long Bone A typical long bone shows the gross anatomical characteristics of bone.

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 6.3.2). In this region, the epiphyses are covered with articular cartilage, a thin layer of cartilage that reduces friction and acts as a shock absorber.

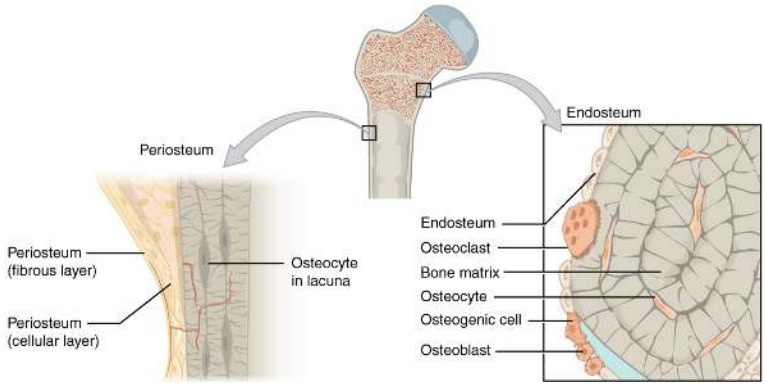


Figure 6.3.2: Periosteum and Endosteum The periosteum forms the outer surface of bone, and the endosteum lines the medullary cavity.

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 6.3.3). 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.

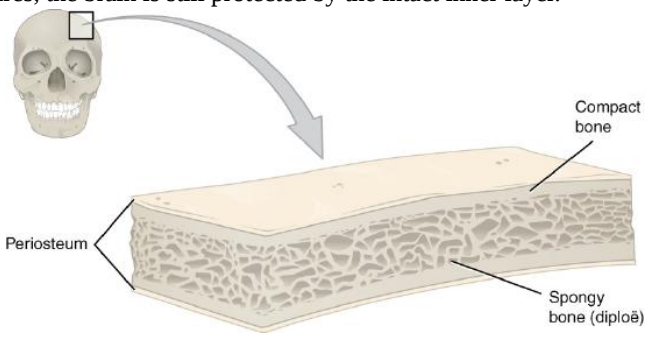
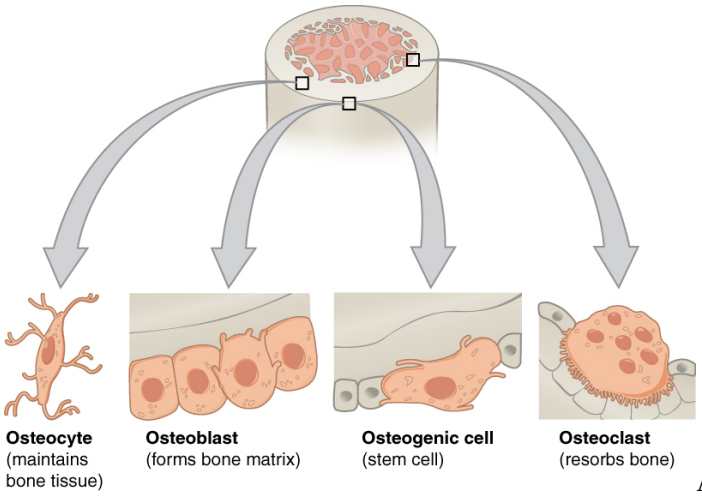


Figure 6.3.3: Anatomy of a Flat Bone This cross-section of a flat bone shows the spongy bone (diploë) lined on either side by a layer of compact bone.

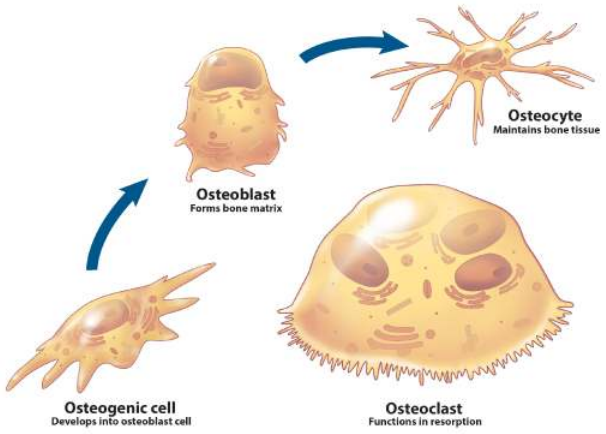
Bone Cells and Tissue

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 6.6.3.5).



A



B

Figure 6.3.5 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. *(Image B Credits: "Bone Cells" by BlueLink is licensed under CC BY-NC 4.0 with notification of the original authors.)*

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 6.3.2 reviews the bone cells, their functions, and locations.

Table 6.3.2: 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
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 6.3.6). It can be found under the periosteum and in the diaphyses of long bones, where it provides support and protection.

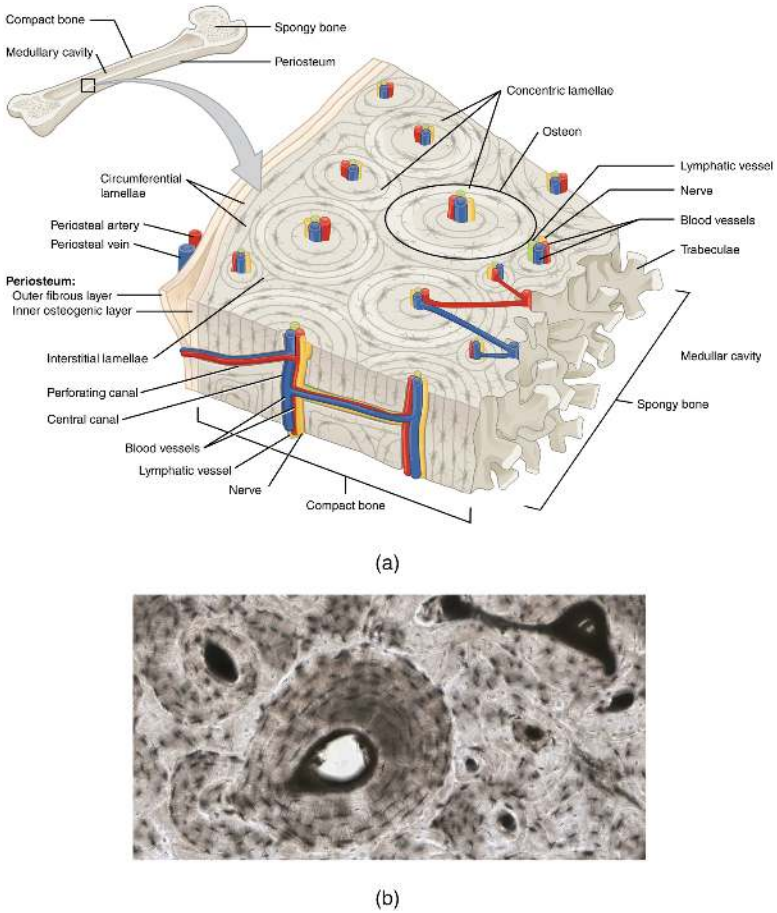


Figure 6.3.6: Diagram of Compact Bone (a) This cross-sectional view of compact bone shows the basic structural unit, the osteon. (b) In this micrograph of the osteon, you can clearly see the concentric lamellae and central canals. LM × 40. (Micrograph provided by the Regents of University of Michigan 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 6.3.7). 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.

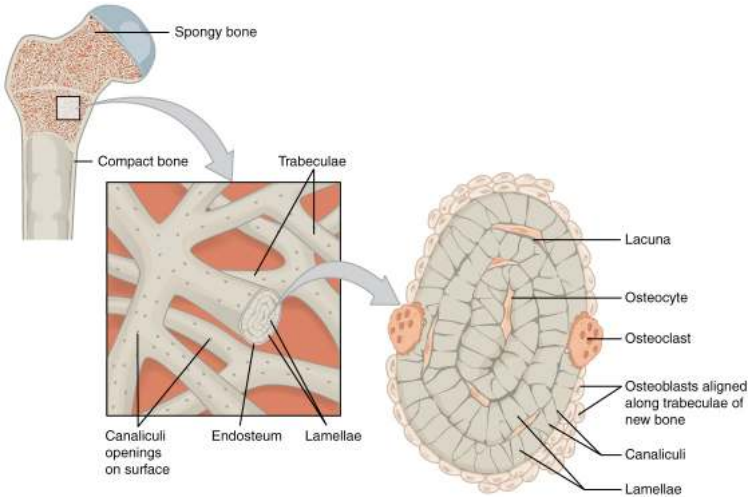


Figure 6.3.7: Diagram of Spongy Bone Spongy bone is composed of trabeculae that contain the osteocytes. Red marrow fills the spaces in some bones.

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 6.3.8). 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.

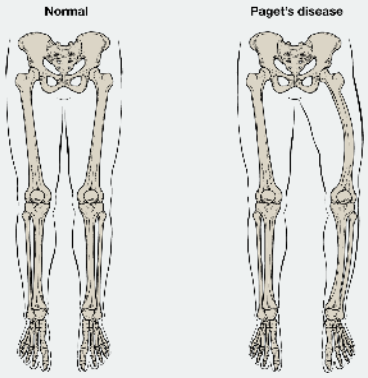


Figure 6.3.8: Paget's Disease Normal leg bones are relatively straight, but those affected by Paget's disease are porous and curved.

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.

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 6.3.9). 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.

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.

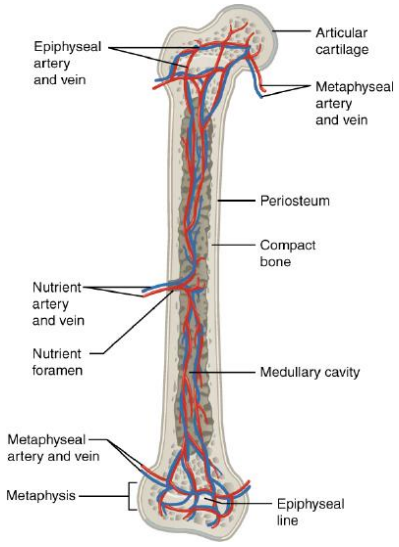


Figure 6.3.9: Diagram of Blood and Nerve Supply to Bone Blood vessels and nerves enter the bone through the nutrient foramen.

Bone Markings

The surface features of bones vary considerably, depending on the function and location in the body. Table 6.2 describes the bone markings, which are illustrated in (Figure 6.3.4). 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 6.3.1: Bone Markings

Marking	Description	Example
Articulations	Where two bones meet	Knee joint

Marking	Description	Example
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
Sinus	Air-filled space in bone	Nasal sinus

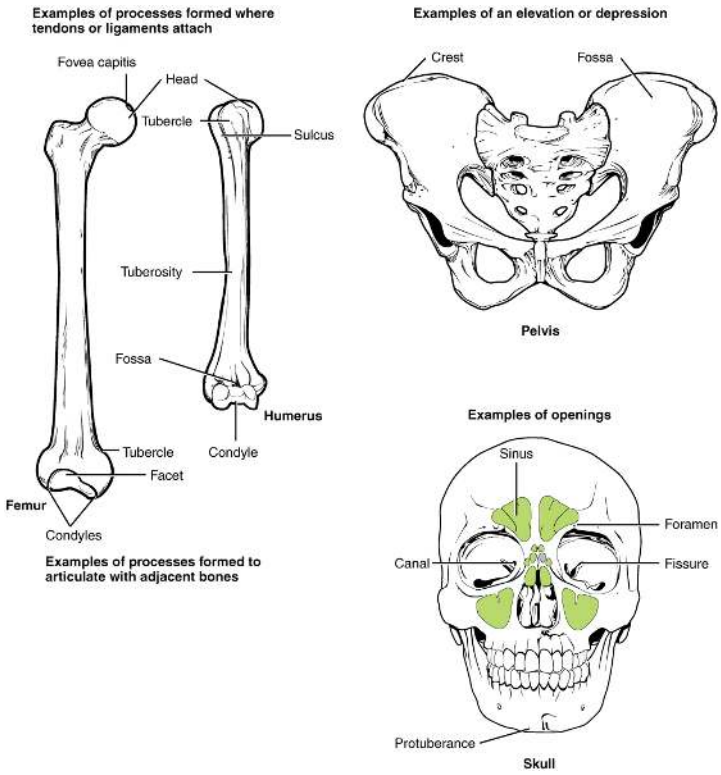


Figure 6.3.4: Bone Features The surface features of bones depend on their function, location, attachment of ligaments and tendons, or the penetration of blood vessels and nerves.

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6.4: Bone Remodeling and Calcium Homeostasis

Learning Objectives

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

- Compare and contrast the processes of modeling and remodeling
- Describe the role of osteoblasts, osteoclasts and osteocytes in bone remodeling
- Explain the negative feedback loop that regulates calcium levels in the blood

Bone Remodeling

Bone deposition is the formation of new bone, accomplished by **osteoblasts**. Osteoblasts secrete the bone matrix, enzymes and calcium ions which calcify bone.

Bone resorption is the removal of old bone, accomplished by **osteoclasts**. Osteoclasts secrete hydrogen ions and enzymes which break down bone. The calcium and other bone components that are released from bone break down can then be used elsewhere.

The process in which bone 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. In childhood, bone deposition occurs at a greater rate than bone resorption.

Bone remodeling is the process 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. Rates of bone deposition and bone resorption should be relatively equal in adulthood.

Bone remodeling occurs for a variety of reasons including:

- Maintaining calcium ion homeostasis
- Repairing bone (such as from injury or exercise)
- Replaces old bone with new bone
- Adapting bone to tension and stress (such as from lifting heavy loads)

Hormones such as testosterone (promotes bone deposition) and estrogen (inhibits osteoclast activity) can also affect bone remodeling. There are other hormones such as thyroxine (from the thyroid gland) and growth hormone (from the pituitary gland) that also affect bone formation and these will be explored in the chapter on the endocrine system.

Calcium Homeostasis

Calcium is not only the most abundant mineral in bone, it is also the most abundant mineral in the human body. It cannot be stressed enough how important calcium is in the body and the many vital processes it is needed for.

Aside from its role in bone formation, calcium is needed for:

- Tooth health
- Heart beat regulation and strength of heart contraction
- Blood coagulation
- Contraction of smooth and skeletal muscle cells
- Regulation of nerve impulse conduction.

That's right, your heart cannot beat properly without calcium, your nerves cannot communicate properly without calcium and your muscles can't even contract without calcium!

For these many reasons, the body needs to regulate the levels of calcium in the body. 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 6.4.1).

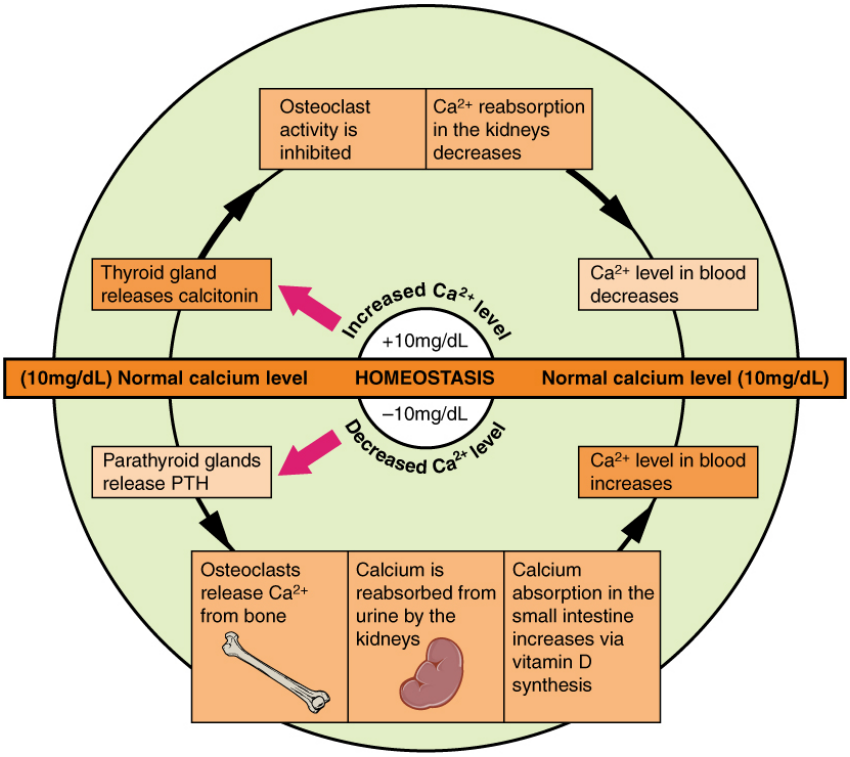


Figure 6.4.1: Pathways in Calcium Homeostasis The body regulates calcium homeostasis with two pathways; one is signaled to turn on when blood calcium levels drop below normal and one is the pathway that is signaled to turn on when blood calcium levels are elevated.

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 **parathyroid hormone (PTH)**, vitamin D, and **calcitonin**.

The regulation of calcium ion levels in the blood is under a negative feedback loop. When calcium levels drop too low, the **parathyroid gland** (the sensor in this negative feedback loop) senses the low levels. In response, the parathyroid gland (also the control center) releases **PTH**. As seen in Figure 6.4.1 above, PTH stimulates osteoclast proliferation and stimulates osteoclasts to break down bone, releasing Ca^{2+} from bone. PTH also stimulates the kidneys to reabsorb calcium from the urine back into the blood and the small intestine to absorb more calcium through increased Vitamin D synthesis. These are effectors or responses in this negative feedback loop. Once calcium levels return to normal, the parathyroid gland stops releasing PTH as homeostasis has now been maintained.

On the other hand, when calcium levels are too high, the **thyroid gland** acts as the sensor and control center. In response to high calcium levels, the thyroid gland releases **calcitonin**. Calcitonin inhibits the osteoclasts (reducing bone resorption). Bone deposition will continue and will deposit calcium into bone, dropping calcium levels in the blood. Additionally, calcitonin will also cause the kidneys to stop reabsorbing as much calcium, allowing excess calcium to be lost to the urine. These are effectors or responses in this negative feedback loop. Once calcium levels have gone back down to normal, the thyroid gland will stop releasing calcitonin and once again, homeostasis has been maintained.

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6.5: Fractures - Bone Repair

Learning Objectives

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

- 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 6.5.1). Table 6.5.1 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).

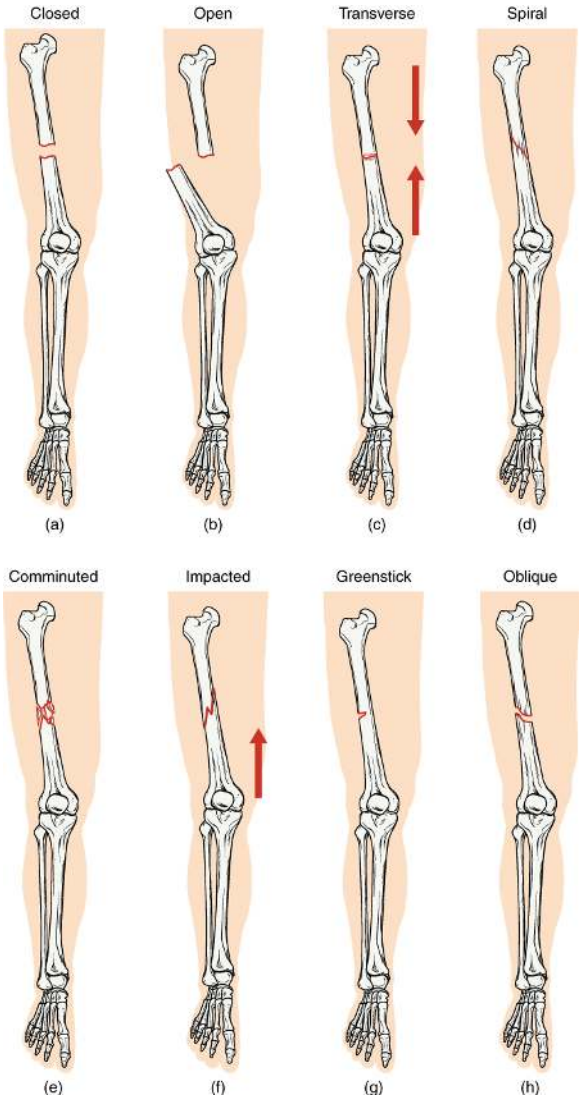

Closed
Open
Transverse
Spiral
(a)
(b)
(c)
(d)
Comminuted
Impacted
Greenstick
Oblique
(e)
(f)
(g)
(h)

Figure 6.5.1: 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 6.5.1: Common 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 6.5.2**a**). The disruption of blood flow to the bone results in the death of bone cells around the fracture.

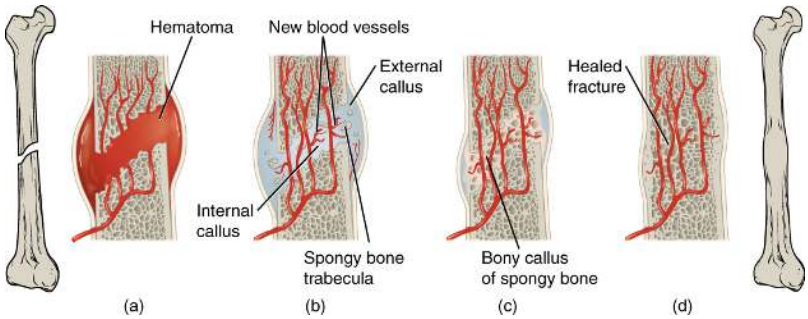


Figure 6.5.2: Stages in Fracture Repair The healing of a bone fracture follows a series of progressive steps: (a) A fracture hematoma forms. (b) Internal and external calli form. (c) Cartilage of the calli is replaced by trabecular bone. (d) Remodeling occurs.

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 6.21**b**). 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 6.21**c**).

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 6.21**d**), and no external evidence of the fracture remains.

Interactive Link

Visit this website to review different types of fractures and then take a short self-assessment quiz.

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6.6: Review Questions

Use the following questions to test your knowledge on the Skeletal System.

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CHAPTER OVERVIEW

7: Joints

7.1: Introduction

7.2: Classification of Joints

7.3: Types of Body Movements

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7.1: Introduction

Chapter Learning Objectives

After studying this chapter, you will be able to:

- Discuss both functional and structural classifications for body joints
- Describe the characteristic features for fibrous, cartilaginous, and synovial joints and give examples of each
- Describe 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, also known as articulations, 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. Importantly, joint stability and movement are inversely 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.

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.



Figure 7.1.1: Yoga. Without joints, body movements would be impossible. (Image credit: Mr. Yoga, CC BY-SA 4.0, via Wikimedia Commons)

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7.2: Classification of Joints

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

- Distinguish between the functional and structural classifications for joints
- Describe the three functional types of joints and give an example of each
- Describe the structural features of fibrous joints and of cartilaginous joints
- Distinguish between a suture, syndesmosis, and gomphosis
- Give an example of each type of fibrous joint and each type of cartilaginous joint
- Distinguish between a synchondrosis and symphysis

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 there is a space **(joint cavity)** between the bones or whether the gap is fully filled by either dense connective tissue or cartilage. Functional classifications describe the degree of movement available between the bones, ranging from immobile, to slightly mobile, to freely moveable joints.

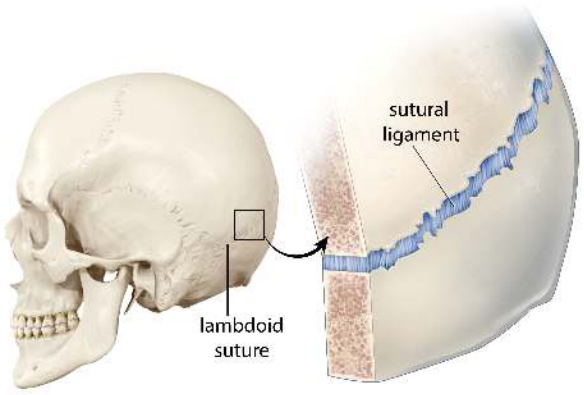
Structural Classification of Joints

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 dense regular connective tissue.
  - A suture is an example of a fibrous joint found in the skull.
- 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. These three structural classifications will be discussed in further detail in the following sections of this chapter.

Suture

All the bones of the skull, except for the mandible, are joined to each other by a fibrous joint called a **suture**. The dense regular 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. (Figure 7.2.1) Thus, skull sutures are functionally classified as a synarthrosis, although some sutures may allow for slight movements between the cranial bones.



(Figure 7.2.1): Suture. The sutures of the skull are very narrow areas of dense regular connective tissue that are immovable. *(Image credit: "Fibrous Joint - Suture" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, based on originals from Anatomy Standard (skull) and BlueLink (illustration).)*

Functional Classification of Joints

The functional classification of joints is determined by the amount of mobility found between the adjacent bones. 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. Joints are thus functionally classified as

- a **synarthrosis** or immobile joint,
- an **amphiarthrosis** or slightly moveable joint, or
- a **diarthrosis**, which is a freely moveable joint.

Depending on their location, fibrous joints may be functionally classified as a synarthrosis or an amphiarthrosis. 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 provides for a strong union between the articulating bones. This is important at locations where the bones provide protection for internal organs. Examples include sutures, such as the coronal, squamous, and lambdoid sutures, which are the fibrous joints between the bones of the skull, and the manubriosternal joint (Figure 7.2.8) that unites the manubrium and body of the sternum for protection of the heart.

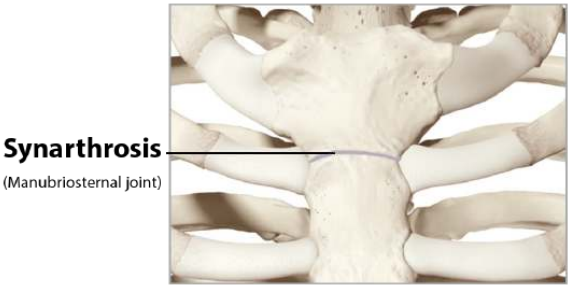


Figure 7.2.8: Synarthrosis - Manubriosternal Joint. The joint between the manubrium and the body of the sternum is an example of a synarthrosis, an immobile or essentially immobile joint. This joint is a synchondrosis that may ossify late in life. *(Image credit: "Synarthrosis - Manubriosternal Joint" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.)*

Amphiarthrosis

An **amphiarthrosis** is a joint that has limited mobility but slight movement is available in many directions. 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. 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 (Figure 7.2.9). 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 because the strength of the pubic symphysis is important in conferring weight-bearing stability to the pelvis. During childbirth this joint loosens so the pelvis can shift to adjust to the fetus passing through the pelvic outlet. Following birth, the joint should tighten again.

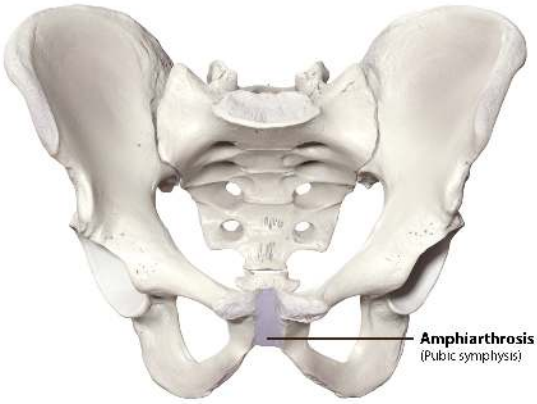


Figure 7.2.9: Amphiarthrosis - Pubic Symphysis. The fibrocartilage joining the right and left symphyseal surfaces allows for limited movement between the right and left os coxae and thus functionally forms an amphiarthrosis type of joint. *(Image credit: "Amphiarthrosis - Pubic Symphysis" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard.)*

Diarthrosis

A freely mobile joint is classified as a **diarthrosis**. These types of joints include all synovial joints (structural classification) 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 7.2.10). The hip joint, where the head of the femur articulates with the acetabulum of the hip bone, is a multiaxial joint. This allows the 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.

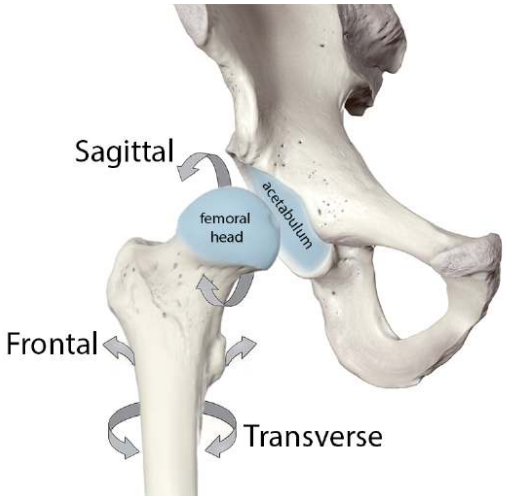


Figure 7.2.10: Diarthrosis - Multiaxial Joint. A multiaxial joint, such as the hip joint, allows for movements in each of the three planes, moving: anterior-posterior, medial-lateral, and rotational. *(Image credit: "Diarthrosis - Multiaxial Joint" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard.)*

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7.3: Types of Body Movements

Learning Objectives

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

- 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 7.3.1). 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. Refer to Figure 7.3.1 as you go through this section.

Interactive Link



Watch this video to learn about anatomical motions. What motions involve increasing or decreasing the angle of the foot at the ankle?

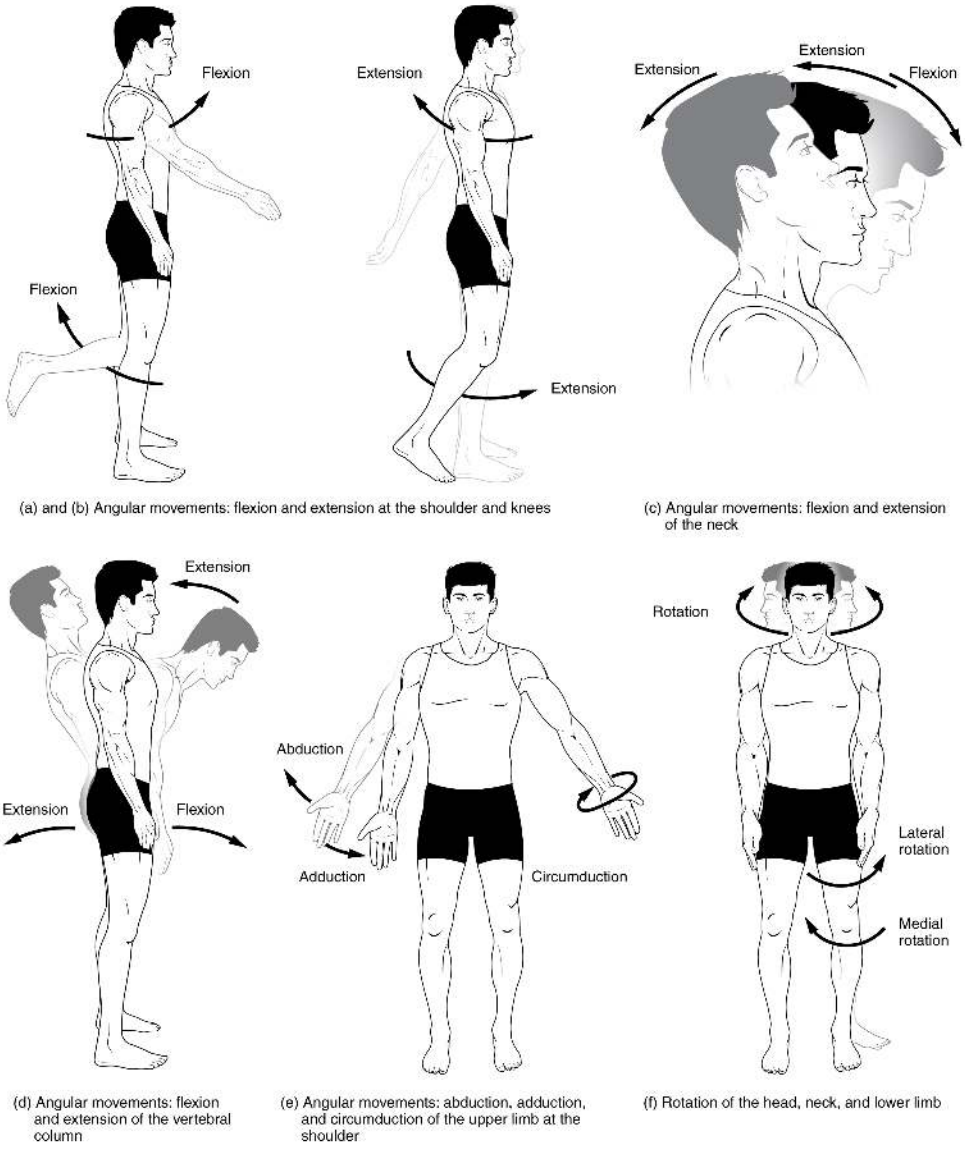


Figure 7.3.1 Movements of the Body, Part 1 Synovial joints give the body many ways in which to move. (a)–(b) Flexion and extension motions are in the sagittal (anterior–posterior) plane of motion. These movements take place at the shoulder, hip, elbow, knee, wrist, metacarpophalangeal, metatarsophalangeal, and interphalangeal joints. (c)–(d) Anterior bending of the head or vertebral column is flexion, while any posterior-going movement is extension. (e) 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. (f) 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).

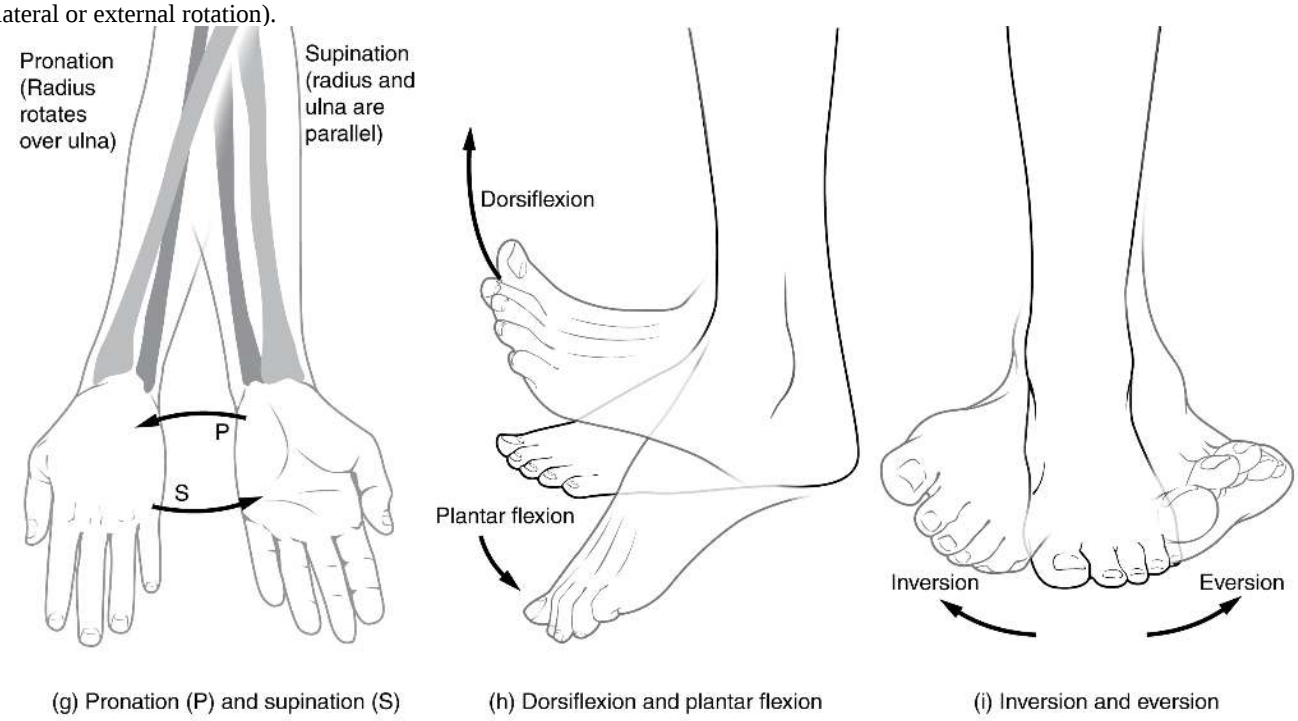


Figure 7.3.2: Movements of the Body, Part 2 (g) Supination of the forearm turns the hand to the palm forward position in which the radius and ulna are parallel, while forearm pronation turns the hand to the palm backward position in which the radius crosses over the ulna to form an "X." (h) Dorsiflexion 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. (i) 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. / Image cropped from original

Flexion and Extension

Flexion and **extension** are typically movements that take place within the sagittal plane and involve anterior or posterior movements of the neck, trunk, or limbs. For the vertebral column, flexion (anterior flexion) is an anterior (forward) bending of the neck or trunk, while extension involves a posterior-directed motion, such as straightening from a flexed position or bending backward. **Lateral flexion** of the vertebral column occurs in the coronal plane and is defined as the bending of the neck or trunk 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 7.3.1 **a-d**).

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 7.3.1 **e**).

> An easy way to remember the difference between the two is to look at the words. Think of **add**uction as "adding" to yourself, you are "adding" your limbs to your body by bringing them closer in. For **abd**uction, although it may sound silly, try to remind yourself of an alien abduction. Typically, an alien would be abducting away a person or a cow in their spaceship. By remembering this image, you can remember that in abduction, you are moving your limbs away from yourself.

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 7.3.1 **e**).

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.

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 7.3.1 **g**).

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 7.3.1 **h**).

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 7.3.1 **i**).

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CHAPTER OVERVIEW

8: Muscle Tissue

8.1: Muscle Tissues
8.2: Skeletal Muscle Organ Structure
8.3: Muscle Fiber Contraction and Relaxation
8.4: Types of Muscle Fibers and Exercise
8.5: Review Questions

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8.1: Muscle Tissues

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

- Compare and contrast the different types of muscle tissue
- Explain the four functional properties of muscle tissue

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 8.1.1). All muscle tissues have four functional properties in common which include **excitability**, **contractility**, **extensibility**, and **elasticity**.

- **Excitability** - the plasma membrane can change electrical states and send an electrical wave called an action potential along the entire surface of each cell.
- **Contractility** - allows muscle tissue to pull on its attachment points as the cells shorten.
- **Extensibility** - the cells of muscle tissue can stretch or elongate.
- **Elasticity** - following contraction or extension, a muscle can recoil to its original length when relaxed due to elastic proteins.

Muscle Tissue Types

Differences among the three muscle types include the microscopic organization of the intracellular contractile proteins—actin and myosin. The actin and myosin proteins are arranged very regularly in the cytoplasm of individual muscle cells (referred to as **myofibers**) in both skeletal muscle and cardiac muscle, which creates a striped pattern across the width of the cell called **striations**. The striations are visible with a light microscope under high magnification (see Figure 8.1.1.*A*, *B*) as an alternating pattern of light - dark - light - dark - etc. along the entire length of the myofiber. These striations are more prominent in skeletal muscle fibers than in cardiac muscle fibers. Because the actin and myosin are not arranged in such regular fashion in smooth muscle, the cytoplasm of a smooth muscle fiber has a uniform, nonstriated appearance (resulting in the name smooth muscle).

Skeletal Muscle Tissue

Skeletal myofibers are long, striated rods that range from a few millimeters to multiple centimeters, extending beyond the sides of the images in Figure 8.1.1.*A* below (individual cell is outlined). The longest muscle in the body is the sartorius that has myofibers that are, on average, 42 centimeters/16.5 inches long! Skeletal muscle comprises approximately 40% of our body weight and contains 50 to 75% of all body proteins. Due to the need to conduct the functioning of such a large cell, each myofiber has many nuclei. The longer the fiber, the more nuclei it has. These nuclei are pushed to the edges of the cell to accommodate all of the intracellular proteins (as indicated by the arrows in Figure 8.1.1.*A*2). Skeletal muscle is under **voluntary control**, so any muscle movement that you can consciously decide to contract or relax has skeletal muscle in it. This includes all of the body's muscles that move the skeleton and the skin, including your muscles of respiration, as well as some of the body's tubular organs: anal sphincters, urinary sphincters, and your throat. Your tongue also contains skeletal muscle!

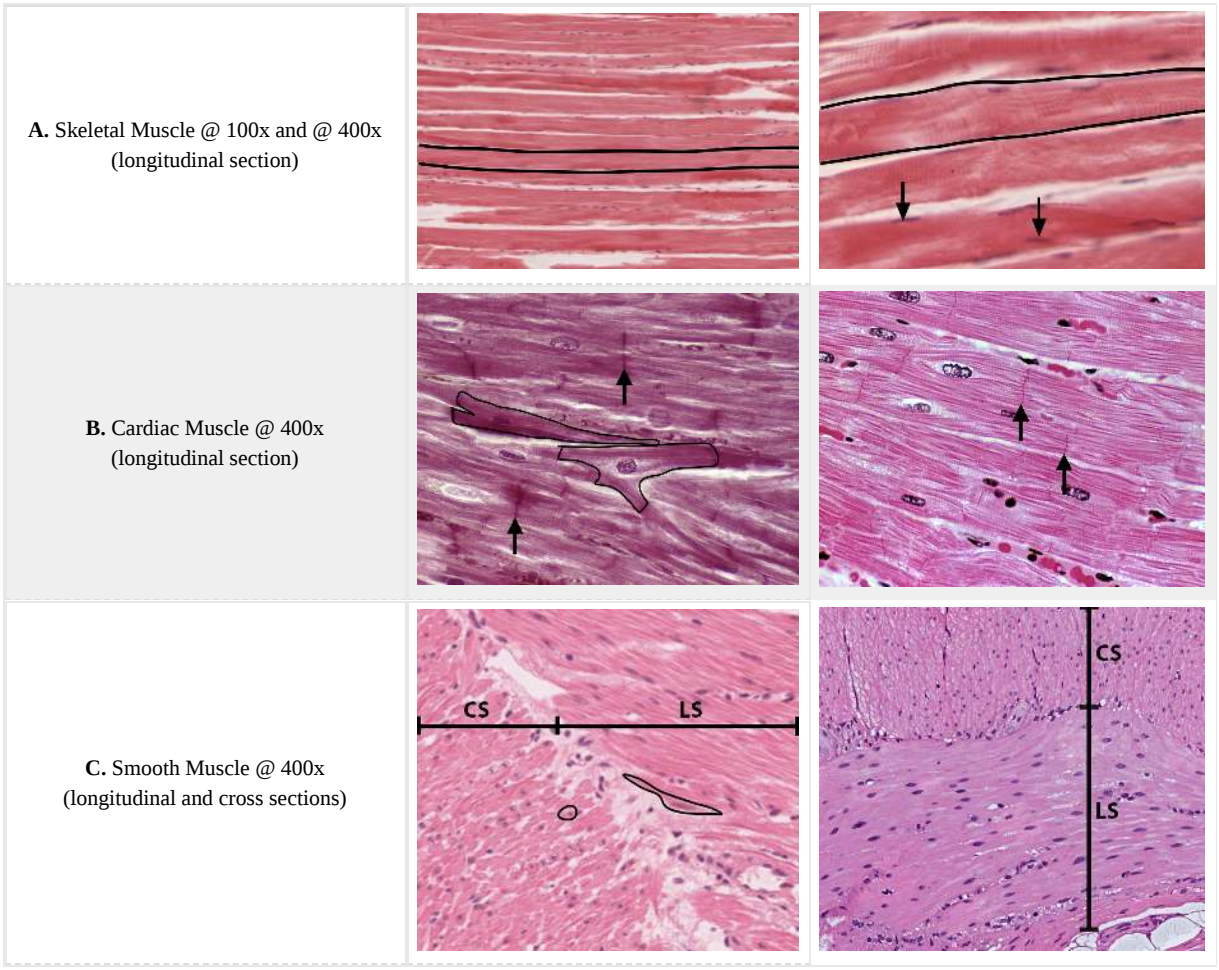


Figure 8.1.1. The Three Types of Muscle Tissue. The body contains three types of muscle tissue: A. skeletal muscle, B. cardiac muscle, C. smooth muscle. *(Image credits: Types of Muscle Tissue by Jennifer Lange are licensed under CC-BY-SA-NC 4.0. Micrographs A1, A2, and C1 provided by the Regents of University of Michigan Medical School, micrographs B1, B2, and C2 provided by Virginia Commonwealth University.)*

Cardiac Muscle Tissue

Cardiac muscle tissue is only found in the heart. Highly coordinated contractions of cardiac muscle pump blood into the vessels of the circulatory system. 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 physically and functionally connected to one another at their ends by specialized cell junctions call **intercalated disks** (indicated by arrows in Figure 8.1.1.*B*). Intercalated disks are part of the sarcolemma and contain two structures important in cardiac muscle contraction: **gap junctions** and **desmosomes** (Figure 8.1.2). A gap junction forms channels between adjacent cardiac muscle fibers that allows the electrical signal to flow quickly from one cardiac myofiber to the next. This joining of cells allows coordinated contraction of

the entire heart. The remainder of the intercalated disk 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. Cardiac muscle is under **involuntary control** as you cannot consciously control its action.

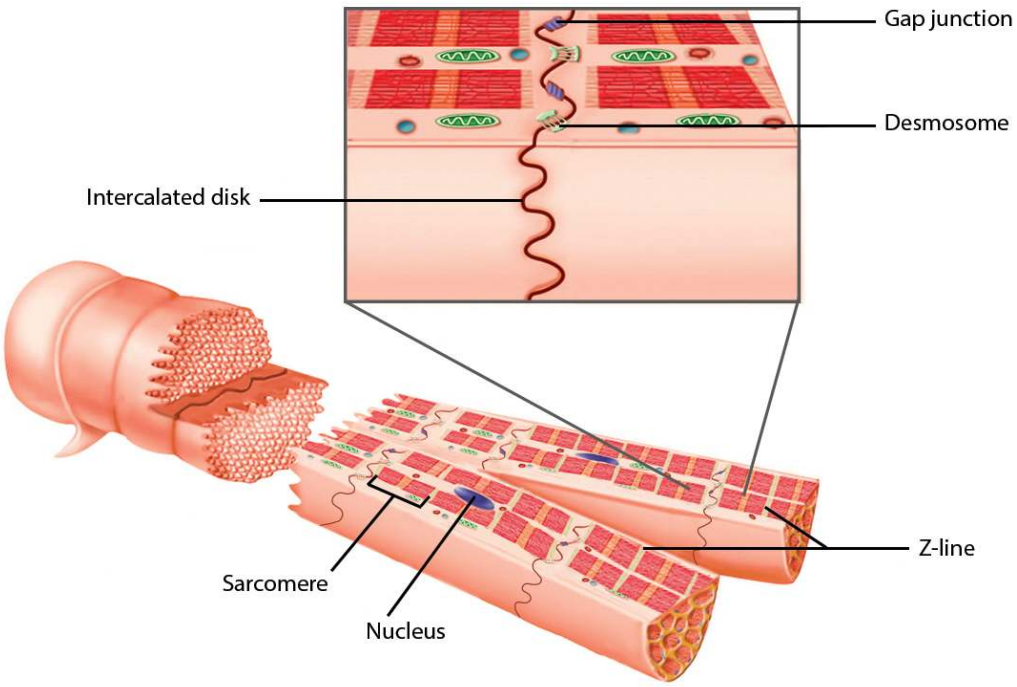


Figure 8.1.2: Cardiac Muscle. Cardiac myofibers are branched so they can connect to mutliple neighboring cells at intercalated disks. Intercalated disks are specialized cell junctions unique to cardiac muscle tissue that contain gap junctions and desmosomes. *(Image credit: "Cardiac Muscle" by Jennifer Lange is licensed under CC-BY-SA-NC 4.0, modification of original work by Cenveo.)*

Smooth Muscle Tissue

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. 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. Smooth muscle fibers are spindle-shaped (wide in the middle and tapered at both ends, somewhat like a football) and have a single nucleus (see outlined cells in (Figure 8.1.1.*C* and in (Figure 8.1.3). 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, smooth muscle fibers do have actin and myosin contractile proteins. Smooth muscle is also under **involuntary control**.

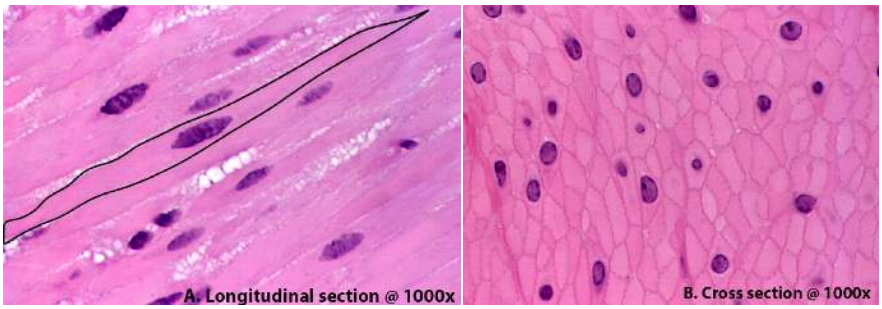


Figure 8.1.3: Smooth Muscle Fibers. Smooth muscle has spindle shaped cells that taper to points at the ends (A) and have a centrally located nucleus. Because of this shape, when viewed in cross section the myofibers will appear to have different diameters and only those cut through the center will show the nucleus (B). *(Image credit: "Smooth Muscle Fibers" by Jennifer Lange is licensed under CC-BY-SA-NC 4.0. Micrographs from Virginia Commonwealth University.)*

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8.2: Skeletal Muscle Organ Structure

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

- Describe the layers of connective tissues and how they package skeletal muscle
- Explain how muscles work with tendons to move the body
- Identify and describe the microscopic anatomy of a muscle fiber and a sarcomere

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 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 structural damage or deformation. Joints can become misaligned or dislocated by excessive or inappropriate forces applied to 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.

Organ Structure

Each skeletal muscle is an organ consisting of multiple integrated tissues acting together to cause movement: skeletal muscle and three layers of proper connective tissue. The connective tissue layers (called “mysia”) provide structure to the muscle as a whole and also compartmentalize the muscle fibers within the muscle (Figure 8.2.1) and (Figure 8.2.2). Wrapping around the organ is a sheath of dense irregular connective tissue called the **epimysium** that 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. Within the epimysium skeletal muscle fibers are organized into bundles, called **fascicles**, by a middle layer of dense irregular connective tissue making up 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 areolar connective tissue layer called the **endomysium**. The endomysium contains the extracellular fluid and nutrients to support the muscle fiber. These nutrients are supplied via blood capillaries located in the areolar tissue.

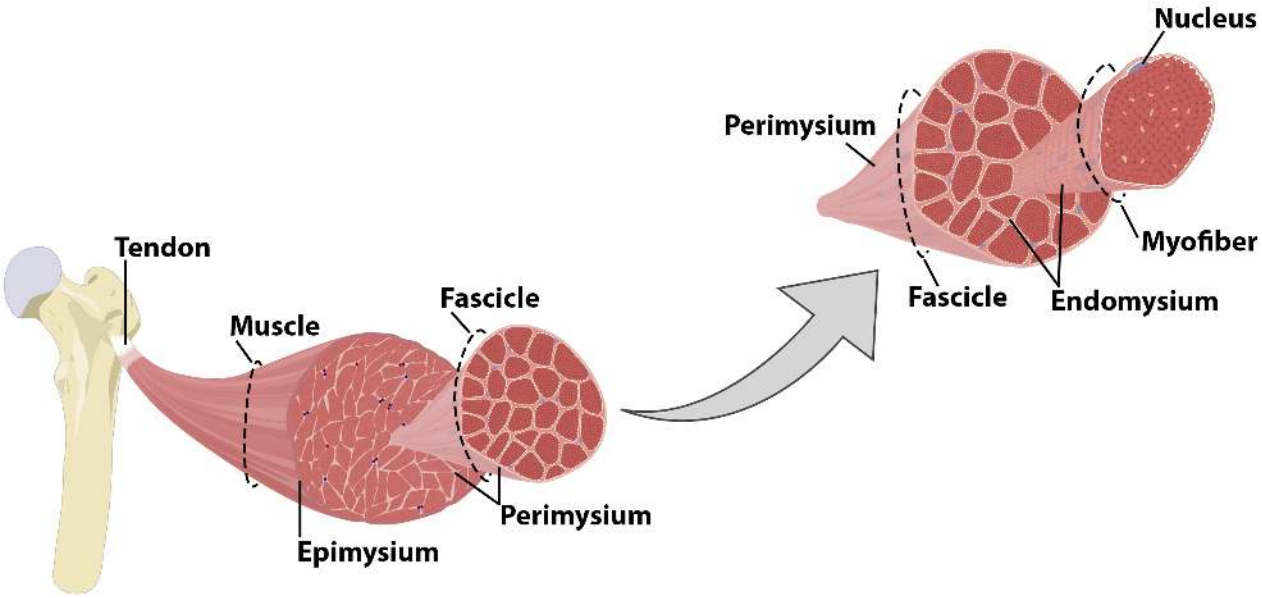


Figure 8.2.1: Skeletal Muscle Organ Structure. Each level of the organization of a skeletal muscle is wrapped in a connective tissue layer: the cell (myofiber) is surrounded by the endomysium, the bundle of cells (muscle fascicle) is surrounded by the perimysium, and the organ (muscle) is surrounded by the epimysium. *(Image credit: "Skeletal Muscle Organ Structure" by Justin Greene is licensed under CC BY-NC-SA 4.0).*

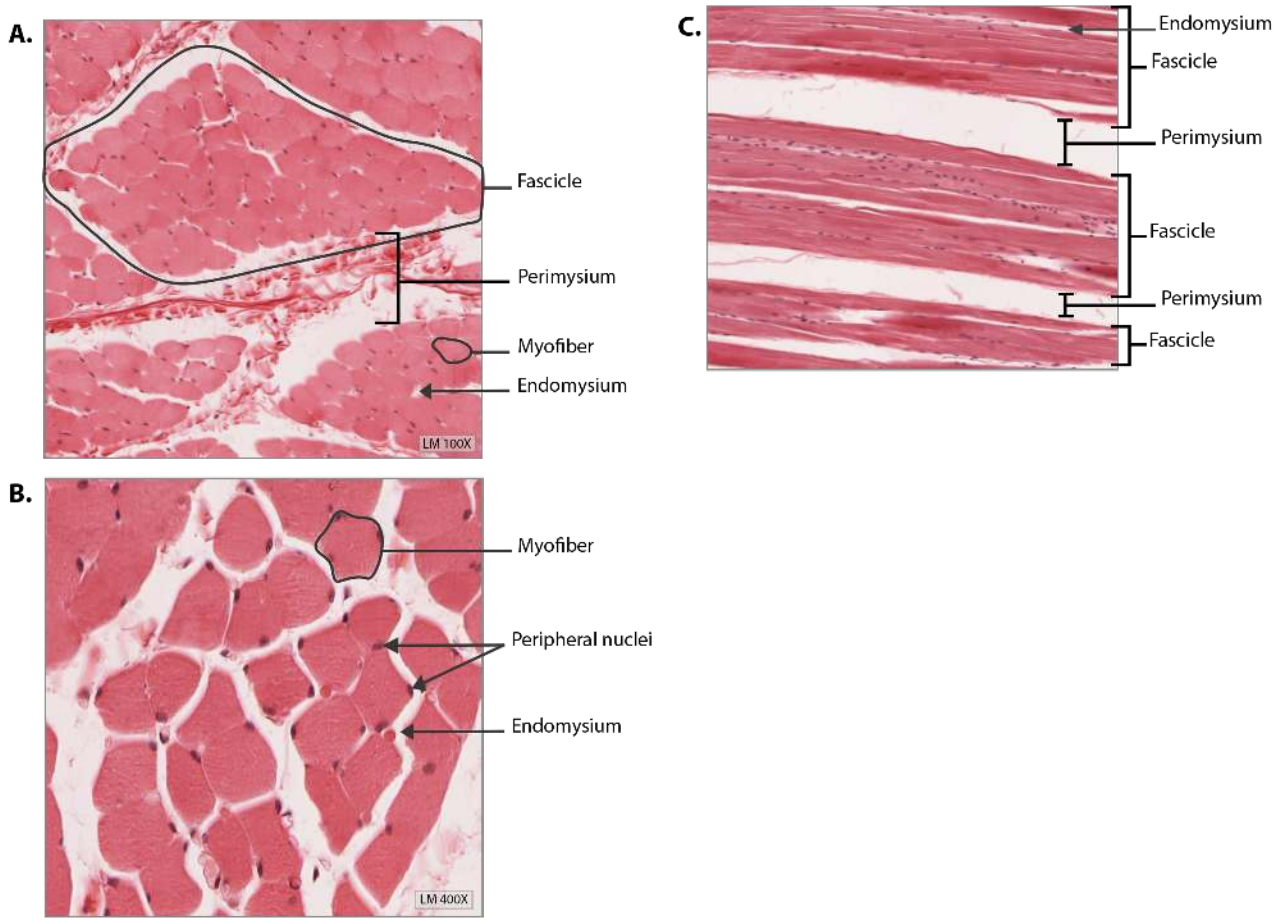


Figure 8.2.2: Histology of Skeletal Muscles in Cross and Long-Sections. Muscles are held together by and transfer force through their connective tissue layers. The perimysium surround the fascicles and can be seen between them. The endomysium surrounds the myofibers and appears thinner than the perimysium. A. Slide cross-section at 100x, B. Slide cross-section at 400x, C. Slide long-section at 100x. *(Image credit: "Histology of Skeletal Muscle" by Jennifer Lange, based on micrographs provided by the Regents of the University of Michigan under CC-BY-NC-SA 3.0)*

Skeletal muscles have **tendons** that attach to bones and transfer the force of contraction to the skeleton. The collagen in the three tissue layers intertwines and integrates with the collagen of a tendon, straightening to form a cord of dense regular connective tissue. At the other end of the tendon, the collagen incorporates into periosteum becoming dense irregular connective tissue once more. Tension created by contraction of the muscle fibers is transferred though the mysia, to the tendon, and then to the periosteum to pull on the bone to move 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 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 **skeletal muscle fibers** or **skeletal myofibers**. Specific terminology associated with myofibers is rooted in the Greek *sarco*, which means “flesh.” The plasma membrane of muscle fibers is called the **sarcolemma** and the cytoplasm is referred to as **sarcoplasm.** Skeletal myofibers can be quite large for human cells, with diameters up to 100 μm and lengths up to 30 cm (11.8 in). Multiple nuclei means multiple copies of genes, permitting the production of the large amounts of proteins and enzymes needed for muscle contraction along the length of the entire muscle fiber. Multiple nuclei also means mitosis would be extremely complicated, so skeletal myofibers do not divide.

Within the sarcoplasm of each muscle fiber are **myofibrils**, rods of protein that run the entire length of the muscle fiber and attach to the sarcolemma at its end (Figure 8.2.3). Each myofibril is composed of a bundle of contractile **thin** and **thick myofilaments**, along with other structural and elastic proteins. As myofibrils contract, the entire muscle cell contracts. Because myofibrils are only approximately 1.2 μm in diameter, hundreds to thousands can be found inside one muscle fiber.

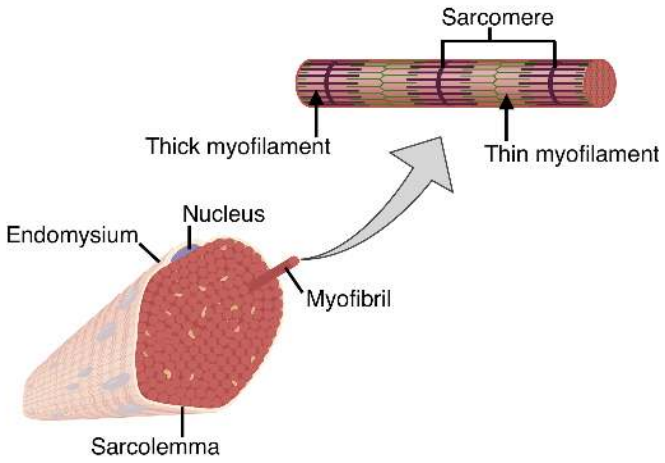


Figure 8.2.3: Myofibrils and Myofilaments. With each cell are multiple rods of proteins that contain two types of myofilaments - thin ones and thick ones. *(Image credit: "Myofibrils and Myofilaments" by Justin Greene is licensed under CC BY-NC-SA 4.0, myofibril enlargement based on original by OpenStax.)*

The Sarcomere, Myofilaments and Protein Organization

The striated appearance of skeletal muscle fibers is due to the arrangement of the thin and thick myofilaments in sequential order from one end of the muscle fiber to the other.

Thin myofilaments, or simply thin filaments, consist of three main proteins: **actin**, **troponin** and **tropomyosin**. Thin filaments are often compared to beads on a string due to their appearance. Several actin subunits form actin strands. These actin subunits each have an "**active site**" where **myosin** from the **thick myofilament** will bind to during muscle contraction. During muscle relaxation, the active site on actin is covered by tropomyosin running along the length of the actin strands. Troponin holds the tropomyosin in place. When muscle contraction begins, calcium (Ca^{2+}) ions bind to troponin, causing tropomyosin to "move out of the way", allowing the active sites on actin to be exposed. Myosin will now bind to these active sites on actin and muscle contraction begins.

As mentioned above, the **thick filaments** are made of thousands of units of **myosin**. Each myosin has a "head" that grabs on to actin's active site. There is also a region on myosin that ATP binds to. Recall that ATP is the major energy molecule of the cell, and so the cell will need energy (ATP) for muscle contraction. The steps of muscle contraction and ATP's role in this process will be discussed in a future section. An illustration of all the components of thin and thick filaments can be seen in Figure 8.2.4.

As mentioned above, actin and myosin are the proteins that are responsible for muscular contraction. The structural differences between these two myofilaments not only leads to the striated appearance of skeletal muscle tissue, but also to the ability of the two to work together to produce the overall function of muscle contraction.

Each segment of these myofilaments and their regulatory proteins, connected on each end to a protein network called the **Z-line** (or Z-disc), is called a **sarcomere**. The sarcomere is the functional unit of the muscle fiber and runs from one Z-line to the next Z-line. A chain of thousands of repeating sarcomeres forms the long tube-like myofibrils.

Each sarcomere is approximately 2 μm in length with a three-dimensional cylinder-like arrangement. The repeating pattern of the myofilaments, along with other proteins, within the sarcomere gives rise to very distinctive regions and structures (Figure 8.2.6). Each sarcomere is bordered by Z-lines to which the thin myofilaments are anchored. The central **M-line** anchors the thick filaments. The difference in protein mass between the two filaments is what causes the striated appearance of skeletal muscle fibers as their positions alternate along the myofibril (Figure 8.2.5).

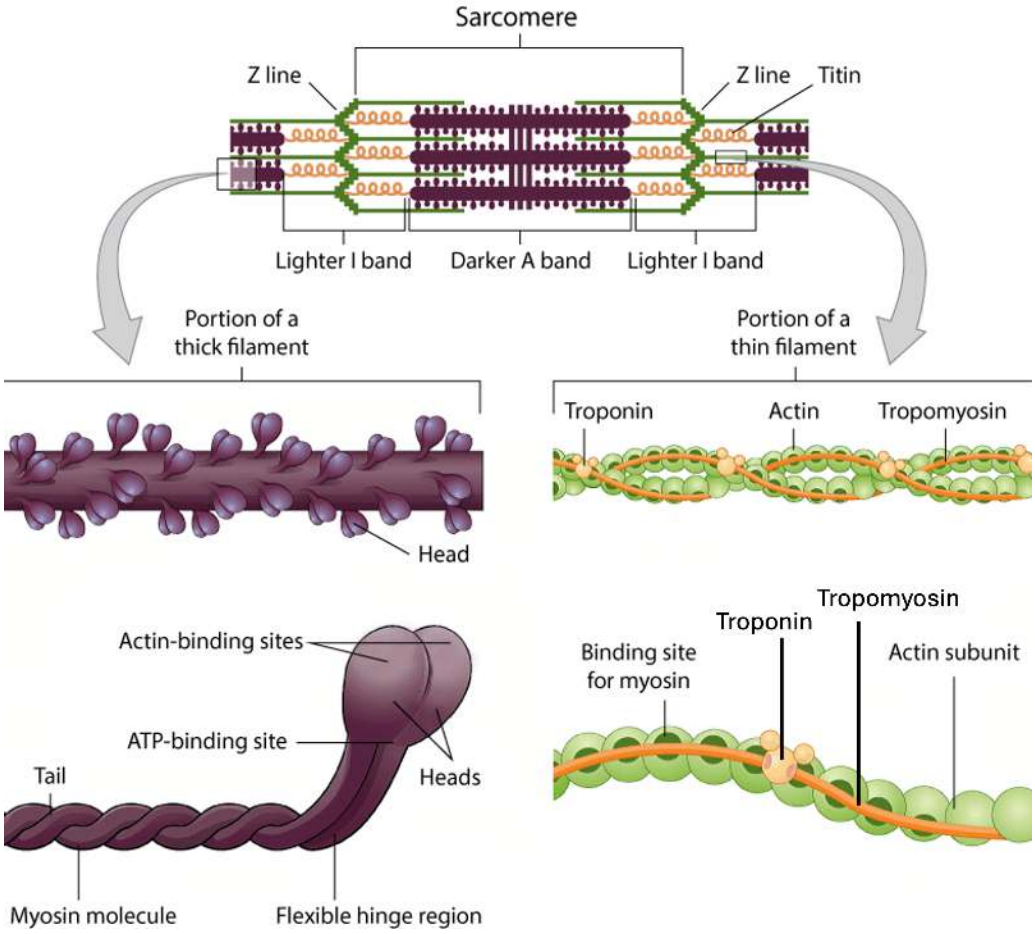


Figure 8.2.4: Myofilaments. The sarcomere, the region from one Z-line to the next Z-line, is the functional unit of a skeletal muscle fiber and is composed of a repeating arrangements of actin and myosin, along with other proteins. *(Image credit: "Sarcomere and Myofilaments" by Mark Schaeffer is licensed under CC BY-NC-SA 4.0, modification of original by Openstax.) / Addtional Troponin and Tropomyosin labels by Harmony Folse*

The zone immediately surrounding the Z-lines is known as the **I band**, or light band, because only thin filaments are present (Figure 8.2.6). The thin composition of actin makes it difficult to see, hence the name the light band. The myosin is anchored to the central M line, from whence it projects toward, but not all to way to, the Z-lines. The area of the sarcomere where myosin is present is known as the **A band**, or dark band. There are some areas where thin and thick myofilaments are both present, known as the zone of overlap. The area in which no overlap occurs is the **H zone,** where only myosin is present. The alternation of I bands and A bands along the length of the myofibril, and thus the myofiber, is what gives the cell its striated appearance.

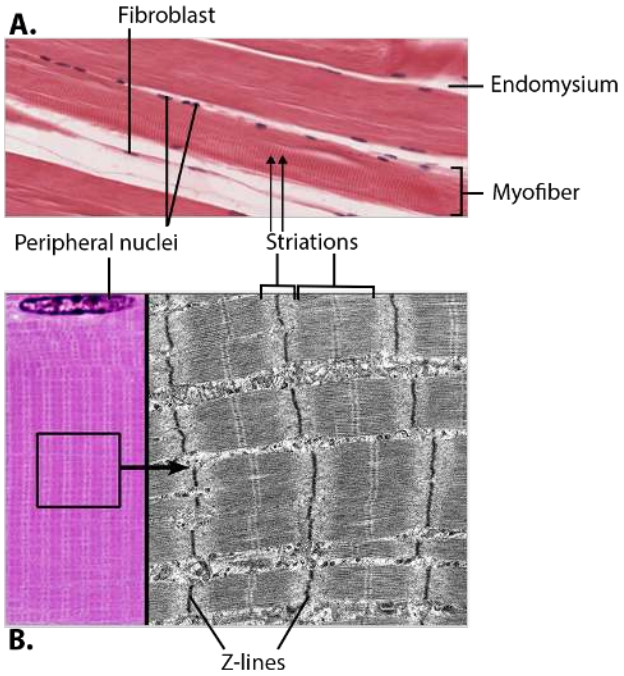


Figure 8.2.5: Skeletal Muscle Striations. The striated pattern of alternating light and dark staining bands results from the regular arrangement of the myofilaments: areas with myosin stain darkly and those without stain lightly. This banding pattern can be visible with a light microscope at 400x (image A) and becomes easier to see at higher magnifications. Image B shows a light microscope at 2,000x as well as a transmission electron microscope (TEM) at 15,000x. With the TEM you can also clearly see the Z-lines. *(Image credit: "Skeletal Muscle Striations" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, slide A provided by the Regents of the University of Michigan Medical School under CC BY-NC-SA 4.0 © 2022; slide B micrographs provided by Virginia Commonwealth University under CC BY-NC-SA 4.0)*

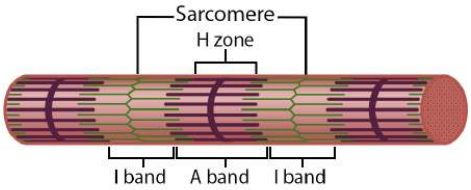


Figure 8.2.6: Myofibril and the Sarcomere. Myofibrils are composed of chains of thousands of repeating sarcomeres. The alternating I bands and A bands give the myofibril (and the myofiber) its striated appearance. *(Image credit: "Myofibril and the Sarcomere" by Justin Greene is licensed under CC BY-NC-SA 4.0, based on original by Openstax.)*

An easy way to remember which is the I band and which is the A band is to remember the other names for these bands, light band and dark band, respectively. The I band is the **li**ght band and the word light has the letter I in it. Only thin filaments are in the I band, this is why it is so "light" and "thin". The A band is the d**a**rk band and the word dark has the A in it. Mostly thick filaments are found in the A band (with some thick overlapping with the thin), this is why it looks so thick or "dark".

Surrounding each myofibril is the **sarcoplasmic reticulum (SR),** the specialized smooth endoplasmic reticulum of myofibers, which stores, releases, and retrieves the calcium ions (Ca^{2+}) needed for contraction to occur (Figure 8.2.7). The signal from a motor neuron stimulates the release of calcium ions (Ca^{2+}) from its storage in the cell's sarcoplasmic reticulum. For the neuron's signal 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 cell membrane can get close to the SR in the sarcoplasm. On each side of the T-tubule is a **terminal cisterna** (plural - cisternae), an enlarged region of the

SR that contains high concentrations of calcium ions. The arrangement of a T-tubule with the terminal cisternae of the SR on either side is called a **triad** (Figure 8.2.7). The triad encircles the cylindrical structure of the myofibril.

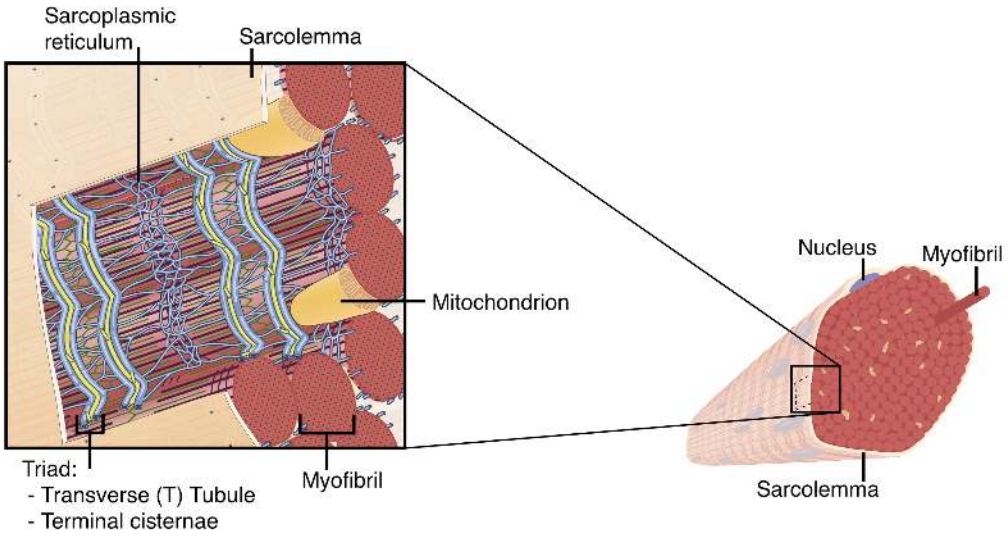


Figure 8.2.7: The Triad. Two terminal cisternae (part of sarcoplasmic reticulum) and one T-tubule comprise a triad—a "threesome" of membranes, with those of sarcoplasmic reticulum on both sides of the T-tubule sandwiched between them. *(Image credit: "Skeletal Myofiber Structure" by Justin Greene is licensed under CC BY-NC-SA 4.0.)*

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8.3: Muscle Fiber Contraction and Relaxation

Learning Objectives

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

- Describe the components and role of the neuromuscular junction
- Describe the components involved in a muscle contraction
- Explain how muscles contract and relax
- Describe the sliding filament model of muscle contraction

The Neuromuscular Junction

The **neuromuscular junction (NMJ)** (Figure 8.3.1) is the site in which a motor neuron contacts a muscle fiber. For a bit of background, a neuron is the basic unit of the nervous system and makes up nervous tissue. A motor neuron is a neuron that specifically stimulates a muscle (or a gland). Neurons communicate with other cells via chemical messengers called **neurotransmitters**.

When the nervous system decides to move a muscle, a signal is sent from the central nervous system (the brain and spinal cord) to a motor neuron at an NMJ. At the NMJ, the motor neuron releases a neurotransmitter called **acetylcholine (ACh).** ACh diffuses across the space between the motor neuron and the muscle fiber. ACh reaches the muscle fiber and binds to a specialized receptor in the sarcolemma of the muscle fiber. The area on the sarcolemma where these receptors are found is called the **motor end-plate**. Once ACh binds to these specialized receptors, a series of events inside the muscle is triggered that leads to muscle contraction. These events will be discussed in the following section.

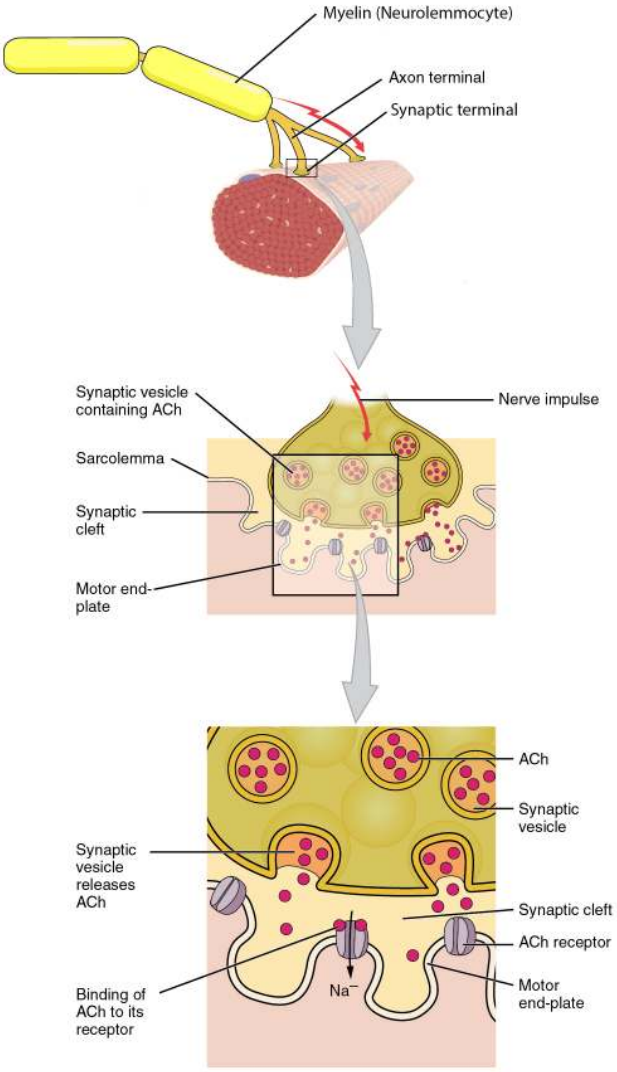


Figure 8.3.1: Motor End-Plate and Innervation. At the NMJ, the axon terminal releases ACh. The motor end-plate is the location of the ACh-receptors in the muscle fiber sarcolemma. When ACh molecules are released, they diffuse across a tiny space called the synaptic cleft and bind to the receptors. *(Image credit: "Motor Endplate and Innervation" by Jennifer Lange and Justin Greene is licensed under CC BY-NC-SA 4.0, modification of original by Openstax.)*

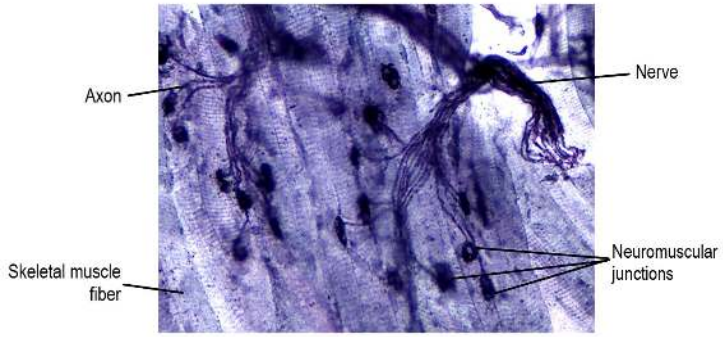


Figure 8.3.2: Neuromuscular Junctions. Every skeletal muscle fiber is innervated by a motor neuron at the neuromuscular junction. Signals from motor neurons initiate the process of muscle contraction. *(Image credit: "Motor End Plate - Labeled" by Whitney Menefee is licensed under CC BY-SA 4.0 / A derivative from the original work.)*

Muscle Contraction

Once ACh binds to the specialized receptors on the sarcolemma of the muscle fiber, it causes the opening of sodium (Na^+) ion channels in the sarcolemma. Na+ will rush into the muscle fiber, electrically exciting the muscle fiber in the form of an action potential. Since the nervous system has not been covered yet, for now, think of an action potential like a change in electrical charge across a cell that triggers different processes inside the cell. In the case of the muscle fiber, as the action potential spreads across the muscle fiber, it causes the release of calcium ions (Ca^{2+}) from the sarcoplasmic reticulum (SR). As Ca^{2+} rushes into the sarcoplasm (the cytoplasm of the muscle cell), it binds to troponin. When Ca^{2+} binds to troponin, troponin will pull tropomyosin away from actin's active site. Actin's active site will now be exposed, allowing the myosin head to bind to it. The binding of the myosin head to the actin's active site forms a complex called a **cross-bridge**. ATP bound to the myosin head will be broken down and 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. See Figure 8.3.3.

As long as Ca^{2+} 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.

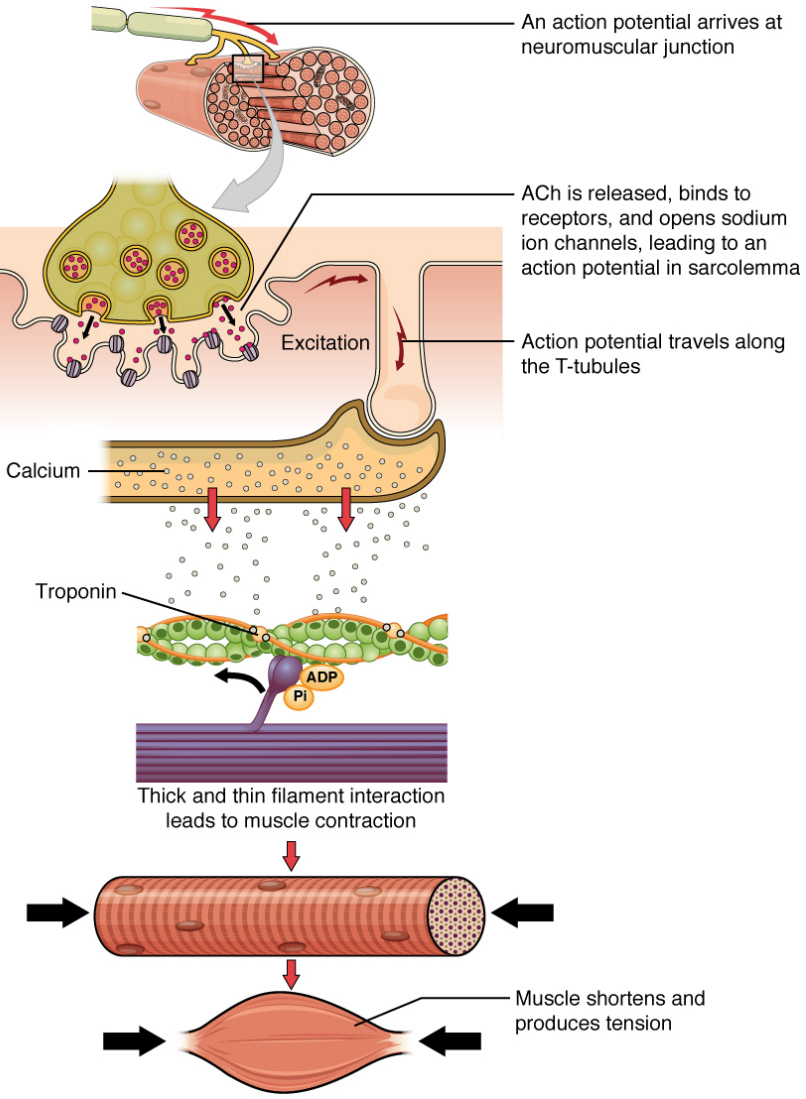


Figure 8.3.3: Contraction of a Muscle Fiber A cross-bridge forms between actin and the myosin heads triggering contraction. As long as Ca^{++} ions remain in the sarcoplasm to bind to troponin, and as long as ATP is available, the muscle fiber will continue to shorten.

Muscle contraction usually stops when signaling from the motor neuron ends, which closes the calcium channels in the SR. Ca^{2+} 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 8.3.4).

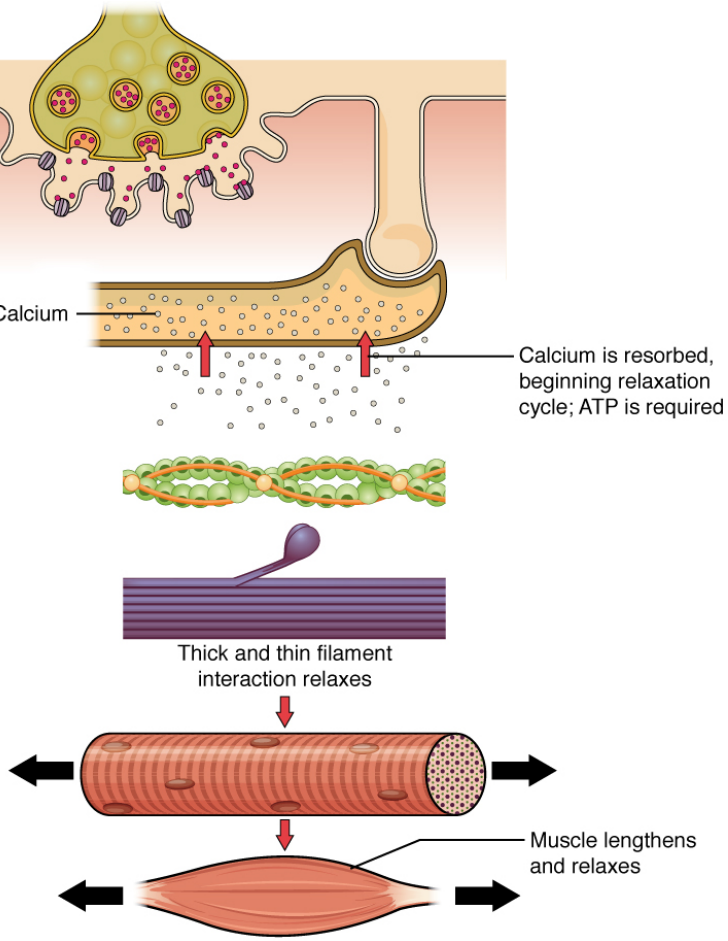
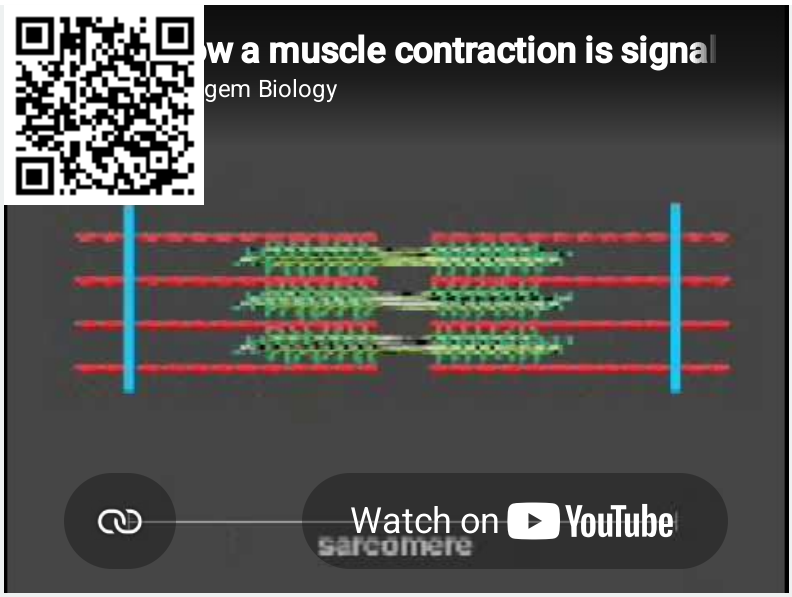


Figure 8.3.4: Relaxation of a Muscle Fiber Ca^{++} ions are pumped back into the SR, which causes the tropomyosin to reshield the binding sites on the actin strands. A muscle may also stop contracting when it runs out of ATP and becomes fatigued.

Interactive Link



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 (Figure 8.3.5). 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 8.3.5). 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.

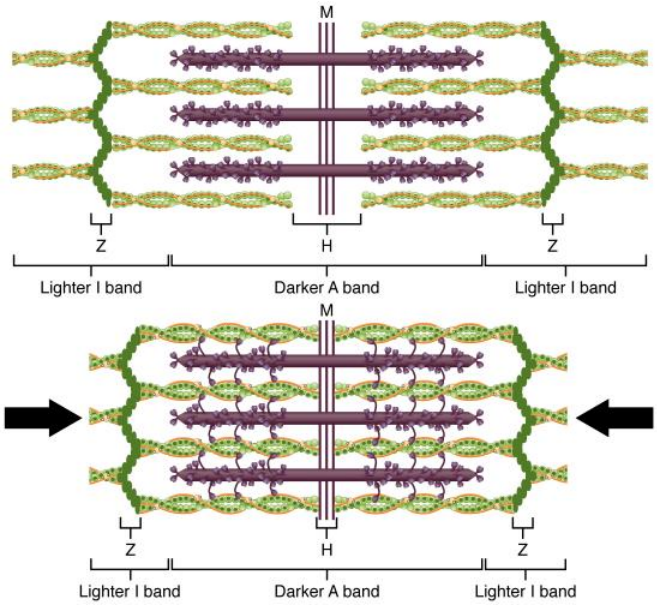


Figure 8.3.5: The Sliding Filament Model of Muscle Contraction When a sarcomere contracts, the Z lines move closer together, and the I band becomes smaller. The A band stays the same width. At full contraction, the thin and thick filaments overlap completely.

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 8.3.6). 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. Recall that ATP stands for adenosine **tri**phospate and ATP has 3 phosphate molecules. When an inorganic phosphate (P_i) is broken off of ATP, it becomes adenoside **di**phosphate or ADP.

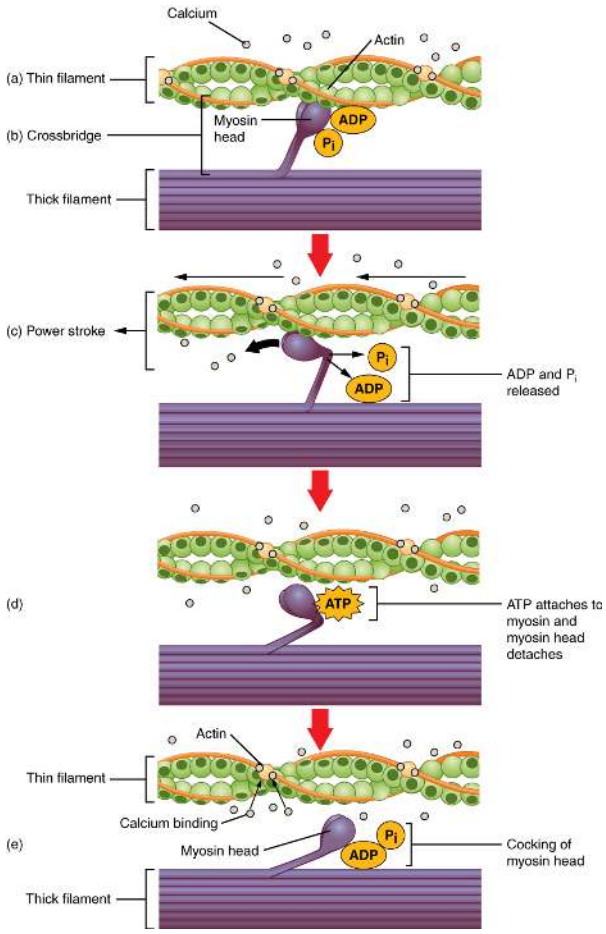


Figure 8.3.6: Skeletal Muscle Contraction (a) The active site on actin is exposed as calcium binds to troponin. (b) The myosin head is attracted to actin, and myosin binds actin at its actin-binding site, forming the cross-bridge. (c) During the power stroke, the phosphate generated in the previous contraction 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 8.3.6**a,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 10nm toward the M-line. This movement is called the **power stroke**, as movement of the thin filament occurs at this step (Figure 8.3.6**c**). 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 8.3.6**d**). After this occurs, ATP is converted to ADP and P_i by the intrinsic ATP breakdown activity of myosin. The energy released during ATP hydrolysis changes the angle of the myosin head into a cocked position (Figure 8.3.6**e**). 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.

Relaxation of a Skeletal Muscle

Relaxing skeletal muscle fibers, and ultimately, the skeletal muscle, begins with the motor neuron. In muscle relaxation, the motor neuron stops releasing its chemical signal, ACh, into the synapse at the NMJ. The muscle fiber will close the gates in the SR where Ca^{2+} was being released. ATP-driven pumps will move Ca^{2+} out of the sarcoplasm and back into the SR. Without Ca^{2+}, troponin allows tropomyosin to fall back into place, blocking the active sites on actin. When these sites are blocked, myosin cannot bind. Without the ability to form cross-bridges between the thin and thick filaments, the muscle fiber loses its tension and relaxes.

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^{2+} 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 in muscle cells: **creatine phosphate** metabolism, **anaerobic glycolysis**, 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 8.3.7).

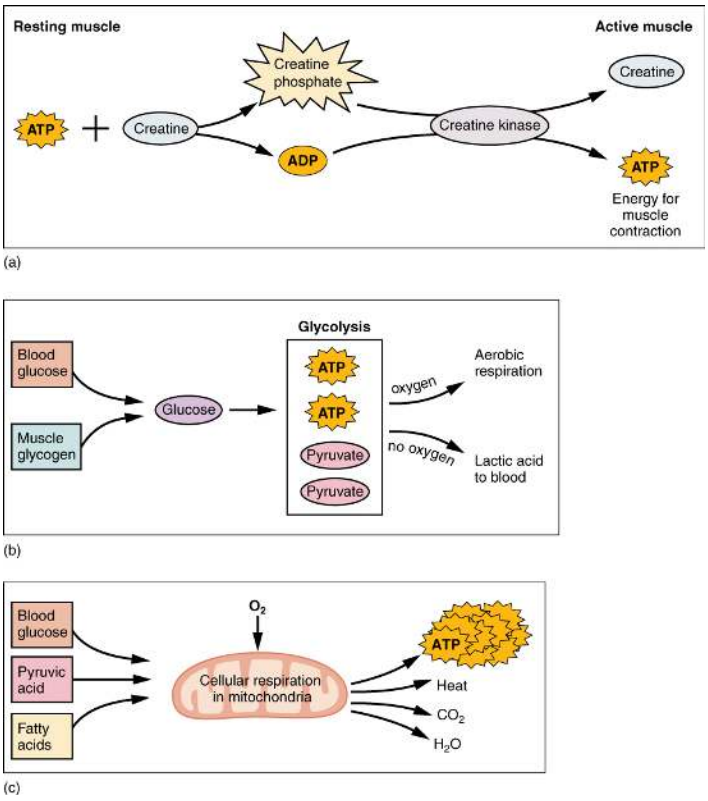


Figure 8.3.7: Muscle Metabolism (a) Some ATP is stored in a resting muscle. As contraction starts, it is used up in seconds. More ATP is generated from creatine phosphate for about 15 seconds. (b) Each glucose molecule produces two ATP and two molecules of pyruvic acid, which can be used in aerobic respiration 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. (c) 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.

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 converting glycogen into glucose. 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, is converted to lactic acid (Figure 8.3.7**b**).

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. 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 only two net 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 two net gain from glycolysis. However, aerobic respiration cannot be sustained without a steady supply of O_2 to the skeletal muscle and is much slower (Figure 8.3.7**c**). 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.

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 may disrupt Ca^{2+} flow out of the SR. Long periods of sustained exercise may damage the SR and the sarcolemma, resulting in impaired Ca^{2+} 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.

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.

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8.4: Types of Muscle Fibers and Exercise

Learning Objectives

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

- Describe the types of skeletal muscle fibers
- Explain fast and slow muscle fibers
- Explain how resistance and endurance exercise affects muscle

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 two types of skeletal muscle fibers: **slow** muscle fibers (also called Type I fibers) and **fast** muscle fibers (also called Type II fibers).

These fibers are then subdivided into the following categories:.

1. **Slow oxidative (SO) fibers** contract relatively slowly and use aerobic respiration (oxygen and glucose) to produce ATP.
2. **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. Also known as Type IIa.
3. **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. Also known as Type IIx.

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.

Endurance Exercise

Slow fibers are predominantly used in endurance exercises that require little force but involve numerous repetitions. The aerobic metabolism used by slow 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.

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 8.4.1). 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.



Figure 8.4.1 Marathoners Long-distance runners have a large number of SO fibers and relatively few FO and FG fibers. (credit: “Tseo2”/Wikimedia Commons)

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 breakdown 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 8.4.2). 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 8.4.2: 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.

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 8.4.3). 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.

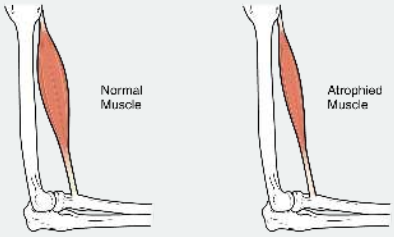


Figure 8.4.3: Atrophy Muscle mass is reduced as muscles atrophy with disuse.

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.

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8.5: Review Questions

Use the following questions to test your knowledge on Muscle Tissue.

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CHAPTER OVERVIEW

9: Overview of the Nervous System

9.1: Organization and Functions of the Nervous System
9.2: Anatomy of Nervous Tissue
9.3: Synapses
9.4: The Function of Nervous Tissue
9.5: The Central Nervous System
9.6: The Peripheral Nervous System
9.7: Review Questions

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9.1: Organization and Functions of the Nervous System

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

- Understand the basic structure of a neuron
- Distinguish between gray and white matter and relate their differences to the structure of neurons
- Identify the structural and functional divisions of the nervous system
- Identify the organs of the central and peripheral divisions of the nervous system
- Understand the basic functions and control 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 in the cranial cavity, 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 an electrophysiology apparatus. 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. For this reason, you will look at the organization of the nervous tissue first and the structures within it. Then you will look at the structural divisions of the nervous system by regions where the organs are located, and then the functional divisions by the specific functions achieved by the organs within it.

Nervous Tissue

Nervous tissue contains two basic types of cells: neurons and glial cells. A **glial cell** performs a supportive role for the neurons and their activities. The **neuron** is the cell type that sends electrical signals throughout the body and both processes and sends motor and sensory information. To describe the functional divisions of the nervous system, it is important to understand the basic structure of a neuron (Figure 9.1.1). 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. Some axons are insulated by a lipid-rich substance called **myelin** that is formed by glial cells. The second type of process that branches off the soma is the **dendrite**. Dendrites are responsible for receiving most of the input from other neurons.

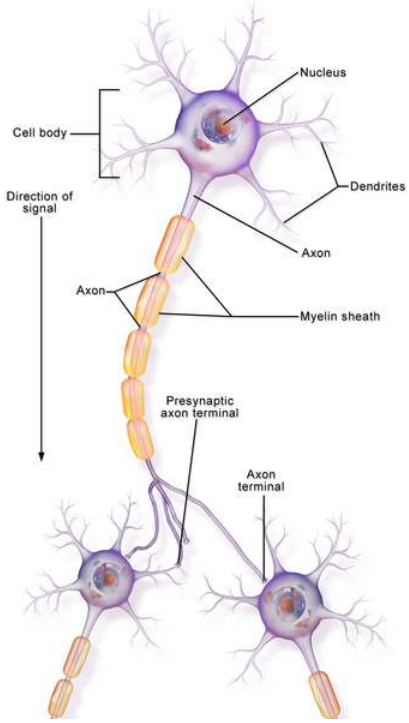


Figure 9.1.1: Basic Structure of a Neuron. Neurons have a soma (or cell body) and processes, which are extensions from the soma that receive or carry information. Processes can be diversified as dendrites which receive information or axon which carries information. The axon shown here is covered by insulating sheaths of myelin. *(Image credit: "Neuron Parts" by BruceBlaus, CC BY-SA 4.0, via Wikimedia Commons.)*

Looking at nervous tissue you can see color differences between the areas: some are white and others are red/pink (if blood is present) or brown/grey (if preserved). there are regions that predominantly contain cell bodies and regions that are largely composed of just axons. Each "color" region contains different neuron parts. The pink/brown/grey areas within nervous system structures are referred to as **gray matter** and these regions contain many cell bodies and dendrites. Those referred to as **white matter** are regions with many axons, particularly axons covered with myelin which give it the white appearance. Figure 9.1.2 demonstrates the appearance of these regions in a freshly dissected brain. 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 the lipids of the myelin.

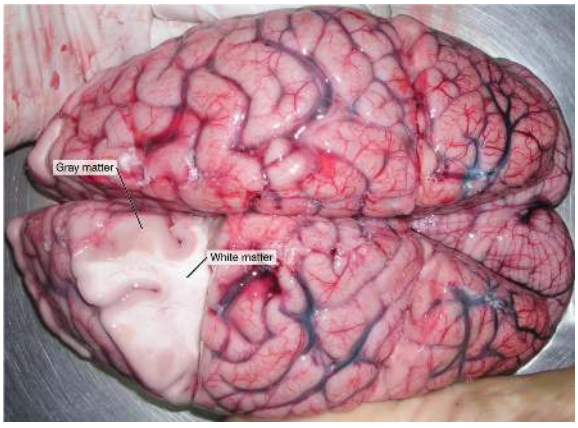


Figure 9.1.2: Gray Matter and White Matter. A brain removed during an autopsy, with a partial section dissected out to show white matter surrounded by gray matter. The gray matter makes up the outer cortex of the brain. *(Image credit: "Human Brain" by Suseno is in the Public Domain / A derivative from the original work.)*

Structural Organization of the Nervous System

The nervous system can be divided into two major regions: the central and peripheral nervous systems. The **central nervous system (CNS)** is composed of the brain and spinal cord, and the **peripheral nervous system (PNS)** is composed of ganglia (structures containing neurons outside of the CNS) and nerves (bundles of axons) (Figure 9.1.3). The brain is contained within the cranial cavity of the skull, and the spinal cord is contained within the vertebral canal 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.

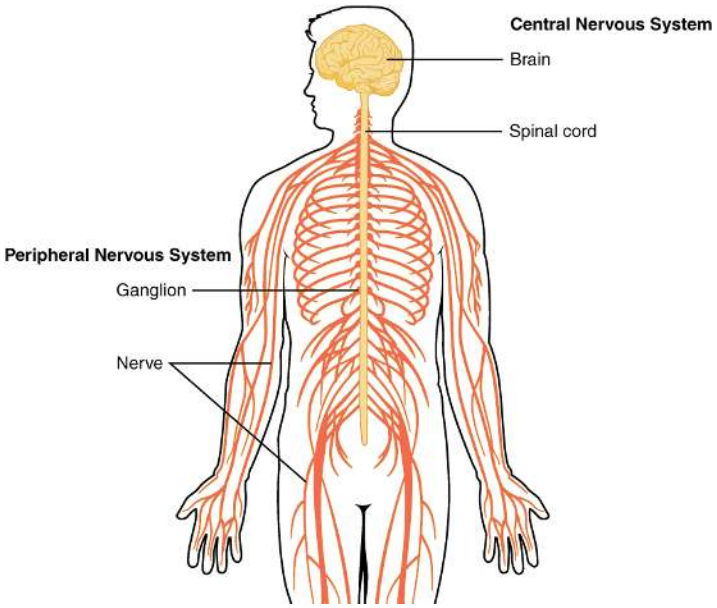


Figure 9.1.3: Structural Divisions of the Nervous System. The structures of the Central Nervous System (CNS) are the brain and spinal cord, located medially within the body. The structures of the Peripheral Nervous System (PNS) are ganglia and nerves. Ganglia are enlarged regions of the nerves that house neuron cell bodies and glial cells within the PNS. *(Image credit: "Structural divisions of the nervous system" by Jennifer Lange is licensed under CC-BY-NC-SA 4.0 , derivative from the original work.)*

The cell bodies or axons of neurons can be located in discrete anatomical structures that 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, cortex, or horn**. In the PNS, a cluster of neuron cell bodies is referred to as a **ganglion**. 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** (or column) 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 in different locations. The most obvious example of this is the axons that project from the retina of the eye into the brain. Those axons are called the optic nerve as they leave the eye, but when they enter the cranium into the brain, they are referred to as the optic tract. Table 9.1.1 helps to clarify which of these terms apply to the central or peripheral nervous systems. There is a further classification of nerves depending on the location where they leave the central nervous system: **cranial nerves** emerge directly from the brain, while **spinal nerves** exit from different segments of the spinal cord.

	CNS	PNS
Group of Neuron Cell Bodies (i.e., gray matter)	Nucleus (brain) Cortex (brain) Horn (spinal cord)	Ganglion
Bundle of Axons (i.e., white matter)	Tract or Column	Nerve

Table 9.1.1: Name of structures depend on the location.

Functional Organization of the Nervous System

The nervous system can also be divided on the basis of its functions, but structural 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 brainstem.

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 **visceral**—divisions that are largely defined by the structures that are involved in the response.

Basic Functions

The nervous system is involved in receiving information about the environment around us**,** and generating responses to that information. Between these inputs and outputs a "decision" needs to be made about how to respond. The process of "thinking" integrates 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 inside the body. The sensory functions of the nervous system register **stimuli** (singular - stimulus), the presence of a change from homeostasis or a particular event in the environment. Stimuli inside the body are those that disturb our resting state, for example pain sensations are perceived by the skin and by internal organs such such as the stomach. Pain, as well as other sensations such as touch and temperature, can occur at any location in the body. These sense are called the **general senses** or **somatic senses**. The environmental stimuli for taste and smell are chemical substances (molecules, compounds, ions, etc.), for vision it is light, for hearing it is sound waves, and for balance it is the perception of where your head is in space. These senses are called **special senses** because they have specialized organs to sense the environment. Special and general senses receive stimuli that can be perceived consciously, meaning that you are aware of them, or unconsciously. Most stimuli that we are unaware of arise inside the internal organs, such as the stretch of an organ wall or the concentration of certain ions in the blood. These unconscious sensations are called **visceral sensations**. Sensory information is perceived by **sensory neurons** within the Peripheral Nervous System and travels towards the Central Nervous System. Sensory neurons are also called **afferent** neurons because they transmit their sensory impulses towards the central nervous system. The word afferent means moving or conducting towards something. (Figure 9.1.4).

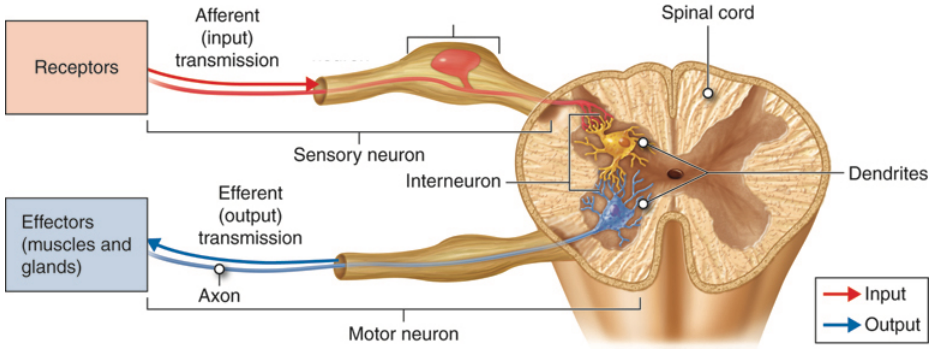


Figure 9.1.4: Sensory information travels along an afferent pathway toward the central nervous system while motor commands travel along an efferent pathway away from the central nervous system. Integration occurs at the interneurons within the spinal cord. *(Image credit: This work by Cenveo is licensed under CC BY 3.0).*

Integration

Stimuli that are received by sensory neurons are communicated to the Central Nervous System where the information is processed. 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.

Response

The nervous system produces a response on the basis of the sensory stimuli. 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 sweat glands found in the skin to lower body temperature. Thus, muscles and glands are the targets of the motor response and they become active when stimulated to carry out the response. For this reason, they are called **effectors**. Responses can be divided into those that are **voluntary** or conscious (contraction of skeletal muscle) and those that are **involuntary** or unconscious (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 is discussed in a future chapter.

Motor information is generated by the Central Nervous System, and carried away from the Central Nervous System by motor neurons to the Peripheral Nervous System. Motor neurons are also called **efferent** neurons. The word efferent means moving or conducting away from something (Figure 9.1.4). In the context of the nervous system, afferent and efferent are used in relation to the central nervous system. If it moves towards the central nervous system, it is afferent, if it moves away from the central nervous system, it is efferent. Afferent and efferent sound similar. One way to remember their differences is using the acronym SAME that stands for Sensory Afferent Motor Efferent.

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 (somatosensation) and voluntary motor responses (also called somatic responses). These are the things you consciously sense and do. 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") such as walking, chewing and riding a bicycle.

The **visceral nervous sytem (VNS)** is responsible for involuntary control of the body. These are the processes that occur without you thinking about them, they operate automatically behind the scenes to keep you alive. Sensory input for visceral 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 to glandular tissue. Because these motor commands operate without CNS conscious control, the visceral motor division is also called the **autonomic nervous system (ANS).** 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.

	Sensation	Integration	Motor Response
Somatic	Conscious perception of environmental changes (light, sounds, molecules in food, movement, temperature, touch, etc) through somatic sensory neurons of PNS	Information processed in brain and spinal cord (CNS)	Voluntary and reflex response via skeletal muscles
Visceral	Unconscious perception of external or internal changes (light, molecules, organ stretch, etc) through visceral sensory neurons in both CNS and PNS	Information processed in brain (particularly hypothalamus and brainstem) and spinal cord (CNS)	Involuntary movement of cardiac muscle, smooth muscle, glands. Also called the ANS.

Table 9.1.2: Basic functions of Somatic and Visceral Divisions of the Nervous System. The basic functions of the nervous system are sensation, integration and motor response (top row). These functions are carried out by all divisions of the nervous system (left column) through different neurons, anatomical regions and targets. What differentiates the somatic nervous system from the visceral nervous system is the ability to perceive and respond to stimuli at the conscious level. The visceral sensory and visceral motor (autonomic) components are unconscious.

Interactive Link

Creeping Weakness

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 9.1.4). 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.

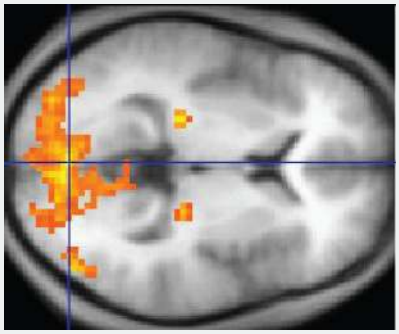


Figure 9.1.4: Functional Magnetic Resonance Imaging (fMRI) map. This imaging represents a transverse plane of the brain with the posterior side on the left and anterior side on the right. The orange areas represent highly active regions. In this particular example, the fMRI map shows activation of the visual cortex in response to visual stimuli. *(Image credit: "1206 FMRI" by OpenStax is licensed under CC BY 4.0)*

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.

Contributors and Attributions

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9.2: Anatomy of Nervous Tissue

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

- Describe the basic structure of a neuron
- Identify the different types of neurons based on their structure and function
- List the glial cells of the CNS and describe their function
- List the glial cells of the PNS and describe their function
- Describe the process of myelination and axon regeneration

Nervous tissue is composed of two types of cells: **neurons** and **glia**, as shown in Figure 9.2.1. 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, or neuroglia, are known to play a crucial supporting role in nervous tissue. Ongoing research pursues an expanded role that glial cells 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.

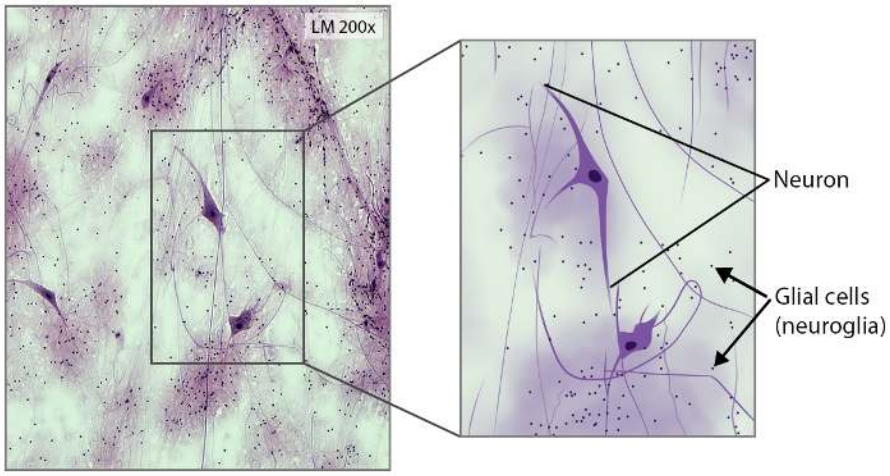


Figure 9.2.1: Nervous Tissue. A small chunk of tissue from the spinal cord was spread on a microscope slide to show neurons and glial cells. Glial cells are smaller and in larger quantities than neurons. The neuron shown is large and has multiple processes coming out of the soma. *(Image credit: "Nervous Tissue Cells" by Jennifer Lange, illustration by Claire McGuire is licensed under CC-BY-NC-SA 4.0. Micrograph provided by Berkshire Community College Bioscience Image Library is in the Public Domain.)*

Neurons

Neurons are the basic functional units of the nervous system. They are large cells with a high metabolic rate. They depend on a continuous and abundant supply of oxygen and glucose. Some neurons live an entire lifespan while others are replaced within days. Neurons do not typically undergo mitosis, thus they are not able to divide and produce new neurons. Only certain areas of the brain and the sense organ of smell house mitotic neurons. They are responsible for the electrical signals that communicate information about sensations, that produce movement in response to those stimuli, and induce 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 previous 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. What makes neurons special is that they have many extensions of their cell membranes, which are generally referred to as **processes**. The two types of processes are axons and dendrites. 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, carrying the electrical signal from the cell body to one or more cells. The region where the axon emerges from the

cell body is called the **axon hillock.** This is a tapering of the cell body toward the axon fiber and it is the location where the outgoing electrical signal is generated. The other processes of the neuron are **dendrites** which branch off of the cell body, 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. Information flows through a neuron from the dendrites, across the cell body, and down the axon. Figure 9.2.2 shows the relationship of these parts to one another.

Many axons are wrapped by an insulating substance called **myelin**, which is actually made of 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 **neurofibril node** (or **node of Ranvier)**. These gaps are exchange points for ions that allow electrical signals to travel down the axon. At the end of the axon is the **axon (synaptic) terminal**, where there are usually several branches extending toward the target cell, each of which ends in an enlargement called a **synaptic knob**. These knobs are what make the connection with the target cell at the synapse.

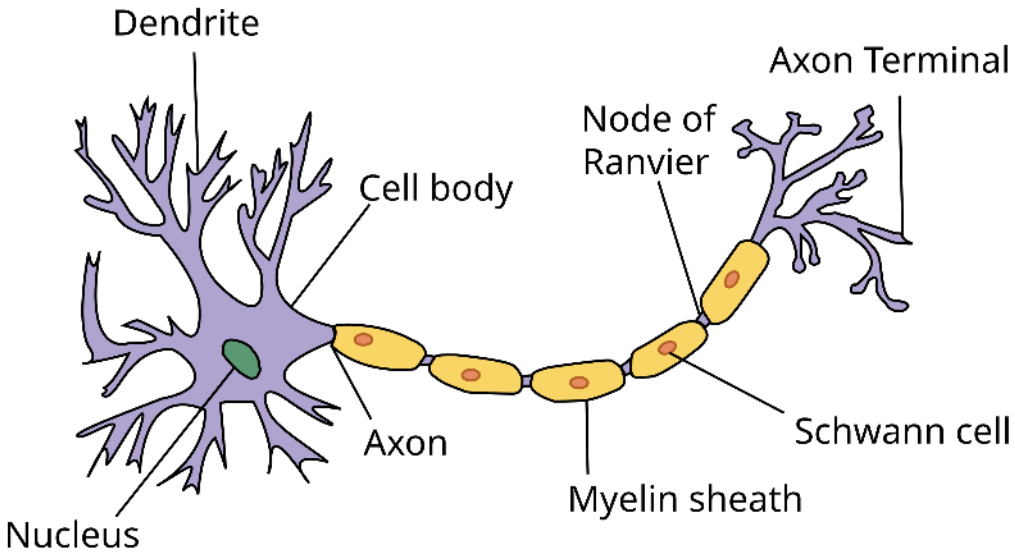


Figure \(\
PageIndex
{2}\) The Neuron: The dendrites that branch off the cell body (soma) receive signals from other neurons. Those signals are transmitted from the dendrites and cell body down the axon to the axon terminals. At the axon terminals, the signal is then propagated to the target cell.
(Image credit: "Neuron description" by Dhp1080 is licensed under CC BY-SA 3.0, via Wikimedia Commons.)

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 both their structure and their function. **Structural classification** depends on the number of processes attached to the cell body: one, two, or multiple (Figure 9.2.3). **The functional classification** depends on which function the neuron is carrying out: sensation, integration, or motor.

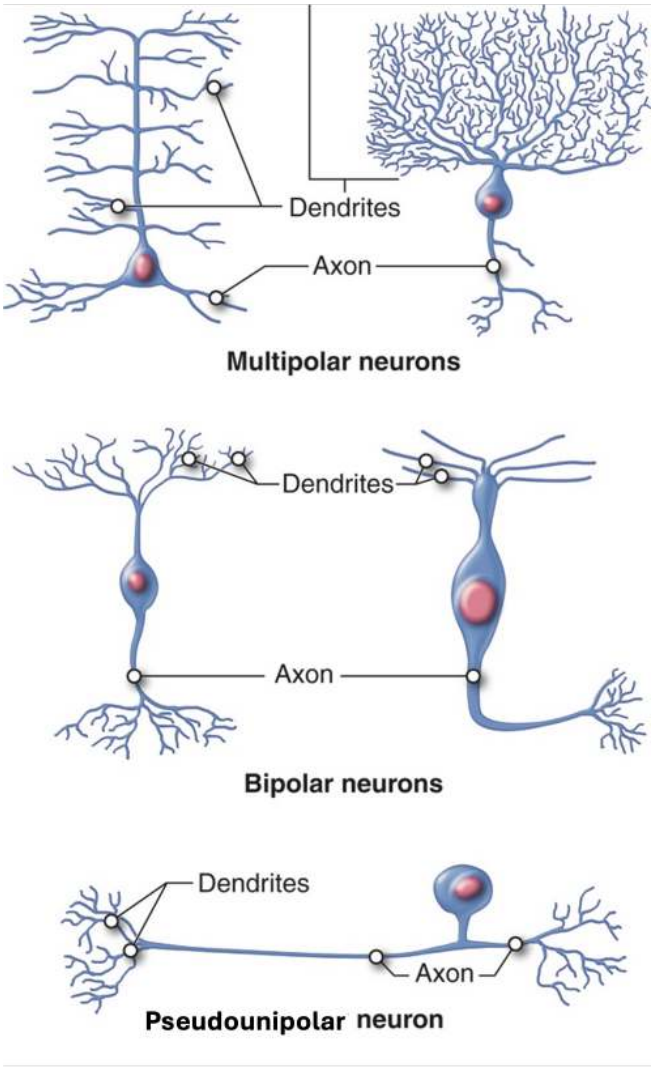


Figure \(\PageIndex{3}\): Neuron Classification by Structure. Pseudounipolar neurons have one process emerging from the soma which contains both the axon and dendrites. Bipolar neurons have two processes emerging from the soma: one is an axon and the other is a dendrite. Multipolar neurons have more than two processes emerging from the soma: one is an axon and two or more other are dendrites. *(Image credit: This work by Cenveo is licensed under CC BY 3.0). / Labels modified and cropped from original by Harmony Folse*

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 pseudo-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. Pseudo-unipolar cells are exclusively **sensory neurons** and have two unique characteristics. First, their dendrites are receiving sensory information, sometimes directly from the stimulus itself, as is the case for sensory neurons perceiving pressure, temperature change, touch, or pain from the skin. Secondly, the cell bodies of unipolar neurons are always found in ganglia. Sensory reception is a peripheral function (those dendrites are in the periphery, perhaps in the skin) so the cell body is in the periphery, though closer to the CNS in a ganglion. The axon projects from the dendrite endings, past the cell body in a ganglion, and into the central nervous system.

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

and as part of the retina, and thus are sensory neurons.

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). Multipolar neurons can have multiple functions. Multipolar neurons can be **motor neurons** which carry commands from the brain and spinal cord to muscles and glands. Motor neurons are located in the brain, spinal cord or autonomic ganglia. Multipolar neurons can also be classified as **interneurons** which constitute the majority of neurons. These neurons carry out integrative functions (such as retrieve, process and store information) and facilitate communication between sensory and motor neurons. Interneurons are found exclusively in the central nervous system.

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,". 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 9.2.1 outlines some common characteristics and functions.

Table 9.2.1: Glial Cell Types by Location and Basic Function.

CNS glia	PNS glia	Basic function
Astrocyte	Satellite cell	Structural and physiological support of the nervous tissue Form the blood-brain barrier (BBB) (Only applies to astrocytes in CNS)
Oligodendrocyte	Schwann Cell (Neurolemmocyte)	Insulation, myelination
Microglia	-	Immune surveillance and phagocytosis
Ependymal cell	-	Creating and circulating 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 9.2.6). Generally, they are supporting cells for the neurons in the central nervous system.

Some ways in which glia support neurons in the central nervous system are:

1. forming a structural network that strengthens the nervous tissue
2. maintaining the homeostasis of signaling molecules, water and ions in the extracellular space
3. providing an energy storage
4. defending the nervous tissue from oxidative stress
5. reacting to tissue damage and replacing dead neurons
6. assisting neuronal development in the fetal brain.
7. contributing to the blood-brain barrier (described below).

The **blood-brain barrier (BBB)** (Figure 9.2.5) 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. 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.

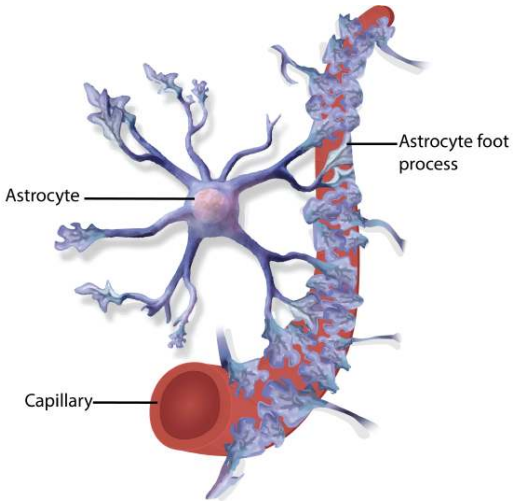


Figure 9.2.5: Blood-Brain Barrier. The foot processes of the astrocytes cover the capillaries in the brain. Having this additional layer makes passage from the blood to the brain more difficult, but immune cells such as monocytes can pass through. *(Image credits: "Astrocyte with Foot Processes" by Sofia Elizondo is licensed under CC-BY-NC-SA 4.0, modification of image by BruceBlaus)*

Also found in CNS tissue is the **oligodendrocyte**, sometimes called just "oligo," which is the glial cell type that insulates axons in the CNS (Figure 9.2.6). 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.

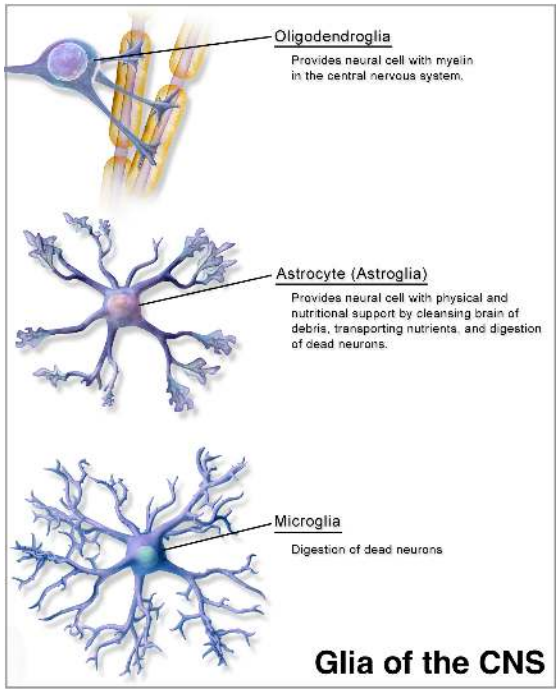


Figure 9.2.6: Glial Cells of the CNS. Astrocytes form a barrier (blood-brain barrier) between the capillaries and the nervous tissue to protect it. Microglial cells act as defenders of the nervous tissue. Finally, oligodendrocytes wrap around multiple axons to insulate them. *(Image credit: "Glia of the CNS" by BruceBlaus, CC BY-SA 4.0, via Wikimedia Commons)*

Microglia are, as the name implies, smaller than most of the other glial cells (Figure 9.2.6). 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.

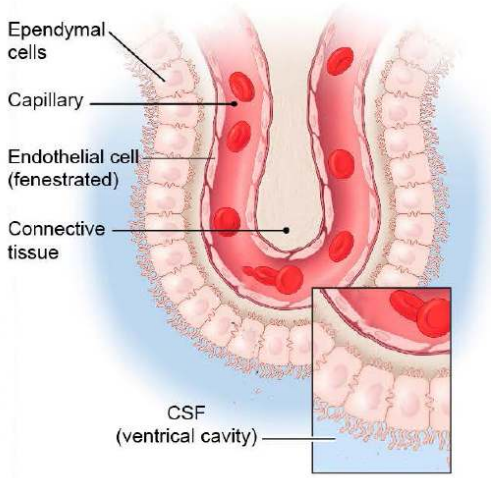


Figure 9.2.7: Ependymal Cells. The ependymal cells cover specialized capillaries in brain's fluid filled spaces. They filter the blood to produce, and then circulate, cerebrospinal fluid (CSF). *(Image credit: "Ependymal Cells - Blood-CSF Barrier" by Jennifer Lange is licensed under CC-BY-NC-SA 4.0, modification of image by NIH Medical Arts.)*

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. They provide support, performing similar functions in the periphery as astrocytes do in the CNS—except, of course, for establishing the BBB.

The second type of glial cell is the **Schwann cell (neurolemmocyte)**, 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 (Figure 9.2.8).

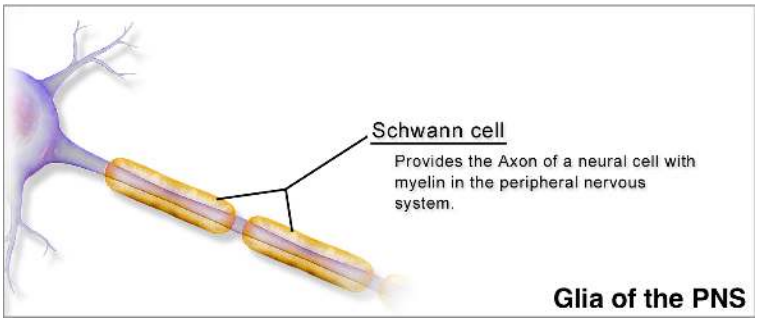


Figure 9.2.8: Glial Cells of the PNS. Satellite cells are wrapped around a unipolar neuron of a peripheral ganglion to support and protect it. Schwann cells are wrapped onto the neuron's axon to insulate it with their myelin sheath. *(Image credit: "Glia of the PNS" by BruceBlaus, CC BY-SA 4.0, via Wikimedia Commons.)*

DISORDERS OF THE...

Glial cells: Gliomas

Glioma is a type of tumor that occurs in the glial cells of the brain or spinal cord (Figure 9.2.9). Remember that tumor begins when the cell loses control over the checkpoints of mitosis and start proliferating excessively. Since neurons do not go under mitosis and can't produce new neurons, the only cells undergoing mitosis in the nervous system are the glial cells. Three types of glial cells can produce tumors. Gliomas are classified according to the type of glial cell involved in the tumor, as well as the

tumor's genetic features, which can help predict how the tumor will behave over time and the treatments most likely to work. Types of glioma include:

- Astrocytomas, involving astrocytes
- Ependymomas, involving ependymal cells
- Oligodendrogliomas, involving oligodendrocytes

A glioma can affect the brain function and be life-threatening depending on its location and rate of growth. Gliomas are one of the most common types of primary brain tumors.

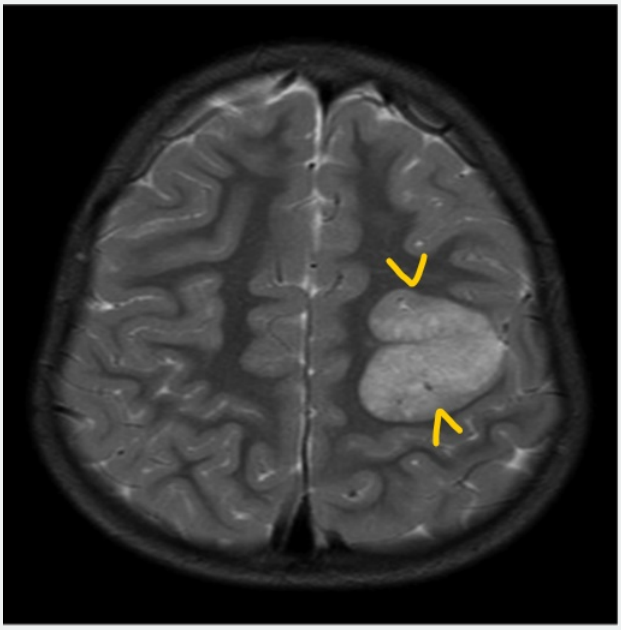


Figure 9.2.9: MRI of a 4-year old boy with a glioma. *(Image credit: "Glioma" by Manoj Kumar Raghu H Ramakrishnaiah Rohan Samant is licensed under CC BY-SA 4.0, via Wikimedia Commons.)*

Myelin

The insulation for axons in the nervous system is provided by oligodendrocytes in the CNS and Schwann cells in the PNS. These cells use the same mechanism to insulate axon segments. 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. The axon has parts that are not covered by myelin called nodes of Ranvier which ensure the propagation of the electrical signal. Axons can be completely enclosed by myelin (**myelinated**) (Figure 9.2.10 and Figure 9.2.11) or not fully enclosed by it (**unmyelinated**). In the PNS, unmyelinated axons generally are less than 2 µm in diameter and myelinated axons are more than 1–2 µm in diameter. In the CNS, almost all axons with diameters greater than 0.2 µm are myelinated. In unmyelinated axons, their speed of electrical transmission is slower than myelinated nerves. Unmyelinated axons are primarily sensory fibers (transmitting sensations like dull pain, temperature changes, and itch) and autonomic fibers.

In myelinated axons, 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 in the CNS, 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 in the PNS, 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. During myelination, 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. At the end of myelination, the myelin sheath is a thick layer that covers the axon. (Figure 9.2.10) demonstrates the different myelination patterns of oligodendrocytes and Schwann cells.

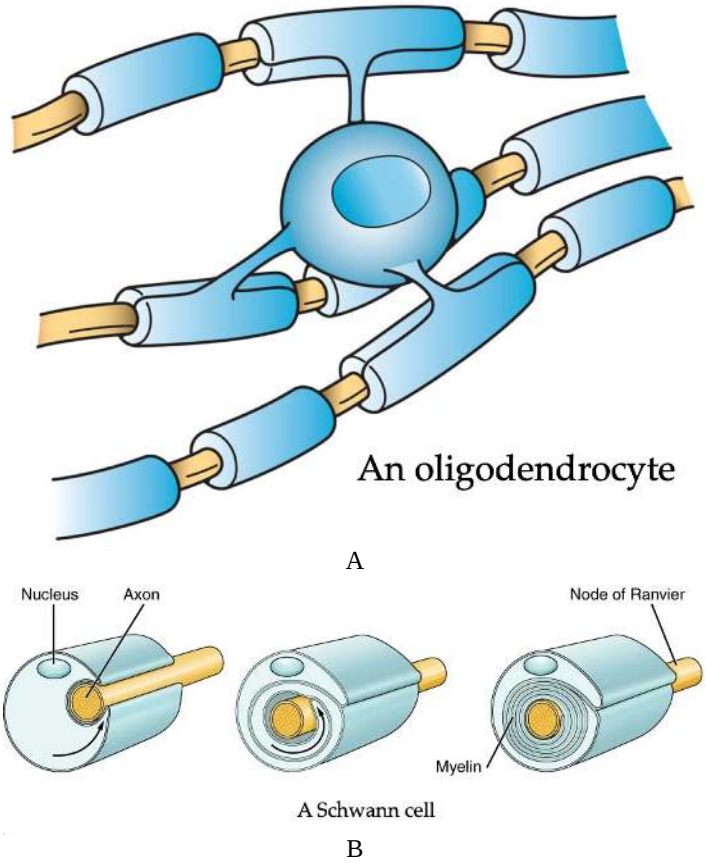


Figure 9.2.10 Myelination in the CNS and PNS: A) One oligodendrocyte in the CNS is able to myelinate multiple axons. It's multiple processes branch out and wrap themselves around multiple axons. B) One Schwann cell in the PNS forms myelin by wrapping itself multiple times over one segment of the axon. One Schwann cell is only able to myelinate one segment of the axon. *(A: Image credit: "Oligodendrocyte illustration" by* Holly Fischer, *CC BY 3.0, via Wikimedia Commons) (B: Image credit: "Dorsal Ventral Body Cavities" by OpenStax is licensed under CC BY 4.0) / Labels modified by Harmony Folse*

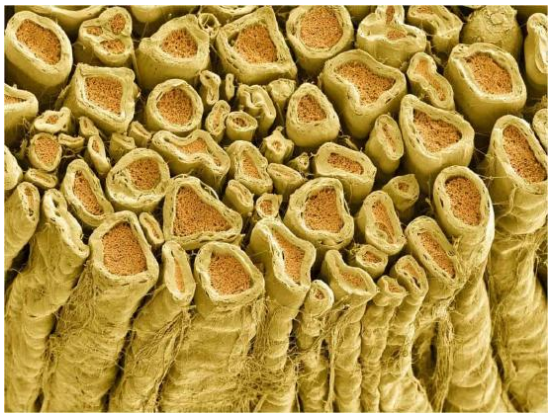


Figure 9.2.11: Myelinated Axons. This false colored scanning electron micrograph image shows the myelinated axons in a rat spinal cord. In the CNS axons are myelinated by oligodentrocytes. *(Image credit: "Myelinated Axons" by Tom Deerinck and Mark Ellisman, National Center for Microscopy and Imaging Research (NCMIR) is licensed under CC BY NC 2.0.)*

Regeneration of Axons

Traumatic injuries can cause damage to nerves. When nerves are damaged within the PNS as in the case of a laceration, the axons distal to the injury degenerate. The Schwann cells that were wrapping the injured axons proliferate to form a new tube of myelin that guides the growing axons through physical and chemical support (Figure 9.2.12). Most of the times, axons can cross the injury site and can successfully grow back to the original targets. Sometimes the injury can affect also the surrounding tissues and form a scar that axons cannot cross. In that case, the axons are not able to grow back, unless surgery is performed to eliminate the scar tissue. The situation is different when injuries affect the CNS as in the case of spinal cord injuries. The oligodendrocytes respond to

injury by undergoing apoptosis or becoming inactive. This contributes to the formation of scar tissue. Moreover, injury-activated astrocytes release molecules that inhibit axonal growth. Consequently, injured axons in the CNS are not able to grow back to their original target and nerve injuries in the CNS are permanent.

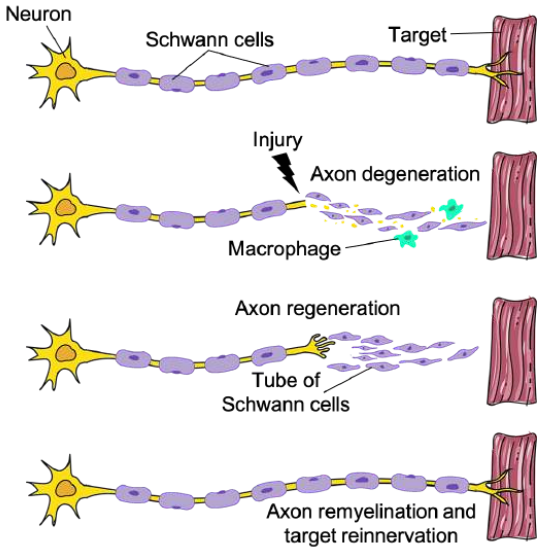


Figure 9.2.12: Axon Regeneration in the PNS. A neuron of the PNS innervates its target with its myelinated axon covered by Schwann cells. Following an injury, the part of the axon distal to the injury degenerates, leaving an axonal stump. The Schwann cells proliferate and produce new Schwann cells that form a tube to guide the axon back to its original target. Macrophages help clear up the debris from the axonal degeneration. The axonal stump grows following the tube of Schwann cells, which wrap it with myelin. The axon reaches the original target and the axon regeneration is complete. *(Image credit: "Axon Regeneration in the PNS" by Chiara Mazzasette is a derivative from the original work of Daniel Donnelly and is licensed by CC BY 4.0.)*

DISORDERS OF THE...

Nervous Tissue: Demyelinating Diseases

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 (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.

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9.3: Synapses

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

- Describe the components of synapses
- Compare electrical and chemical synapses

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. Neurons communicate with other neurons, muscles or glands through the generation and conduction of nerve impulses called **action potentials**. These electrical impulses propagate from the axon hillock to the axon terminals via changes in the electrical properties of the neuronal cell membrane. All cells have an electrical charge associated with their membrane. However, neurons and other cells are able to change their electrical charge by moving ions across the membrane. At the axon (or synaptic) terminals the action potential needs a way to pass the signal on to the next cell, which they do at structures called **synapses**.

Synapses

Neurons and their targets form synapses. The neuron that generates and conducts the action potential to the target is called a **presynaptic cell**. The target cell receiving the action potential is called a **postsynaptic cell**. While the presynaptic cell is always a neuron (because only neurons have axons and can form a synapse), the postsynaptic cell can be a neuron or another type of cell such as skeletal, cardiac or smooth muscle cells, or glands. In Figure 9.3.1, a presynaptic neuron forms synapses with two postsynaptic neurons. The nerve impulse (or signal) travels from a presynaptic neuron to a postsynaptic cell by crossing the gap between them, the **synaptic cleft**. The two methods by which the cleft is crossed are 1) electrical and 2) chemical, with chemical being the most common and most diverse.

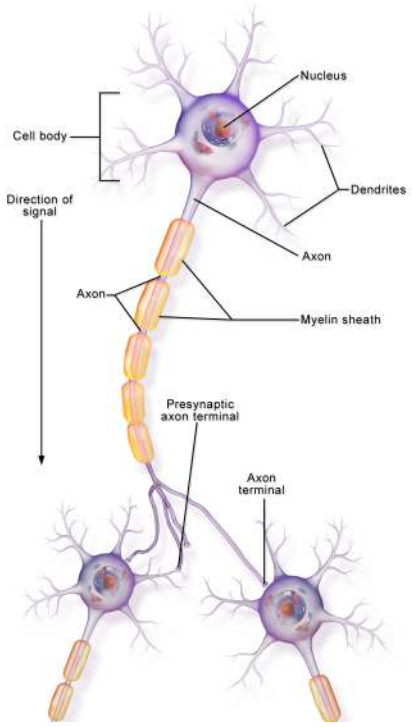


Figure 9.3.1: Presynaptic and postsynaptic neurons. A presynaptic neuron on top forms synapses with two postsynaptic neurons at the bottom. The parts of the presynaptic neuron are labeled as cell body, nucleus, dendrites and axon covered in a myelin sheath. The direction of signal shows that the electrical signal (action potential) travels from the axon of the presynaptic neuron to the axon terminals of the presynaptic neuron that are in contact with the dendrites and cell body of the postsynaptic neurons. *(Image credit: "Neuron Part 1" by BruceBlaus is licensed under CC BY-SA 4.0.)*

Chemical Synapses

Chemical synapses involve the transmission of chemical information from one cell to the next and they represent the majority of the synapses found within the nervous system. In a **chemical synapse**, a chemical signal called a **neurotransmitter**, is released

from the presynaptic cell and it affects the postsynaptic cell. There are many different types of neurotransmitters, for example acetylcholine, serotonin, dopamine, adrenaline, glutamate, etc. Each neurotransmitter has its own specific receptor on the postsynaptic membrane. Chemical synapses can then be classified based on the neurotransmitter that the cells use to communicate (for example glutamatergic synapses use glutamate). Different neurotransmitters and different receptors will determine the overall response to the stimulus. All chemical synapses have common characteristics, which can be summarized in this list and are shown in Figure 9.3.2:

- synaptic end bulb of presynaptic neuron
- neurotransmitter (packaged in vesicles)
- synaptic cleft
- receptors for neurotransmitter
- postsynaptic membrane of postsynaptic neuron

The process of communication from a presynaptic neuron to a postsynaptic neuron via a chemical synapse is as follows. An action potential arrives at the axon terminal of the presynaptic neuron. The arrival of the action potential at the axon terminal causes Ca^{2+} to open in the axon terminal. Ca^{2+} rushes into the axon terminal, causing the release of neurotransmitters into the synaptic cleft. The neurotransmitters then diffuse across the synaptic cleft and bind to specific receptors in the cell membrane of the postsynaptic neuron (or target cell which could be a muscle or gland). The target cell will then respond to the binding of a neurotransmitter in a variety of ways. For example, if the target cell is another neuron (post synaptic neuron), then the neurotransmitters binding to the postsynaptic neuron's receptors may then trigger an action potential in the postsynaptic neuron. If the target cell is a muscle, the binding of neurotransmitters (in this case, acetylcholine) to their specific receptors on the muscle fiber will then trigger muscle contraction, as described in the chapter on muscle tissue.

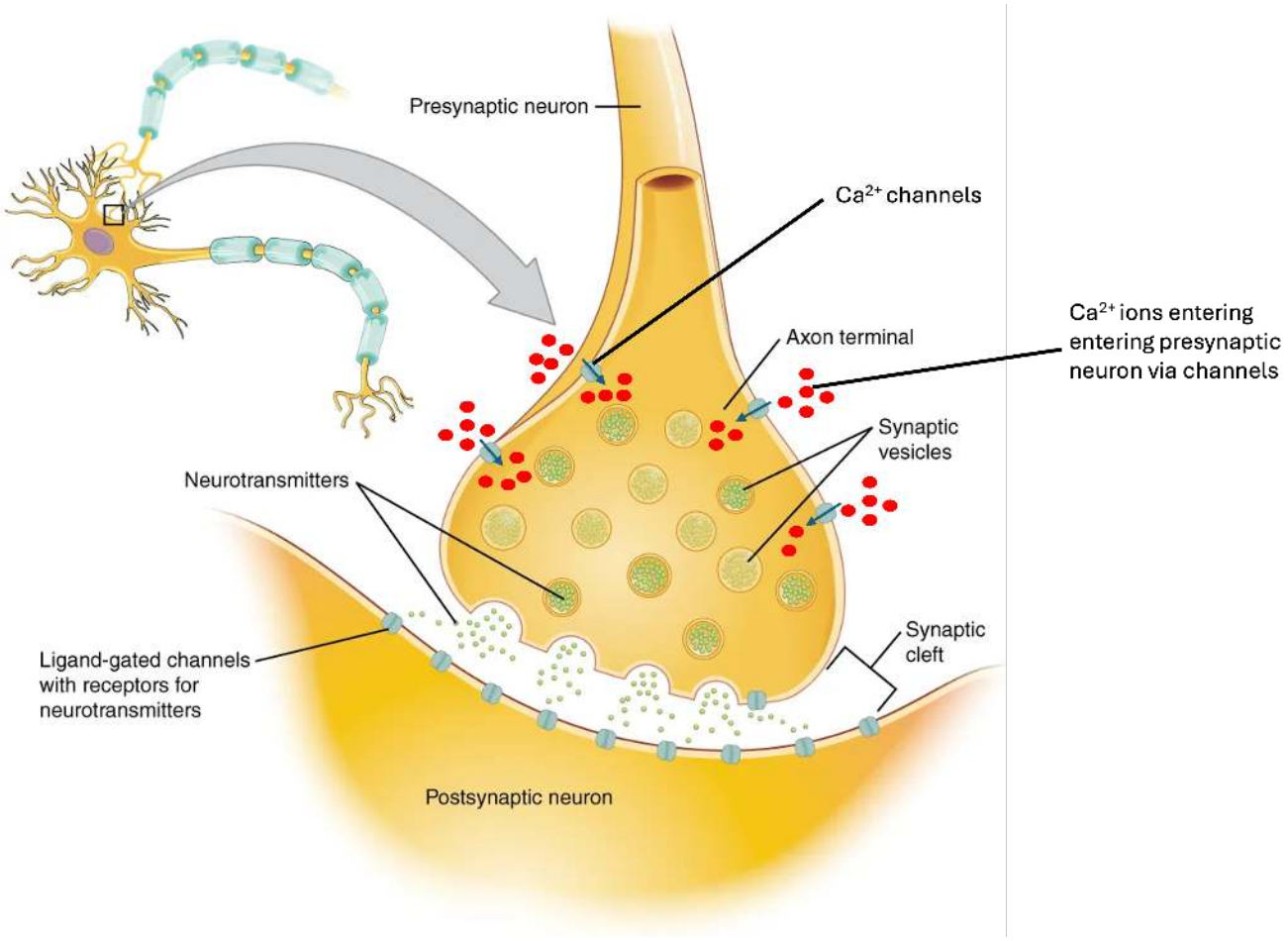


Figure \(\PageIndex{2}\) Chemical Synapse: An action potential arriving at the axon terminal triggers the entrance of Ca^{2+} ions into the axon terminal. This then triggers the release of neurotransmitters from the presynaptic neuron into the synaptic cleft. The neurotransmitters will then bind to receptors on the postsynaptic neuron (or target cell) triggering a response. *(Image credit: "Chemical Synapse" by OpenStax is licensed under CC BY 4.0.) / Ca2+ ions and related Ca2+ labels added by Harmony Folse*

There are a variety of ways to terminate synaptic transmission and end signaling from the presynaptic neuron to the target cell. Synaptic transmission can be ended via:

- The neurotransmitters may diffuse away from the synaptic cleft and then are reabsorbed into the presynaptic neuron's axon terminal (reuptake).
- The neurotransmitters may be degraded by specialized enzymes in the synaptic cleft. For example, acetylcholinesterase is an enzyme that breaks down acetylcholine and lead to muscle relaxation at the neuromuscular junction.

Electrical Synapses

In an **electrical synapse**, there is a direct connection between the presynaptic and postsynaptic cells and the connection is formed by gap junctions. Thus, the electrical charges of an action potential can pass directly from one cell to the next. If one cell delivers an action potential in an electrical synapse, the joined cell will also generate an action potential because the electrical charges will pass between the cells (Figure 9.3.3). Although representing the minority of synapses, electrical synapses are found throughout the nervous system. These synapses also occur between excitable cells other than neurons, for example between smooth muscle cells in the intestines and cardiac muscle cells in the heart.

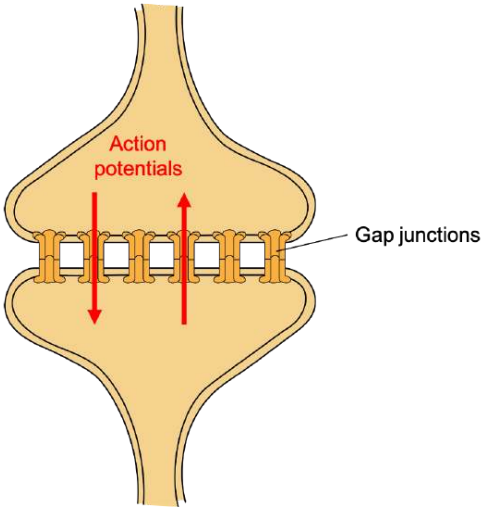


Figure 9.3.3: Electrical Synapse. Two synaptic end bulbs form an electrical synapse where gap junctions allow the passage of action potentials from one cytoplasm to the other, and vice versa. *(Image credit: "Electrical Synapse" by Chiara Mazzasette is a derivative from the original work of Daniel Donnelly and is licensed by CC BY 4.0.)*

DISORDERS OF THE...

Nervous System: Alzheimer's and Parkinson's Disease

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 fragment that aggregates instead of being broken down by microglia. 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.

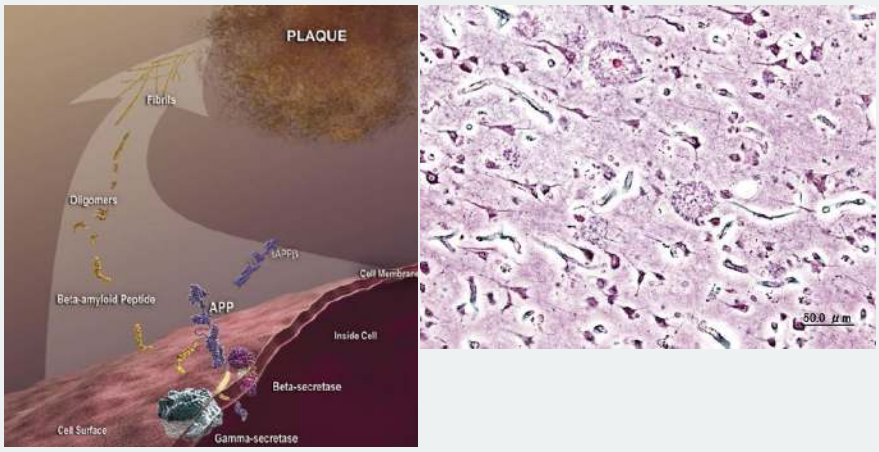


Figure 9.3.4: Beta-amyloid plaques form in the brain of Alzheimer's disease patients. These plaques form when a normal process, the slicing of the amyloid precursor protein to remove the beta-amyloid fragment, is disrupted and these fragments are not metabolized normally. Instead, the stick to each other and disrupt neuronal function.*(Image credits: Illustration: "Alzheimers_disease-Beta-amyloid_plaque_formation" by National Institute on Aging is in the Public domain, via Wikimedia Commons; Histology: "Alzheimer_dementia_(3)_presenile_onset " by KGH is licensed under CC BY-SA 3.0, via Wikimedia Commons.)*

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 (Figure 9.3.4). 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.

CAREER CONNECTIONS

Neurophysiologist



Figure 9.3.5 A neuroscience student can participate in research projects by monitoring and running various tests during experiments as well as doing data collection and analysis. Student Cammi Borden worked with research psychologist Dr. Kara Blacker at the Naval Medical Research Unit studying low-oxygen conditions impact on brain activity. *(Image credit: Public Domain Dedication. Public Use Notice of Limitations: https://www.dvidshub.net/about/copyright.)*

Understanding how the nervous system works could be a driving force in your career. Studying neurophysiology (Figure 9.3.5) 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, or a neurologist, a neurosurgeon, or an anesthesiologist.

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9.4: The Function of Nervous Tissue

Learning Objectives

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

- 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. The most basic pathway your nervous system consists of a sensory receptor sending a stimuli to interneurons which determine a response, and then motor neurons that conduct that response.

Before getting to the nuts and bolts of how this works, an illustration of how the components come together will be helpful. An example is summarized in Figure 9.4.1.

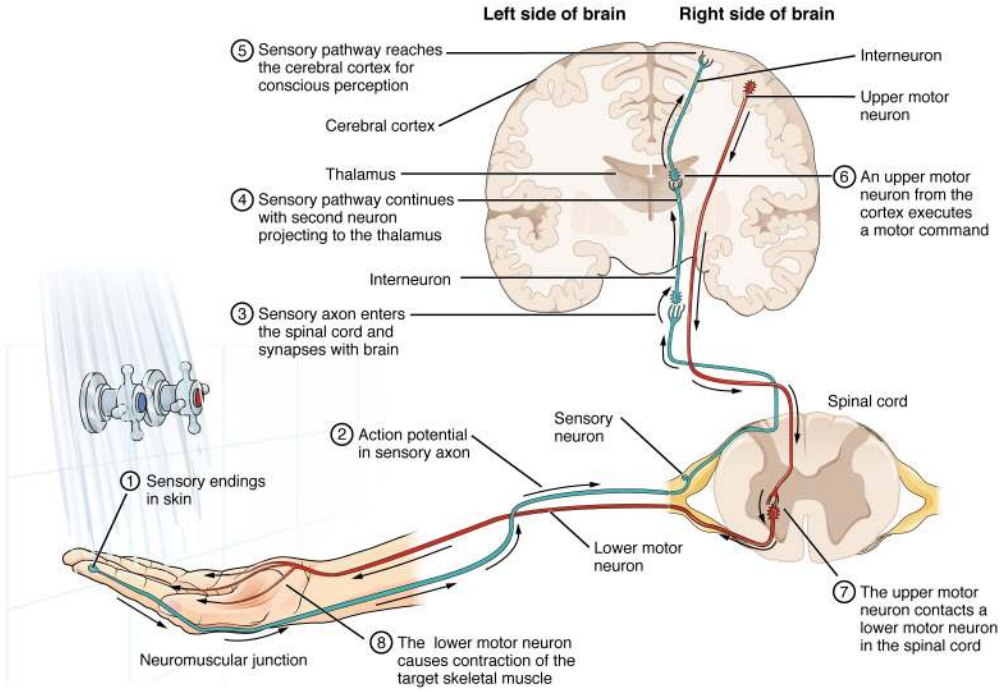


Figure 9.4.1: Testing the Water: Posterior View (1) The sensory neuron has endings in the skin that sense a stimulus such as water temperature. The strength of the signal that starts here is dependent on the strength of the stimulus. (2) The graded potential from the sensory endings, if strong enough, 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.

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.

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 9.4.2), the thermoreceptors send action potentials that transmit the signal to interneurons in your spinal cord. These spinal cord interneurons then pass the signal along to interneurons in your brain. Interneurons in a region of your brain called the **thalamus** then send the signal to the sensory regions of your cerebral cortex for the signal to be integrated and processed into a **perception** of the water temperature and your surroundings. The role of the thalamus will be discussed in the chapter on the CNS.

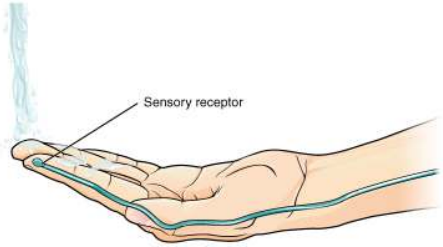


Figure 9.4.2: The Sensory Input Receptors in the skin sense the temperature of the water.

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 9.4.3).

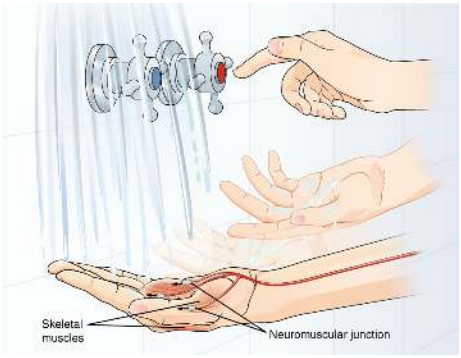


Figure 9.4.3: The Motor Response On the basis of the sensory input and the integration in the CNS, a motor response is formulated and executed.

Just like your cerebral cortex has specialized sensory regions, it also has specialized motor regions which determine your motor response to any given situation. In this case, in response to the sensory information just received in your cerebral cortex, **motor neurons** in your cerebral cortex will send signals all the way down your spinal cord and from your spinal cord to the muscles that will contract for the appropriate reaction. In this situation with the water temperature, your response may be to use your muscles to adjust the temperature until it is to your liking. What has just been described is a typical **sensory-motor pathway** used by your nervous system.

Career Connection

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.

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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.

Basic Reflex Pathways

Reflexes are automated responses by your nervous system to stimuli, especially pain. For example, lifting your foot up after stepping on something sharp or closing your eyes when being sprayed with water are responses due to reflexes. Reflexes occur before you have a chance to consciously react to the stimuli. Many reflexes occur without even reaching your brain, instead causing a reaction only by reaching the spinal cord. This is one of the reasons that reflex responses occur so quickly. A basic reflex pathway or **reflex arc** will be described in the following paragraphs.

We will use an example of the **withdrawal** reflex, where a limb is withdrawn in response to pain stimuli. When you place your finger on a hot flame, sensory receptors in your finger respond to the exceedingly hot temperature and pain by sending signals to your spinal cord. An interneuron in your spinal cord immediately processes this harmful stimuli by signaling a motor neuron in the spinal cord to cause the limb muscles to pull the hand away. The motor neuron immediately contacts your arm muscles and you pull your finger away from the hot flame. Note how the stimuli did not need to reach your brain for your body to have a response. The basic steps of this reflex arc can be seen in Figure 9.4.4 below.

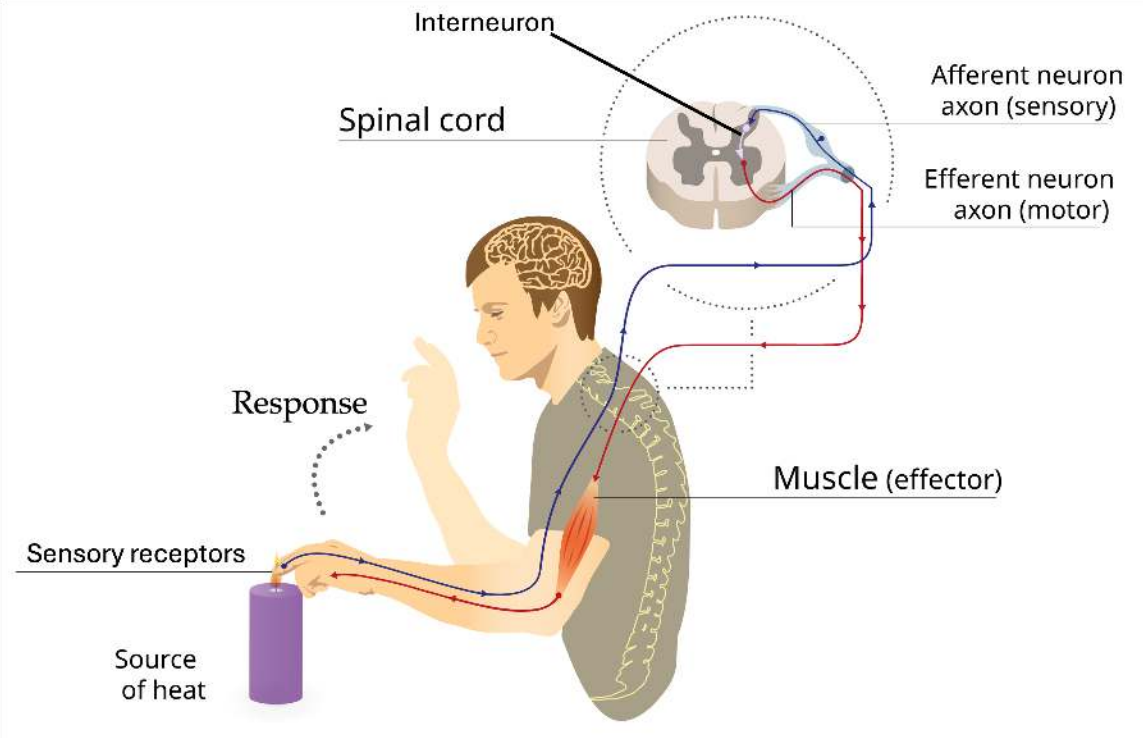


Figure 9.4.4 A basic reflex arc: The withdrawal reflex can be seen, with sensory stimuli triggering a withdrawal reflex, all without contacting the brain allowing for a rapid response. *(Image credit: "*Imgnotraçat arc reflex eng*" by Jmarchn, CC BY-SA 3.0, via Wikimedia Commons) / Labels modified by Harmony Folse*

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9.5: The Central Nervous System

Learning Objectives

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

- 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 9.5.1 =). 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.

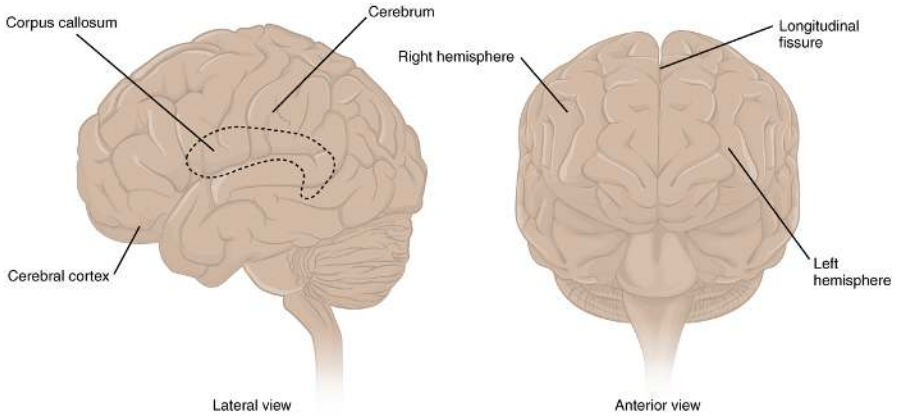


Figure 9.5.1: The Cerebrum The cerebrum is a large component of the CNS in humans, and the most obvious aspect of it is the folded surface called the cerebral cortex.

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. 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 9.5.2).

The lobes of the brain are:

- **Frontal lobe**
- **Parietal lobe**
- **Temporal lobe**
- **Occipital Lobe**
- **Insula**

The lobes of the brain are seperated by sulci. The l**ateral sulcus** that separates the temporal lobe from the other regions. 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. Lastly, the insula is deep to the lateral sulcus and cannot be seen without peeking under this sulcus.

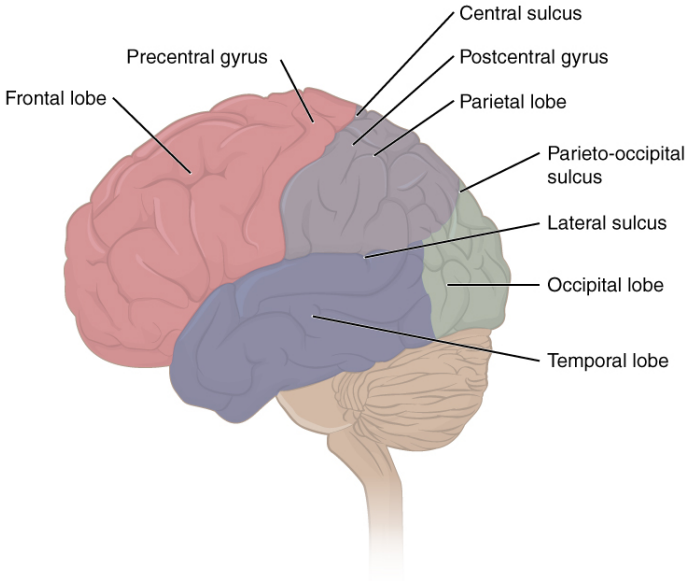


Figure 9.5.2: Lobes of the Cerebral Cortex The cerebral cortex is divided into four lobes. Extensive folding increases the surface area available for cerebral functions.

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. This areas can be seen in Figure 9.5.3.

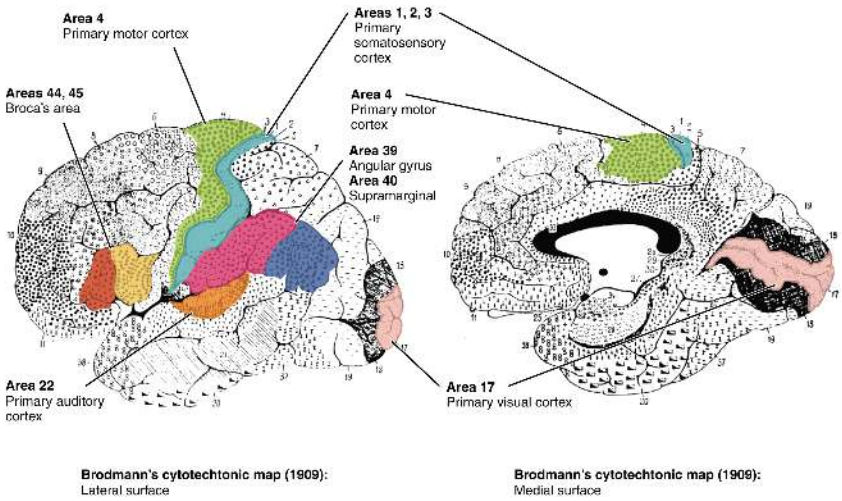


Figure 9.5.3: Brodmann's Areas of the Cerebral Cortex Brodmann mapping of functionally distinct regions of the cortex was based on its cytoarchitecture at a microscopic level.

Today, we more frequently refer to these regions by their function (i.e., primary visual cortex) than by the number Brodmann assigned to them. The **primary cortical areas** are where sensory information is initially received for conscious perception or where descending motor commands are sent down to the brainstem or spinal cord to execute movements. The regions near the primary areas are each referred to as **association areas**.

We can broadly categorize the cortices found within each lobe and their functions.

The **frontal lobe** contains the following regions of cerebral cortex:

- **Prefrontal cortex**
  - Responsible for decision making, planning, personality, social behavior, among other roles
- **Primary motor cortex**
  - Located within the precentral gyrus
  - Contains motor neurons that determine muscle movement
- **Premotor cortex and supplementary motor cortex**
  - Aid in planning and coordinate movement
- **Broca's area**
  - Ability to produce language and make the movements needed for speech

The **parietal lobe** contains the following regions of cerebral cortex:

- **Primary somatosensory cortex**

- 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

- **Somatosensory association area**
  - Aids primary somatosensory cortex in somatic processing

The **temporal lobe** contains the following regions of cerebral cortex:

- **Primary auditory cortex**
  - Where sound from the cochlear nerve is processed
- **Auditory association area**
  - Aids in processing sound
- **Wernicke's area**
  - Understanding and comprehending language
- **Primary olfactory cortex** (deep)
  - Processes smell

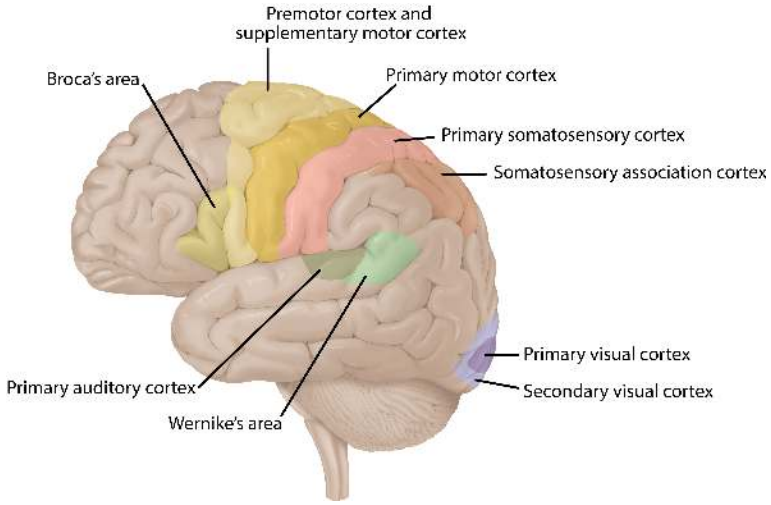
The **occipital lobe** contains the following regions of cerebral cortex:

- **Primary visual cortex**
  - Where visual information from the optic nerve arrives and is processed
- **Visual association areas**
  - Aids in visual processing

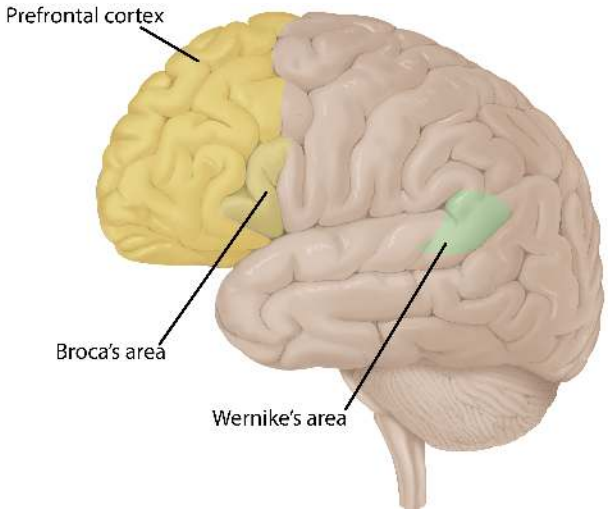
The **insula** contains the following regions of cerebral cortex:

- **Primary gustatory cortex**
  - Processing sense of taste

Refer to Figure 9.5.4 below to visually locate each region of cortex within each lobe.



A



B

Figure 9.5.4 Functional and Cortical Areas: The functions of the cerebral cortex are localized within their respective lobes. Although the exact boundaries can vary from person to person, their general area and their relative positions remain the same. The prefrontal cortex is responsible for executive functions such as decision making, reasoning, and working memory. *(A: Image and caption credit: "Functional Areas of the Cerebral Cortex" by Justin Greene and Jennifer Lange is licensed under CC BY-NC-SA 4.0.) (B: Image credit: "Functional Areas of the Cerebral Cortex - Language and Executive Functions" by Justin Greene and Jennifer Lange is licensed under CC BY-NC-SA 4.0.)*

Everyday Connection

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.

The diencephalon is deep beneath the cerebrum. 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 9.5.5). 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.

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 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 such as temperature control. 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.

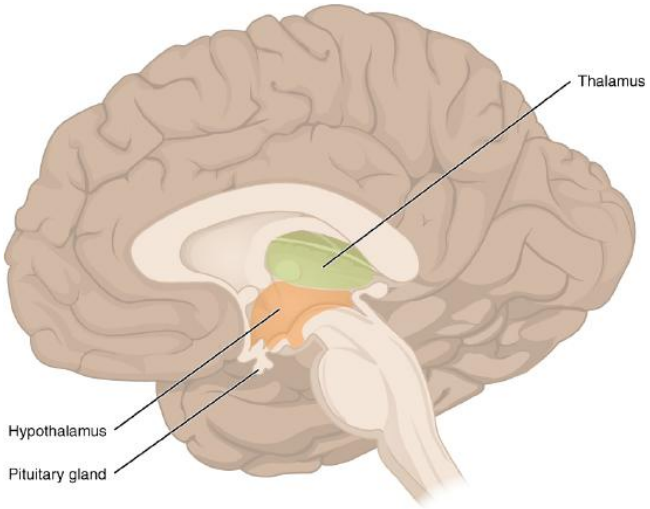


Figure 9.5.5: The Diencephalon The diencephalon is composed primarily of the thalamus and hypothalamus, which together define the walls of the third ventricle. The thalami are two elongated, ovoid structures on either side of the midline that make contact in the middle. The hypothalamus is inferior and anterior to the thalamus, culminating in a sharp angle to which the pituitary gland is attached.

Brain Stem

The **midbrain** and hindbrain (composed of the **pons** and the **medulla**) are collectively referred to as the **brain stem** (Figure 9.5.7). 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.

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.

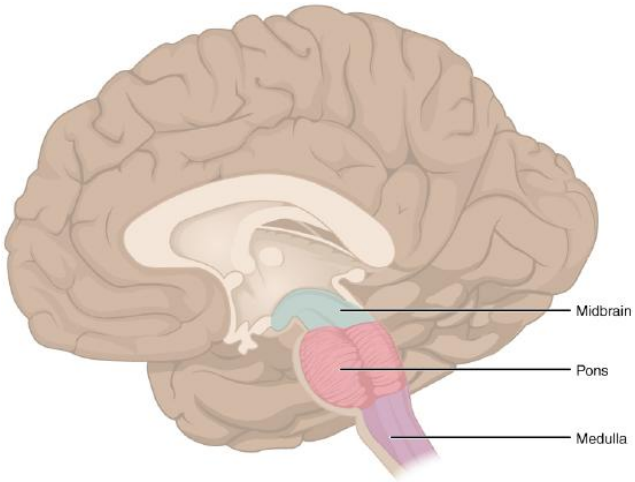


Figure 9.5.6: The Brain Stem The brain stem comprises three regions: the midbrain, the pons, and the medulla.

Midbrain

The midbrain 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 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 9.5.8). 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.

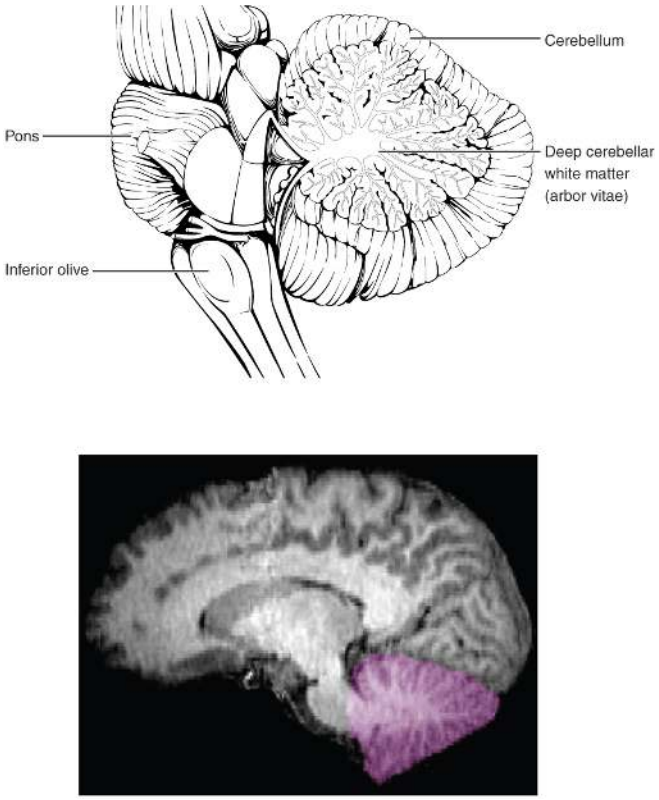


Figure 9.5.7: The Cerebellum The cerebellum is situated on the posterior surface of the brain stem. Descending input from the cerebellum enters through the large white matter structure of the pons. Ascending input from the periphery and spinal cord enters through the fibers of the inferior olive. Output goes to the midbrain, which sends a descending signal to the spinal cord.

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 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**. Axons enter the posterior side of the spinal cord 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. Please memorize these words as they will be used interchangeably.

On the whole, the **posterior regions of the spinal cord are responsible for sensory functions and the anterior regions are associated with motor functions**.

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 foramina 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 9.5.8, 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, contains cell bodies of motor neurons 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.

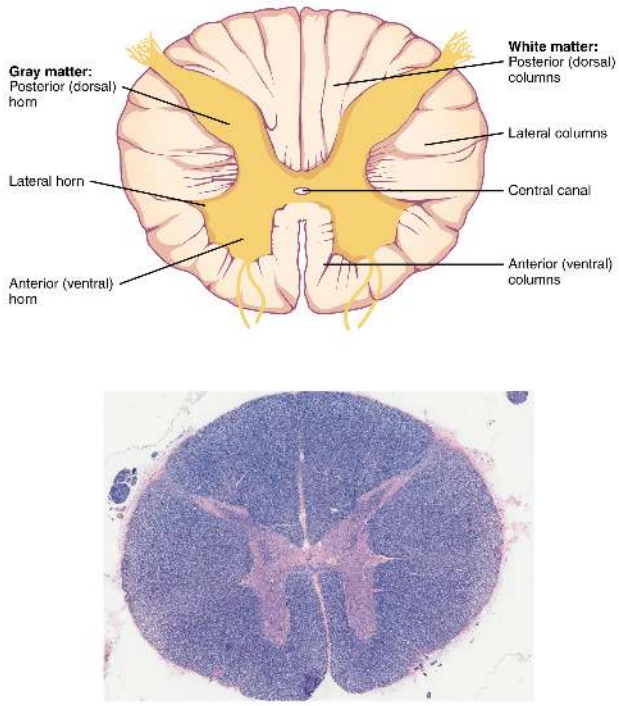


Figure 9.5.8: Cross-section of Spinal Cord The cross-section of a thoracic spinal cord segment shows the posterior, anterior, and lateral horns of gray matter, as well as the posterior, anterior, and lateral columns of white matter. LM × 40. (Micrograph provided by the Regents of University of Michigan 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**. 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** and carry sensory information to the brain. 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.

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.

Interactive Link

Visit this site for a thorough explanation of Parkinson's disease.

Interactive Link

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?

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9.6: The Peripheral Nervous System

Learning Objectives

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

- 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.

Ganglia

A **ganglion** is a group of neuron cell bodies in the peripheral nervous system (recall that a group of neuron cell bodies in the CNS is called nuclei). 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 9.6.1). The cells of the dorsal root ganglion are pseudounipolar 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. Recall that satellite cells are glial cells that provide a supportive role to neurons in the PNS.

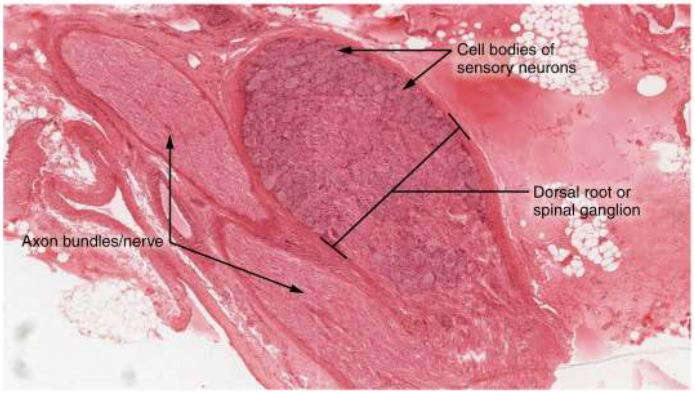


Figure 9.6.1: Dorsal Root Ganglion The cell bodies of sensory neurons, which are unipolar neurons by shape, are seen in this photomicrograph. Also, the fibrous region is composed of the axons of these neurons that are passing through the ganglion to be part of the dorsal nerve root (tissue source: canine). LM × 40. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

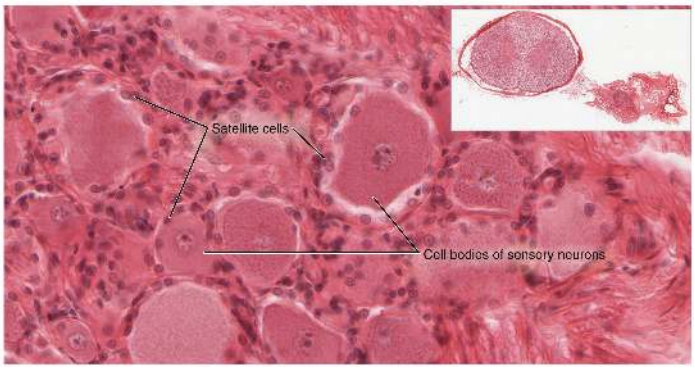


Figure 9.6.2 Spinal Cord and Root Ganglion The slide includes both a cross-section of the lumbar spinal cord and a section of the dorsal root ganglion (see also Figure 9.6.1) (tissue source: canine). LM × 1600. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

Interactive Link

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?

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.

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**.

Nerves

Bundles of axons in the PNS are referred to as nerves. This is in contrast to bundles of axons in the CNS, which are called tracts. 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 9.6.3). 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.

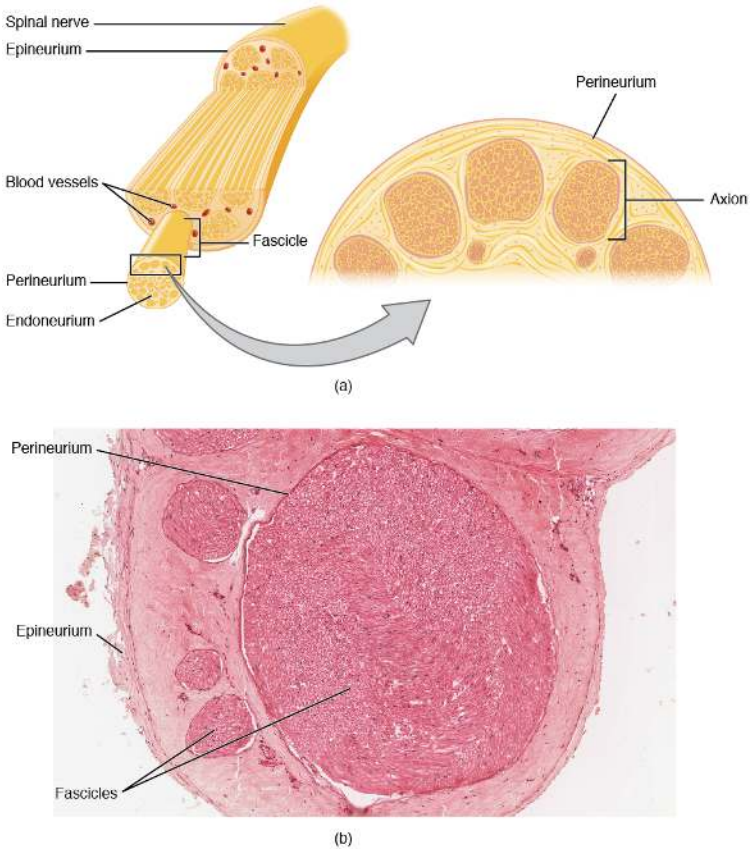


Figure 9.6.3: Nerve Structure The structure of a nerve is organized by the layers of connective tissue on the outside, around each fascicle, and surrounding the individual nerve fibers (tissue source: simian). LM × 40. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

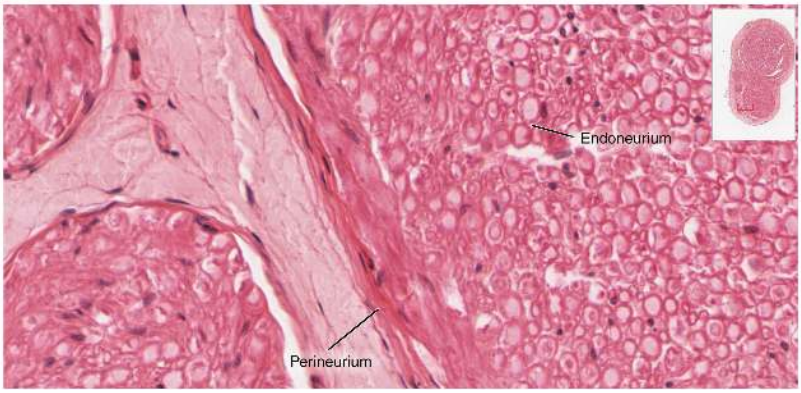


Figure 9.6.4 Close-Up of Nerve Trunk Zoom in on this slide of a nerve trunk to examine the endoneurium, perineurium, and epineurium in greater detail (tissue source: simian). LM × 1600. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

Interactive Link

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 CN I through CN XII for "Cranial Nerve (CN)," using Roman numerals for 1 (I) through 12 (XII). They can be classified as sensory nerves, motor nerves, or mixed nerves, meaning that these nerves transmit both sensory and motor information. 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, "**O**h **O**nce **O**ne **T**akes **T**he **A**natomy **F**inal **V**ery **G**ood **V**acations **A**re **H**appening," in which the initial letter of each word corresponds to the initial letter in the name of each nerve. For reference, the first letter of each cranial nerve is as follows: OOOTTAFVGVAH. If you find the traditional mnemonic hard to remember, try to come up with your own that has a personal significance to you! The names of the cranial nerves are listed in Table 13.3 along with a brief description of their function, their source (sensory ganglion or motor nucleus), and their target (sensory nucleus or skeletal muscle). They are listed here with a brief explanation of each nerve (Figure 9.6.5).

The **olfactory nerve (CN I)** and **optic nerve (CN II)** are responsible for the sense of smell and vision, respectively.

The **oculomotor nerve (CN III)** 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 (CN IV)** and the a**bducens nerve (CN V)** are both responsible for eye movement, but do so by controlling different extraocular muscles.

The **trigeminal nerve (CN VI)** is responsible for cutaneous (skin) sensations of the face and controlling the muscles of mastication.

The **facial nerve (CN VII)** 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 (CN VIII)** is responsible for the senses of hearing and balance.

The **glossopharyngeal nerve (CN IX)** 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 (CN X)** is responsible for contributing to homeostatic control of the organs of the thoracic and upper abdominal cavities.

The **spinal accessory nerve (CN XI)** is responsible for controlling the muscles of the neck, along with cervical spinal nerves.

The **hypoglossal nerve (CN XII)** is responsible for controlling the muscles of the lower throat and tongue.

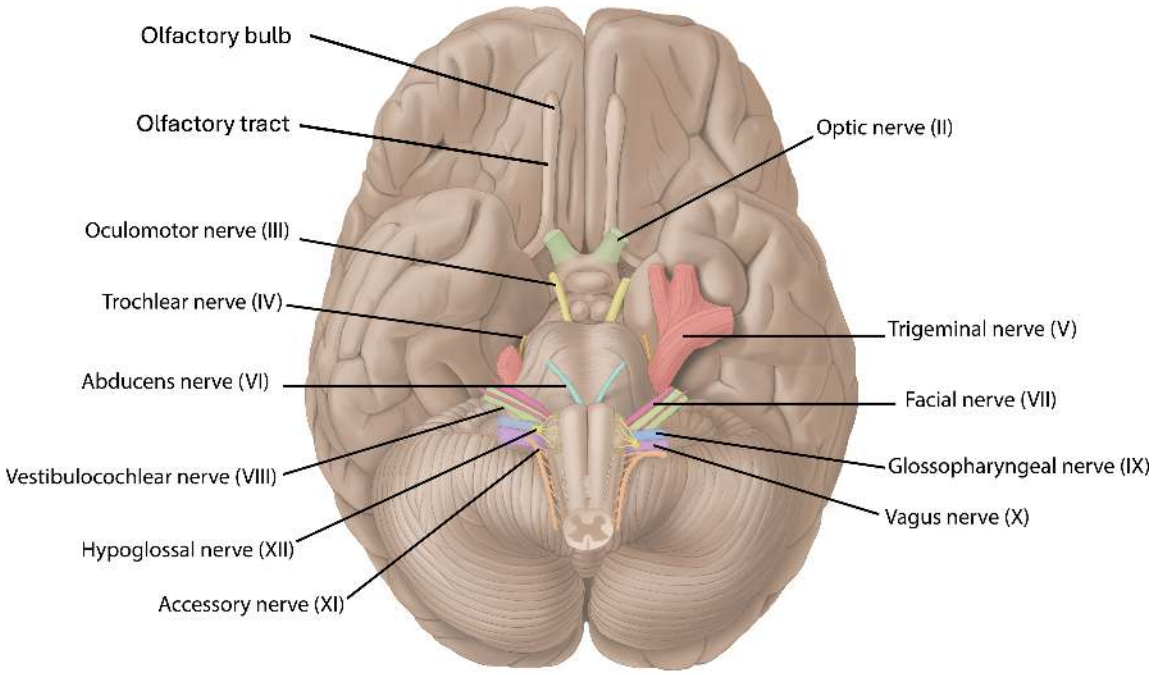


Figure 9.6.5 The Cranial Nerves. The cranial nerves are labelled above but keep in mind that only the olfactory bulb and olfactory tract are visible when viewing the brain hence the olfactory nerve not being labelled directly.*(Image credit: "Cranial Nerves" by Justin Greene and Jennifer Lange is licensed under CC BY-NC-SA 4.0.) / Olfactory bulb and tract labels by Harmony Folse*

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.

Interactive Link

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 address 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 (S), motor (M), or for mnemonic purposes, mixed nerves will be referred to as **both (B)**, as in both sensory and motor) (see Table 9.6.1). For reference, the function of each cranial nerve in order is SSMMBMBSBBMM. This can be converted into the following mnemonic: "**S**ome **S**ay **M**arry **M**oney **B**ut **M**y **B**rother **S**ays **B**rains **B**eauty **M**atter **M**ore," corresponds to the basic function of each nerve. The first, second, and eighth nerves are purely sensory: the olfactory (CN I), optic (CN II), and vestibulocochlear (CN VIII) nerves. The three eye-movement nerves are all motor: the oculomotor (CN III), trochlear (CN IV), and abducens (CN VI). The spinal accessory (CN XI) and hypoglossal (CN XII) nerves are also strictly motor. The remainder of the nerves contain both sensory and motor fibers. They are the trigeminal (CN V), facial (CN VII), glossopharyngeal (CN IX), and vagus (CN X) 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.

Table 9.6.1: Cranial Nerves

Mnemonic	#	Name	Function (S/M/B)	Central connection (nuclei)	Peripheral connection (ganglion or muscle)
Oh	I	Olfactory	Smell (S)	Olfactory bulb	Olfactory epithelium
Once	II	Optic	Vision (S)	Hypothalamus/thalamus/midbrain	Retina (retinal ganglion cells)
One	III	Oculomotor	Eye movements (M)	Oculomotor nucleus	Extraocular muscles (other 4), levator palpebrae superioris, ciliary ganglion (autonomic)
Takes	IV	Trochlear	Eye movements (M)	Trochlear nucleus	Superior oblique muscle
The	V	Trigeminal	Sensory/motor – face (B)	Trigeminal nuclei in the midbrain, pons, and medulla	Trigeminal
Anatomy	VI	Abducens	Eye movements (M)	Abducens nucleus	Lateral rectus muscle
Final	VII	Facial	Motor – face, Taste (B)	Facial nucleus, solitary nucleus, superior salivatory nucleus	Facial muscles, Geniculate ganglion, Pterygopalatine ganglion (autonomic)
Very	VIII	Vestibulocochlear	Hearing/balance (S)	Cochlear nucleus, Vestibular nucleus/cerebellum	Spiral ganglion (hearing), Vestibular ganglion (balance)
Good	IX	Glossopharyngeal	Motor – throat Taste (B)	Solitary nucleus, inferior salivatory nucleus, nucleus ambiguus	Pharyngeal muscles, Geniculate ganglion, Otic ganglion (autonomic)

Mnemonic	#	Name	Function (S/M/B)	Central connection (nuclei)	Peripheral connection (ganglion or muscle)
Vacations	X	Vagus	Motor/sensory – viscera (autonomic) (B)	Medulla	Terminal ganglia serving thoracic and upper abdominal organs (heart and small intestines)
Are	XI	Accessory	Motor – head and neck (M)	Spinal accessory nucleus	Neck muscles
Happening	XII	Hypoglossal	Motor – lower throat (M)	Hypoglossal nucleus	Muscles of the larynx and lower pharynx

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 pairs of 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 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 as 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 innervate the periphery. Axons from different spinal nerves will come together into a systemic nerve. Spinal nerves at the cervical, lumbar and sacral segments of the spinal cord form complex networks of nerves called **nerve plexuses.**

Of the four nerve plexuses, two are found at the cervical level, one at the lumbar level, and one at the sacral level (Figure 9.6.6). 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 lumbar plexus splits into an anterior and posterior division. The **femoral nerve** is the largest nerve from the posterior division of this plexus. The **obturator nerve** is the largest nerve from the anterior division of this plexus. 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.

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. These 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.

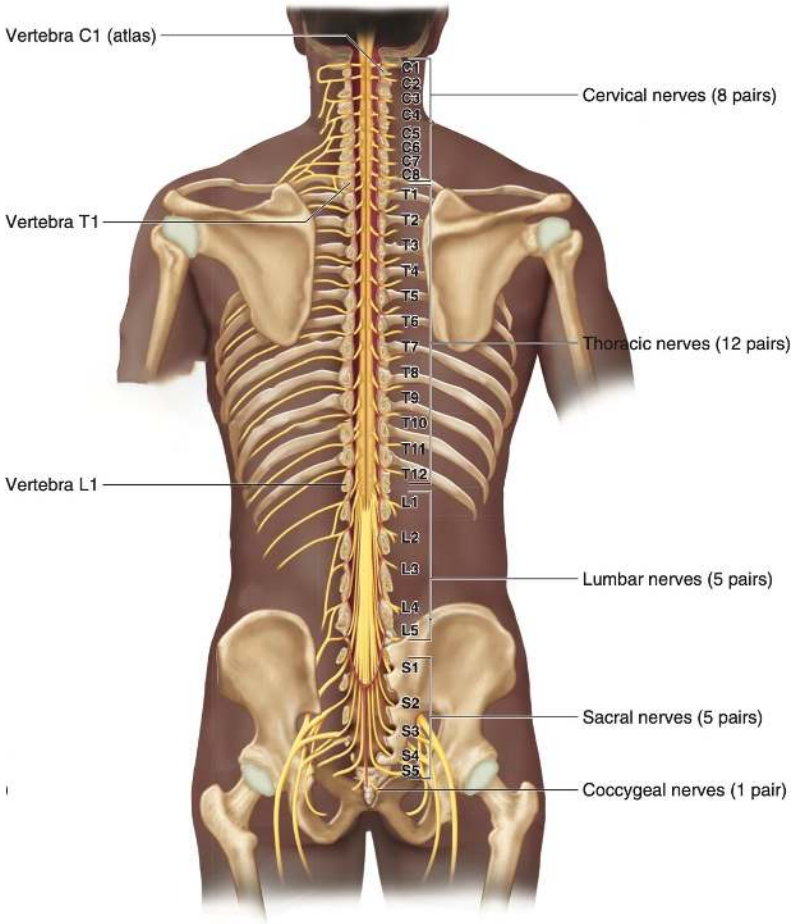


Figure 9.6.6 Spinal Cord and Spinal Nerves: The spinal nerves emerge laterally from the vertebral column with 8 in the cervical region, 12 in the thoracic region, 5 in the lumbar region, 5 in the sacral region, and 1 in the coccygeal region. *(Image credit: "Spinal Cord and Spinal Nerves" by Gabrielle Spurlock is licensed under CC BY-NC-SA 4.0, based on original by "KnowledgeWorks - Drawing Spinal nerves and plexuses - English labels" by KnowledgeWorks Global Ltd.)*

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.

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9.7: Review Questions

Use the following questions to test your knowledge on the Nervous System.

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CHAPTER OVERVIEW

10: Sensory Perception

10.1: General and Special Senses
10.2: Special Senses - Eyes
10.3: Special Senses - Ears
10.4: Review Questions

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10.1: General and Special Senses

Learning Objectives

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

- 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 how the sense of smell is conducted

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.** These receptors are found in the cell membrane of these sensory neurons. Certain receptors are activated by chemicals called ligands. For example, a molecule in food can serve as a ligand for taste receptors. Other cell membrane proteins, which are not accurately called receptors, are sensitive to mechanical or thermal changes. Physical changes in these proteins increase ion movement across the membrane, and can generate an action 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. Sensory receptor cells can be classified based on their location as well as their function.

There are two classifications for sensory receptors based on the location of stimuli in the body. Sensory receptors that detect stimuli originating from outside your body are classified as **exteroceptors**. Exteroceptors are usually found near the body's surface. An example of **exteroceptors** are the sensory receptors in your skin which detect temperature and pressure. Another example are the sensory receptors in your eye which detect light that is then processed as vision in your brain. Note that the "ex" portion of the name exteroceptor refers to the outside.

Sensory receptors that detect stimuli originating from inside the body are **interoceptors**. Interoceptors will thus be found inside your body, further from the surface. An example of interoceptors are the sensory receptors that detect chemical changes in your blood, or those that detect the stretch of your bladder, indicating a need to urinate. Note that the "int" portion of the name refers to the internal environment.

Sensory receptors can also be classified based on the type of stimuli they detect. These types of receptors are as follows:

- **Chemoreceptors** respond to different chemicals in the body such as in the blood or in the air in the lungs.
- **Osmoreceptors** respond to solute concentrations of body fluids.
- **Thermoreceptors** respond to changes in temperature. There are "hot" receptors which respond to hot temperature ranges (90-118°F) and "cold" receptors which respond to cold temperature ranges (50-104°F). Temperatures outside of this ranges activate **nociceptors**.
- **Nociceptors** respond to pain stimuli. Pain is primarily a chemical sense interpreted by the presence of chemicals from tissue damage, or similar intense stimuli.
- **Proprioceptors** detect movement and position of the body in the surrounding space.
- **Photoreceptors** detect light stimuli and are only found in the eye.
- **Mechanoreceptors** to mechanical stimuli such as pressure, touch, and vibration.

Lastly, sensory receptors can also be classified by how quickly or slowly they *adapt* to stimuli. Certain sensory receptors initially send rapid signals to the brain in response to stimuli but if this stimuli continues, these receptors decrease their firing rate. These

sensory receptors are classified as **rapidly adapting receptors** and include receptors that detect vibration, touch, smell and thermoreceptors. For example, when you start the day in the morning and get dressed, you may initially feel your shirt on your skin as you get dressed. However, as you continue about your day, you tend not to notice the sensation of the shirt fabric on your skin. Your receptors have rapidly adapted to this sensation.

In contrast, **slow adapting receptors** are those that continue to send signals to the brain as long as the stimuli is present. Slow adapting receptors include nociceptors for pain, chemoreceptors and proprioceptors. These receptors are critical for maintaining homeostasis so if pain is present, you brain will want to be aware of it to address the issue. Similarly, your body needs to constantly monitor the chemical composition of the fluids in your body so your chemoreceptors will be constantly firing.

Types of Senses

We can classify the senses into the **general senses** and **special senses**. The general senses include touch, temperature, pain, and proprioception. The special senses include vision, hearing (and balance), taste, and smell. The special senses of taste and smell will be covered below while the special senses of vision, hearing and equilibrium will be covered in their own separate chapters.

Special Sense - 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. 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.

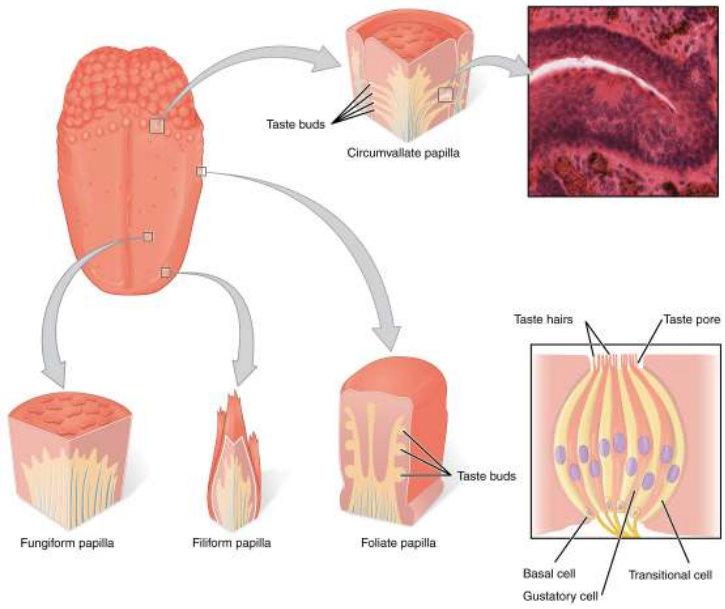


Figure 10.1.2: The Tongue The tongue is covered with small bumps, called papillae, which contain taste buds that are sensitive to chemicals in ingested food or drink. Different types of papillae are found in different regions of the tongue. The taste buds contain specialized gustatory receptor cells 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 specialized receptors in the cell membrane of taste buds. The sweet taste is the sensitivity of taste buds 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 specialized receptors However, there are a number of different ways in which this can happen because there are a large diversity of bitter-tasting molecules. 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 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 specialized 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.

Interactive Link



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. 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 10.1.3). 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.

Olfactory stimuli travels to the primary olfactory cortex that is located in the inferior and medial areas of the temporal lobe. Olfactory stimuli also reaches 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.

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.

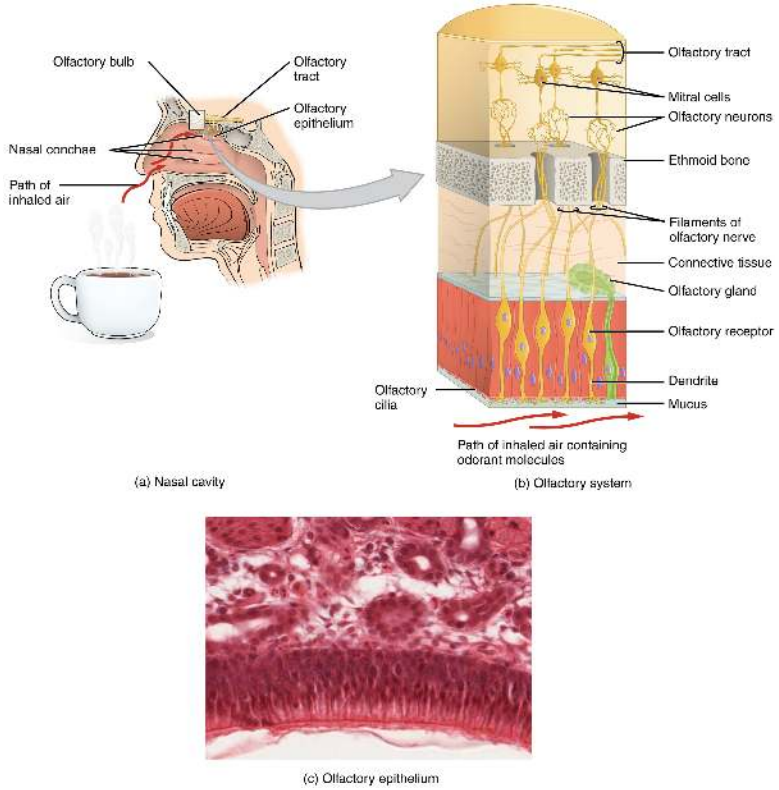


Figure 10.1.3: The Olfactory System (a) The olfactory system begins in the peripheral structures of the nasal cavity. (b) The olfactory receptor neurons are within the olfactory epithelium. (c) Axons of the olfactory receptor neurons project through the cribriform plate of the ethmoid bone and synapse with the neurons of the olfactory bulb (tissue source: simian). LM × 812. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

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.

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10.2: Special Senses - Eyes

Learning Objectives

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

- List the supporting structures around the eye and describe the structure of the eyeball
- Describe the processes of phototransduction

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 10.2.1). 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 just inside the orbit, superior and lateral to the eyeball. 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.

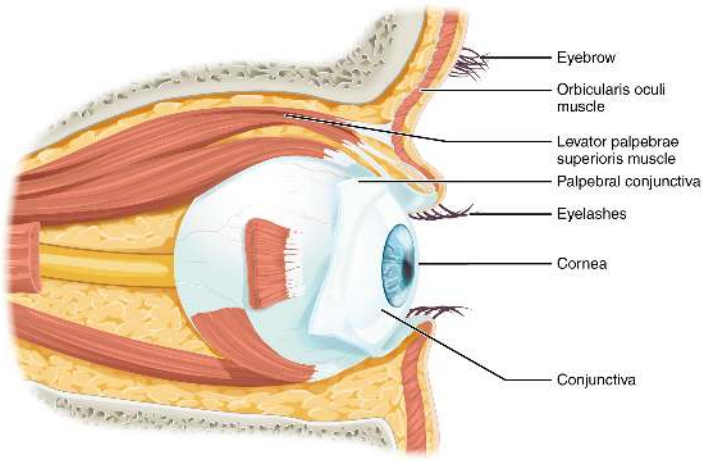


Figure 10.2.1: The Eye in the Orbit The eye is located within the orbit and surrounded by soft tissues that protect and support its function. The orbit is surrounded by cranial bones of the skull.

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 10.2.2). 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 moves toward the contracting muscle. For example, when the superior rectus contracts, the eye rotates to look up. 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 angle of the tendon through the trochlea means that contraction of the superior oblique rotates the eye laterally. When the inferior oblique muscle 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 10.2.1).

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.

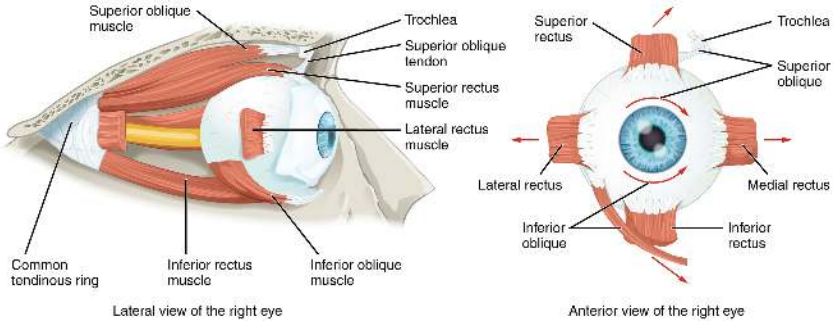


Figure 10.2.2: Extraocular Muscles The extraocular muscles move the eye within the orbit.

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 10.2.3). 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 **suspensory ligaments**, or 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 containing **photoreceptors**.

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 aqueous humor helps bring nutrients to the structures of the anterior cavity and drains wastes. 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 vitreous humor helps support the eyeball internally, helping it maintain its spherical shape.

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. 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 10.2.3). 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.

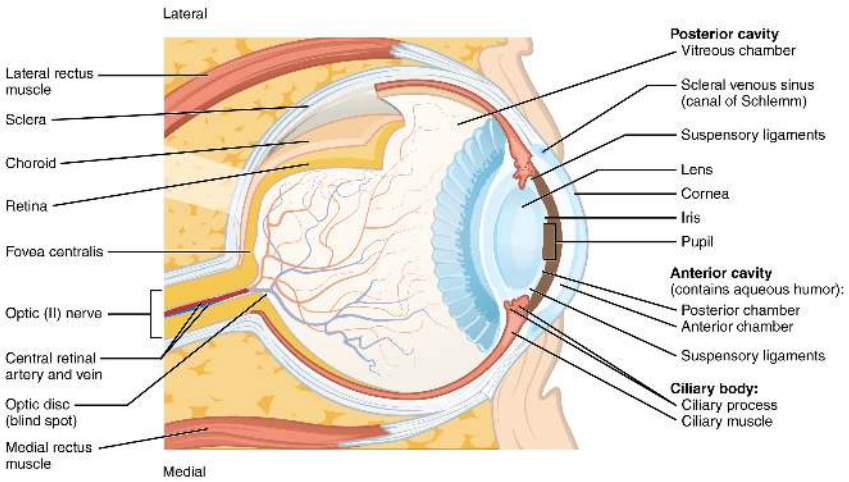


Figure 10.2.3: Structure of the Eye The sphere of the eye can be divided into anterior and posterior chambers. The wall of the eye is composed of three layers: the fibrous tunic, vascular tunic, and neural tunic. Within the neural tunic is the retina, with three layers of cells and two synaptic layers in between. The center of the retina has a small indentation known as the fovea.

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 centralis**. At the **fovea centralis**, 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 10.2.4). 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 10.2.5). 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. **Rods** are specialized for low-light levels and black and white vision. **Cones** are specialized for high definition color vision in high light levels.

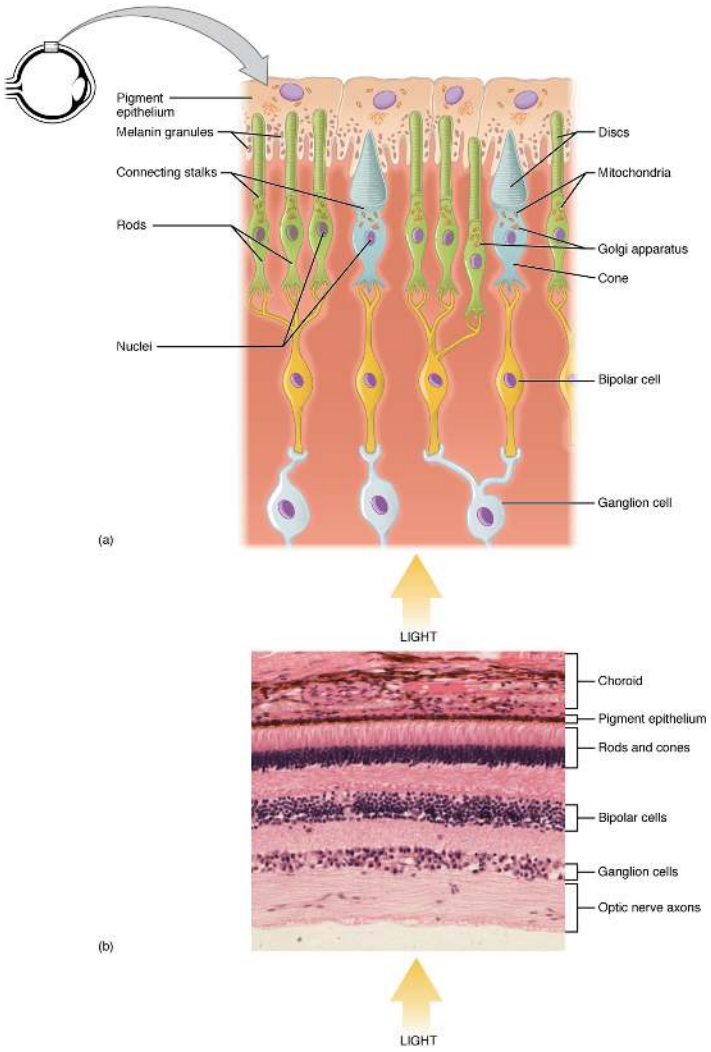


Figure 10.2.5: Photoreceptor (a) All photoreceptors have inner segments containing the nucleus and other important organelles and outer segments with membrane arrays containing the photosensitive opsin molecules. Rod outer segments are long columnar shapes with stacks of membrane-bound discs that contain 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)

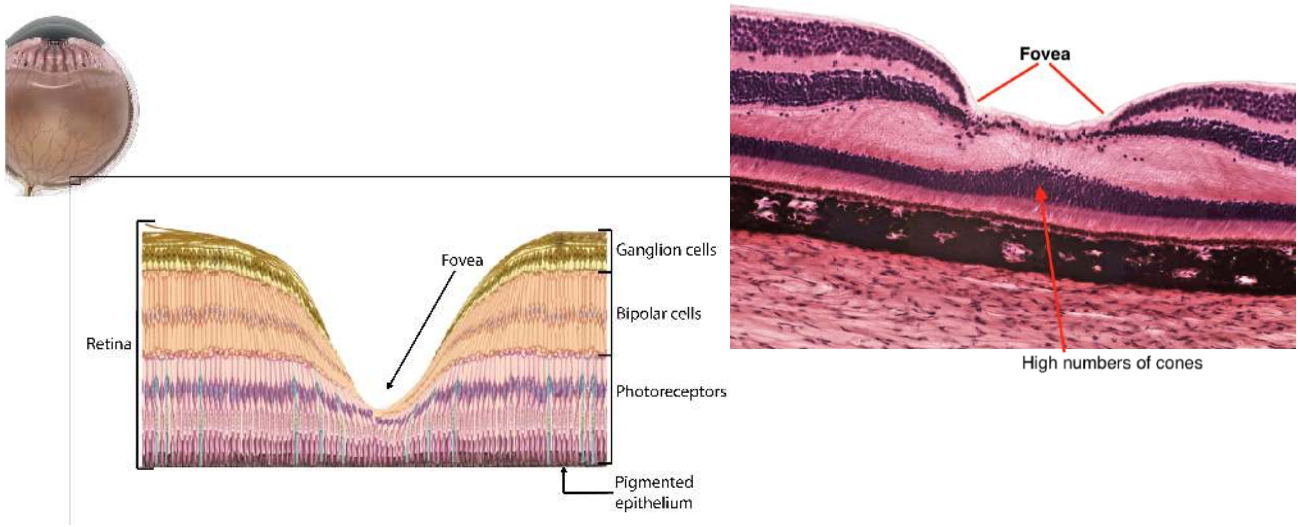


Figure 10.2.6 Fovea: At the exact center of the retina is a region called the macula lutea with a depression called the fovea. At the fovea there are no blood vessels, ganglion cells or bipolar cells to interrupt light reaching the receptor cells and only cones are present. Because more light passes to the receptor cells at the fovea, it is in this region that visual acuity is the greatest. *(Image and caption credits: "Retinal Cell Layers at Fovea Illustration" by Sofia Elizondo is licensed under CC BY-NC SA 4.0, modification of original "Cenveo - Drawing Anatomy of the fovea - English labels" by Cenveo. "Fovea Histology" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, slide provided by the Regents of the University of Michigan Medical School © 2022.)*

Errors of Refraction

Refraction refers to the ability of the lens to bend light rays as they enter on the eye so that they focus on the fovea centralis for most optimum vision. However, often due to the shape of the eye or cornea, the lens is not able to accommodate enough to focus light on the fovea centralis, instead focusing it before or beyond the fovea centralis. This leads to two of the most common vision issues: **myopia** (nearsightedness) and **hyperopia** (farsightedness).

Individuals with **hyperopia** experience blurry vision when viewing objects that are near to the eye. This can occur due to the eyeball being too short or the cornea being too flat. This affects the lens ability to become thick or round, which then causes light rays to focus behind the fovea centralis instead of on the fovea centralis. This leads to the blurry vision close up. Hyperopa is also called farsightedness because individuals with hyperopia can see *far* but they cannot see near. Hyperopia is corrected by placing a convex lens in front of the eye to properly refract light onto the fovea.

The opposite occurs in myopia. Individuals with **myopia** experience blurry vision when viewing objects at a distance. This can occur due to the eyeball being too long or the cornea being too curved. This affects the lens ability to flatten, which then causes light rays to focus in front of the fovea centralis instead of on the fovea centralis. This leads to the blurry vision at a distance. Myopia is also called nearsightedness because individuals with myopia can see *near* but they cannot see far. Myopia is corrected by placing a concave lens in front of the eye to properly refract light onto the fovea.

Figure 10.2.7 below shows the differences inside the eye between myopia and hyperopia.

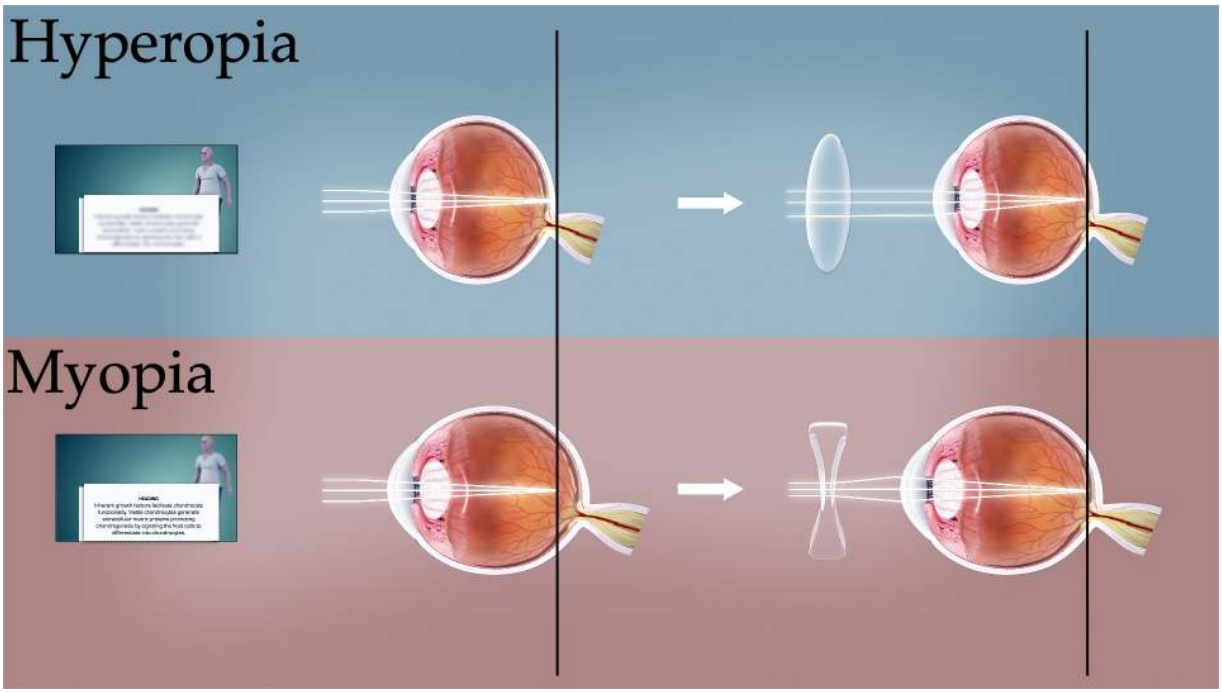


Figure 10.2.7 Errors of Refraction: In hyperopia, light is focused behind the fovea, instead of on the fovea. In myopia, light is focused in front of the fovea instead of on the fovea. *(Image Credit: "Refractive Error" by Scientific Animations is licensed under CC BY-NC-SA 4.0) / Labels by Harmony Folse*

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10.3: Special Senses - Ears

Learning Objectives

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

- Describe the means of mechanoreception for hearing and balance

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 10.3.1). 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.

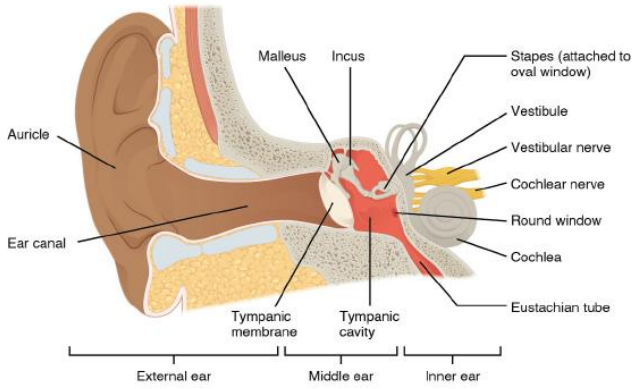


Figure 10.3.1: Structures of the Ear The external ear contains the auricle, ear canal, and tympanic membrane. The middle ear contains the ossicles and is connected to the pharynx by the Eustachian tube. The inner ear contains the cochlea and vestibule, which are responsible for audition and equilibrium, 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 10.3.2). The membrane covering the round window will bulge out or pucker in with the movement of the fluid within the scala tympani.

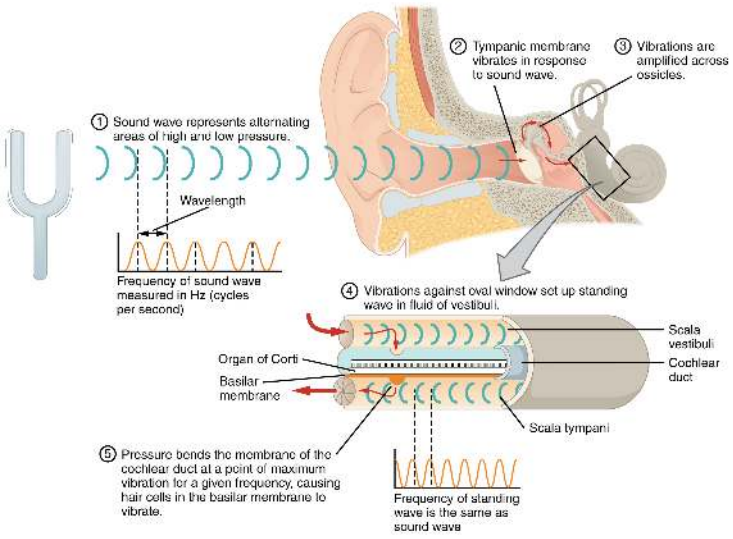


Figure 10.3.2: Transmission of Sound Waves to Cochlea A sound wave causes the tympanic membrane to vibrate. This vibration is amplified as it moves across the malleus, incus, and stapes. The amplified vibration is picked up by the oval window causing pressure waves in the fluid of the scala vestibuli 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 10.3.3). The cochlear duct contains several organs of Corti, which transduce 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.

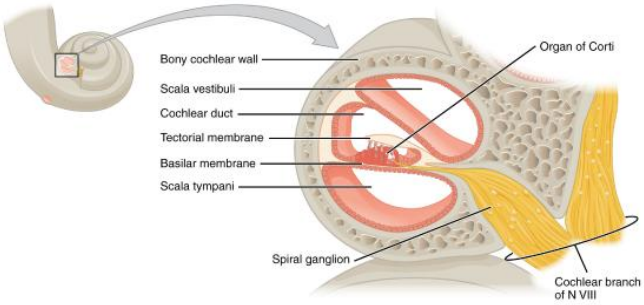


Figure 10.3.3: Cross Section of the Cochlea The three major spaces within the cochlea are highlighted. The scala tympani and scala vestibuli lie on either side of the cochlear duct. The organ of Corti, containing the mechanoreceptor hair cells, is adjacent to the scala tympani, where it sits atop the 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 10.3.4). 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.

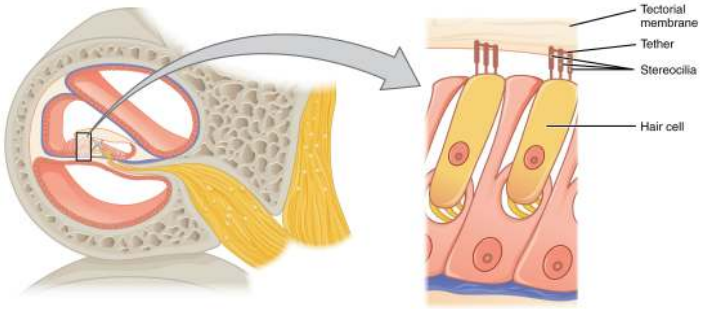


Figure 10.3.5: Hair Cell The hair cell is a mechanoreceptor with an array of stereocilia emerging from its apical surface. The stereocilia are tethered together by proteins that open ion channels when the array is bent toward the tallest member of their array, and closed when the array is bent toward the shortest member of their array.

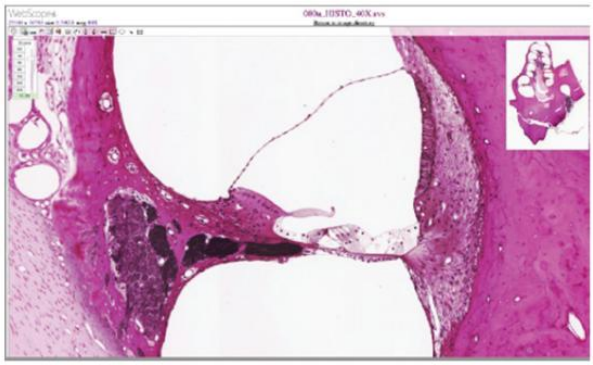


Figure 10.3.6: Cochlea and Organ of Corti LM × 412. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

Interactive Link

View the University of Michigan WebScope to explore the tissue sample 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. 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 10.3.7). 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.

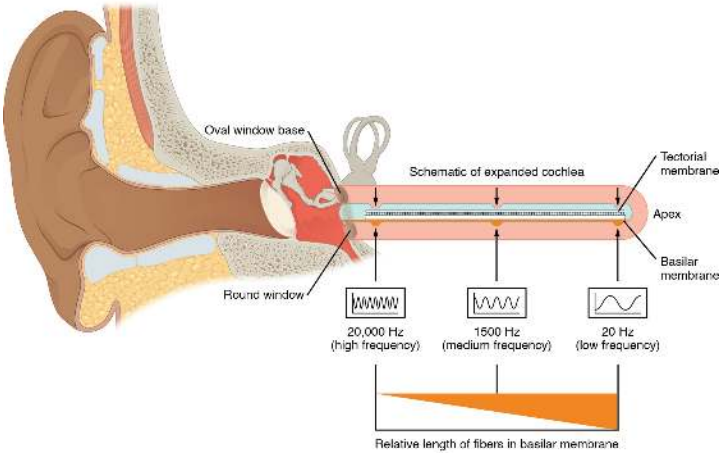
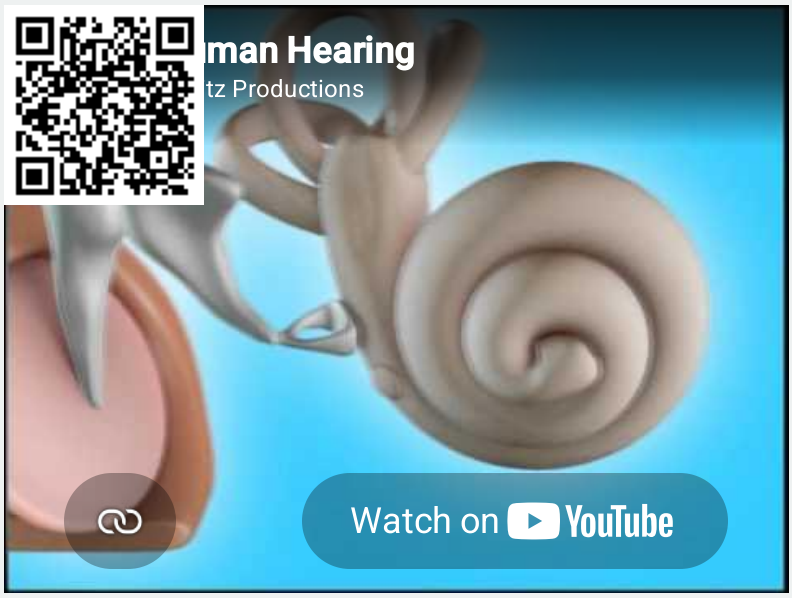


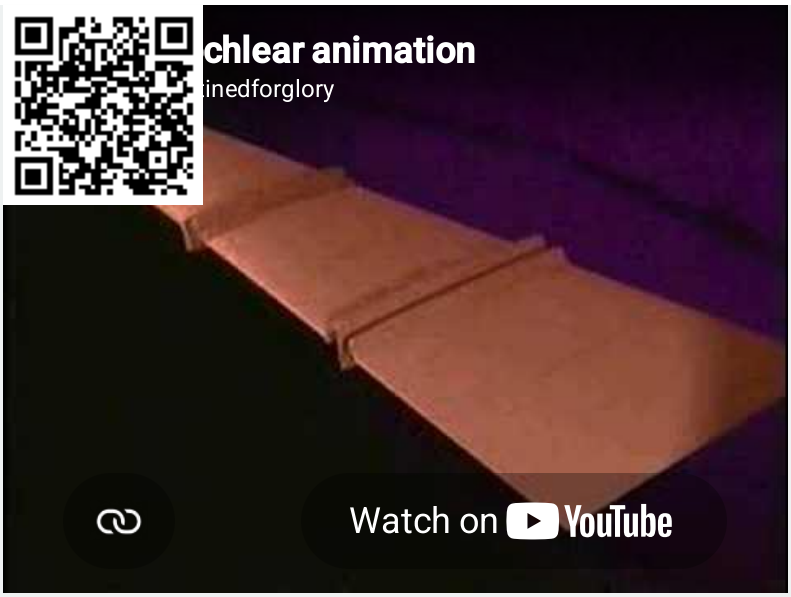
Figure 10.3.7: Frequency Coding in the Cochlea The standing sound wave generated in the cochlea by the movement of the oval window deflects the basilar membrane on the basis of the frequency of sound. Therefore, hair cells at the base of the cochlea are activated only by high frequencies, whereas those at the apex of the cochlea are activated only by low frequencies.

Interactive Link



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. Which ear structures are responsible for the amplification and transfer of sound from the external ear to the inner ear?

Interactive Link



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. 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 otolithic membrane (Figure 10.3.8). On top of the otolithic membrane is a layer of calcium carbonate crystals, called otoliths. The otoliths essentially make the otolithic membrane top-heavy. The otolithic membrane moves separately from the macula in response to head movements. Tilting the head causes the otolithic membrane to slide over the macula in the direction of gravity. The moving otolithic membrane, in turn, bends the sterocilia, causing some hair cells to depolarize as others hyperpolarize. The exact position of the head is interpreted by the brain based on the pattern of hair-cell depolarization.

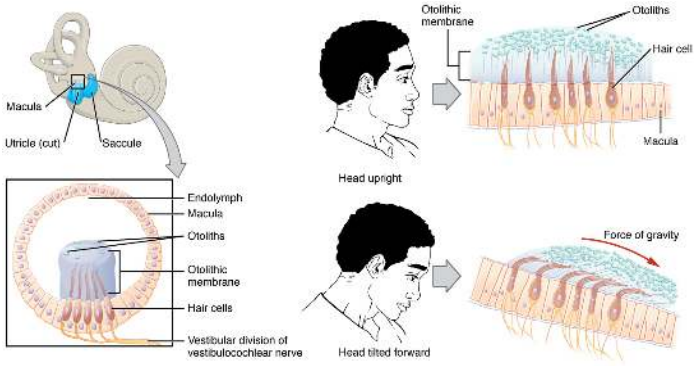


Figure 10.3.8: Linear Acceleration Coding by Maculae The maculae are specialized for sensing linear acceleration, such as when gravity acts on the tilting head, or if the head starts moving in a straight line. The difference in inertia between the hair cell stereocilia and the otolithic membrane in which 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 10.3.9). 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.

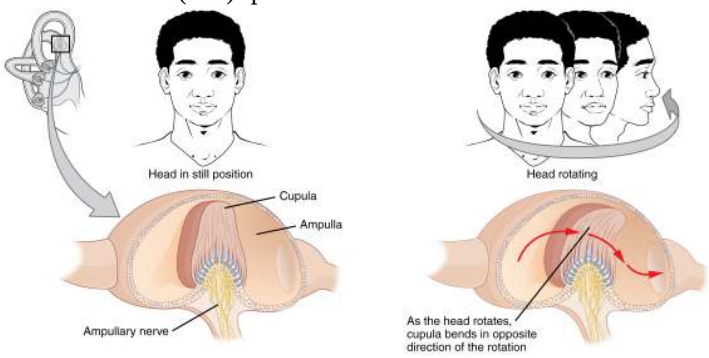


Figure 10.3.9: Rotational Coding by Semicircular Canals Rotational movement of the head is encoded by the hair cells in the base of the semicircular canals. As one of the canals moves in an arc with the head, the internal fluid moves in the opposite direction, causing the cupula and stereocilia to bend. 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.

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10.4: Review Questions

Use the following questions to test your knowledge on Sensory Perception.

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CHAPTER OVERVIEW

11: The Autonomic Nervous System

11.1: Introduction to the Autonomic Nervous System (ANS)
11.2: The Sympathetic Division of the ANS
11.3: The Parasympathetic Division of the ANS
11.4: Review Questions

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11.1: Introduction to the Autonomic Nervous System (ANS)

Learning Objectives

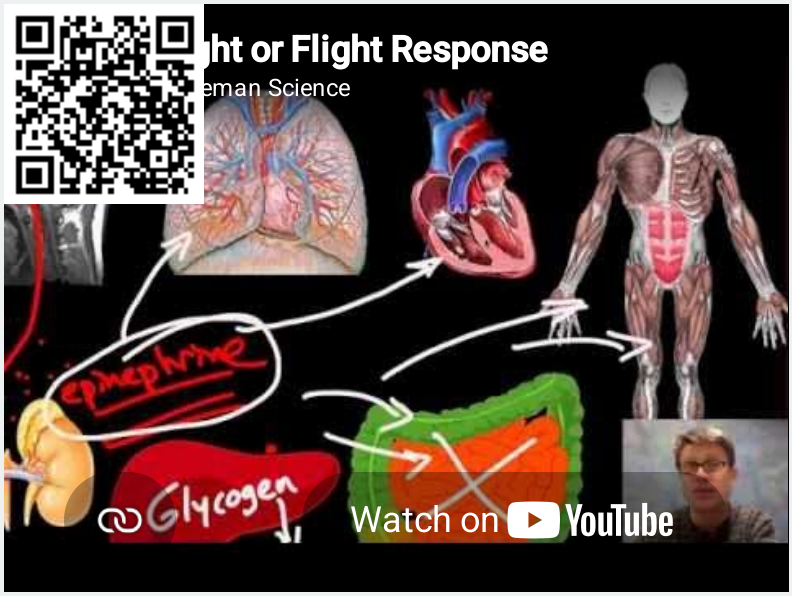
By the end of this section you should be able to:

- Name and describe the divisions of the autonomic nervous system
- Descrone the components of the 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 (ANS)**. 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 addition 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.

Interactive Link



Watch this video to learn more about adrenaline and the fight-or-flight response. 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?

Neurons of the Autonomic Nervous System

The autonomic nervous system is composed of a chain of two lower motor neurons. The cell body of the first of the two ANS motor neurons is located in the brainstem or spinal cord and is called a **preganglionic neuron**. The axon of the preganglionic

neuron extends outside of the CNS through cranial or spinal nerves. These axons project to an **autonomic ganglion** of the peripheral nervous system. The preganglionic axons release acetylcholine (ACh) to excite the **postganglionic neuron.** The cell body of the postganglionic neuron resides within the autonomic ganglion and its axon extends to an **effector** or target organ (cardiac muscle, smooth muscle, or gland). Postganglionic neurons have axons that release either acetylcholine (ACh) or norepinephrine (NE) to either excite or inhibit an effector, depending on the type of receptors present on the effector.

For example, a general pathway of communication in the autonomic nervous system would begin at the preganglionic neuron in the CNS. The axons of the preganglionic neuron extend out from the CNS and synapse onto a postganglionic neuron in the PNS. The preganglionic neuron releases acetylcholine (a neurotransmitter) that stimulate the postganglionic neuron. The axons of the postganglionic neuron synapse onto the effector or target organ. The neurotransmitter release by the postganglionic neuron to the target organ will then activate the target organ's autonomic response. The type of neurotransmitter released at each synapse between the postganglionic neuron and the target organ depends on the division of the ANS and the receptors present at the target organ. These will be discussed in the upcoming sections on the ANS.

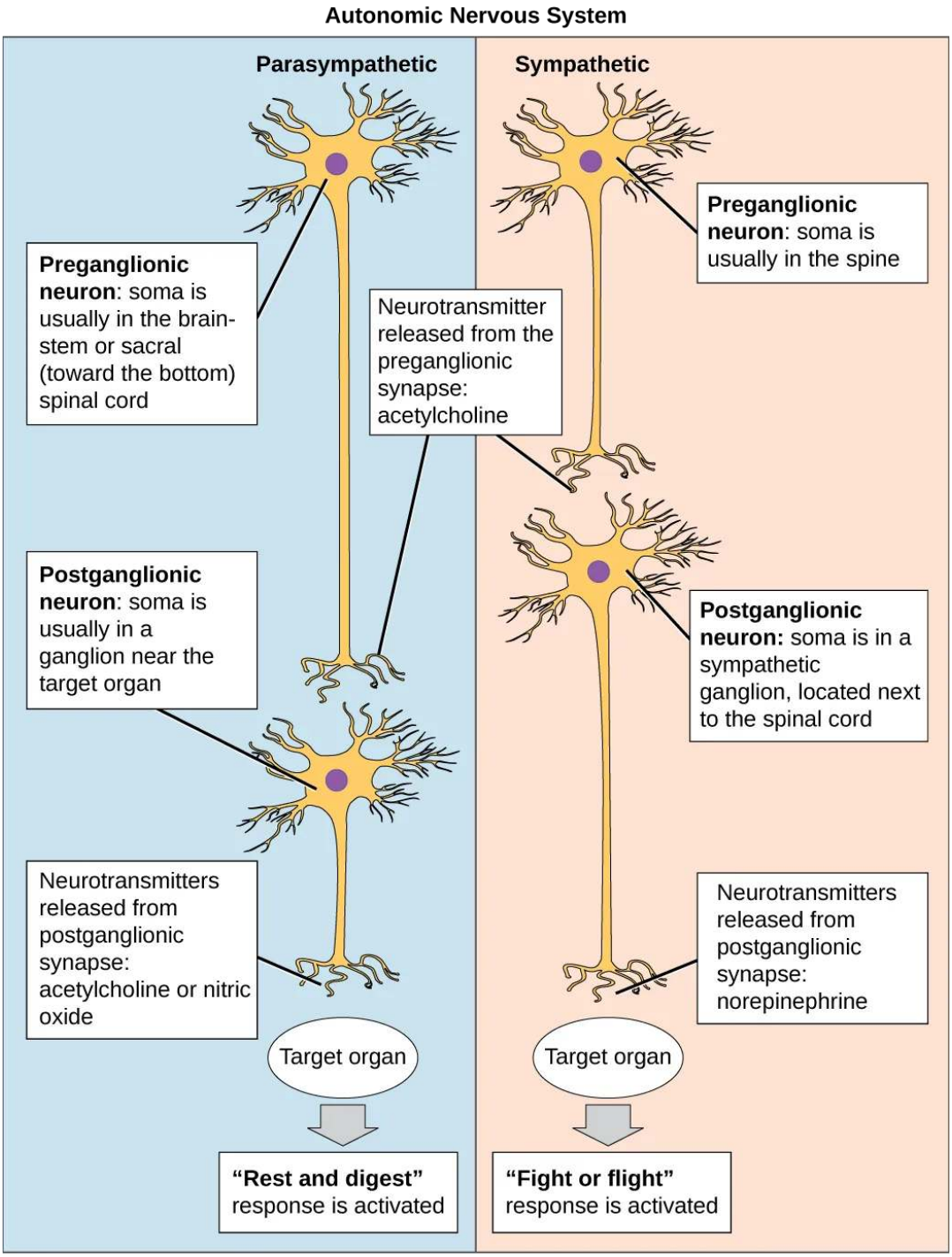


Figure 11.1.1 The Autonomic Nervous System: In the autonomic nervous system, a preganglionic neuron of the CNS synapses with a postganglionic neuron of the PNS. The postganglionic neuron, in turn, acts on a target organ. Autonomic responses are mediated by the sympathetic and the parasympathetic systems, which are antagonistic to one another. The sympathetic system activates the "fight or flight" response, while the parasympathetic system activates the "rest and digest" response. *(Image and caption credit: "Autonomic Nervous System" by OpenStax is licensed under CC BY 4.0)*

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11.2: The Sympathetic Division of the ANS

Learning Objectives

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

- Name the components that generate the sympathetic responses of the autonomic nervous system
- Explain the bodily responses associated with the sympathetic divisions
- Describe the signaling molecules and receptor proteins involved in communication within the sympathetic division

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. Additionally, 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 called the sympathetic chain ganglia that runs alongside the vertebral column. 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.

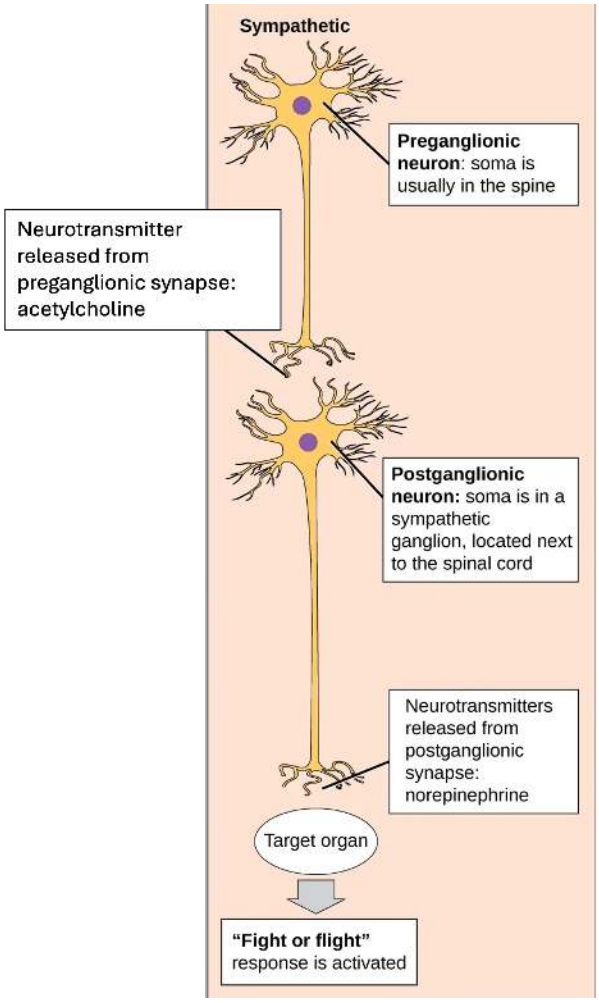


Figure 11.2.1 Sympathetic Division of the ANS. *(Image and caption credit: "Autonomic Nervous System" by OpenStax is licensed under CC BY 4.0) / Cropped from original*

As mentioned previously, the preganglionic neuron projects out to synapse onto a postganglionic neuron. A preganglionic neuron of the sympathetic division will release acetylcholine onto the postganglionic neuron. The postganglionic neuron will then respond by releasing epinephrine or norepinephrine to the target organ. The target organ will bind epinephrine or norepinephrine through **adrenergic** receptors on its cell membrane. The binding of epinephrine or norepinephrine to the adrenergic receptors of the target organ will then trigger the sympathetic response in that organ. An exception exists when the target organ is a sweat gland. A sympathetic postganglionic neuron will release acetylcholine if the target organ is a sweat gland. The sweat gland will bind to acetylcholine via **muscarinic** receptors and sweat will be released.

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 adrenal medulla will release norepinephrine/epinephrine into the bloodstream to enhance the sympathetic nervous system's effects.

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. The variety of responses by the sympathetic nervous system can be seen in Figure 11.2.2 below.

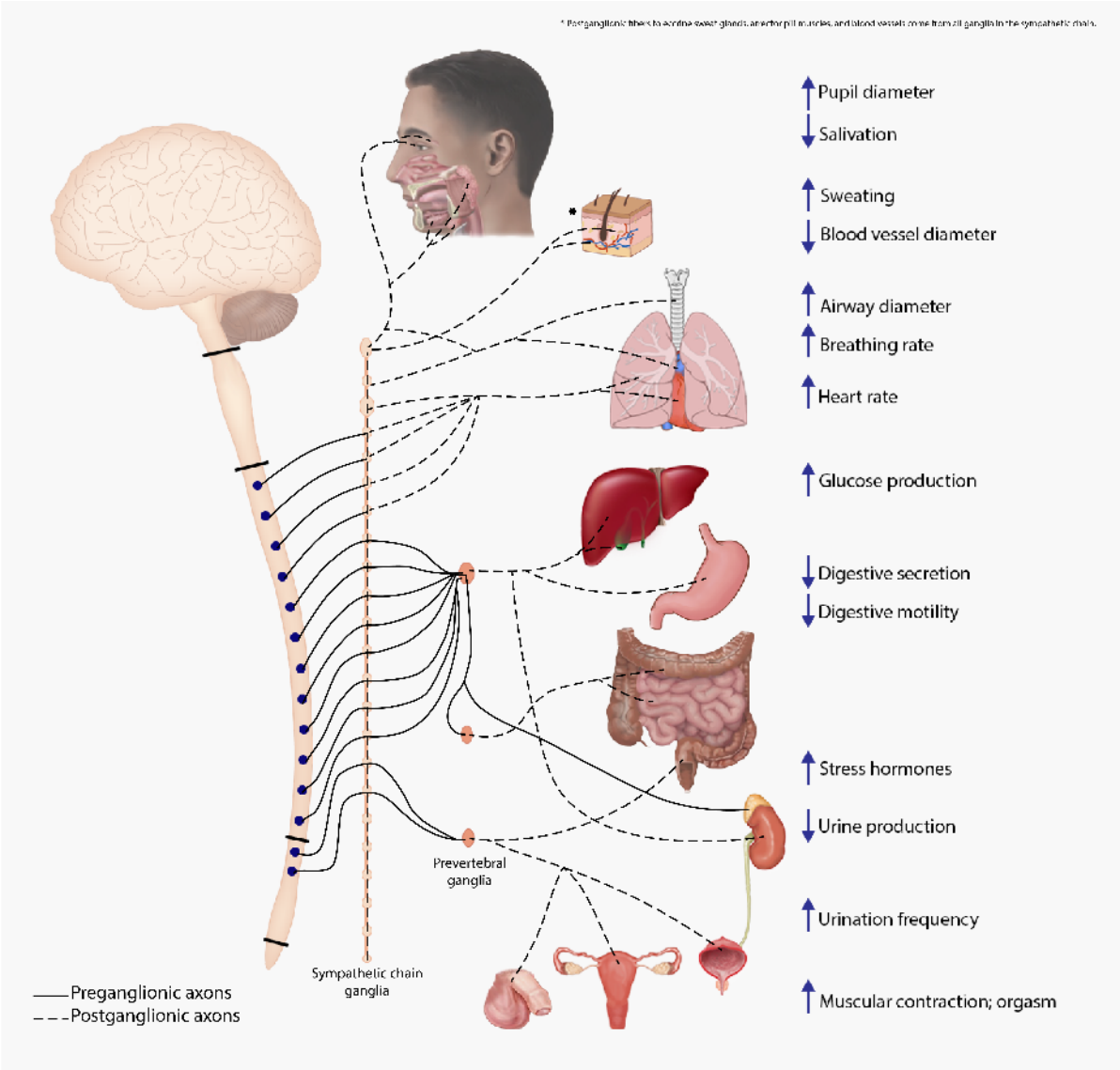


Figure 11.2.2 Sympathetic Innervation: Neurons from the lateral horns of the spinal cord extend their preganglionic nerve fibers (solid lines) to the sympathetic chain ganglia on the lateral sides of the vertebral column. Axons may terminate here or pass through and terminate in prevertebral (collateral) ganglia that are anterior to the vertebral column. Axons from the ganglionic neurons, called postganglionic nerve fibers (dashed lines), then project to target effectors throughout the body. *(Image and caption credit: "ANS - Sympathetic Division Innervation" by Jennifer Lange is licensed under CC BY-NC-SA 4.0. Image incorporates originals from Functional Neuroanatomy, KnowledgeWorks, Patrick J. Lynch, and Ron Slagter.)*

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11.3: The Parasympathetic Division of the ANS

Learning Objectives

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

- Name the components that generate the parasympathetic responses of the autonomic nervous system
- Explain the bodily responses associated with the parasympathetic divisions
- Describe the signaling molecules and receptor proteins involved in communication within the parasympathetic division

Parasympathetic Division of the Autonomic Nervous System

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. 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.

A preganglionic neuron of the parasympathetic division will release acetylcholine onto the postganglionic neuron. The postganglionic neuron will then respond by also releasing acetylcholine to the target organ. The target organ will bind acetylcholine through **muscarinic** receptors on its cell membrane. The binding of acetylcholine to the muscarinic receptors of the target organ will then trigger the parasympathetic response in that organ.

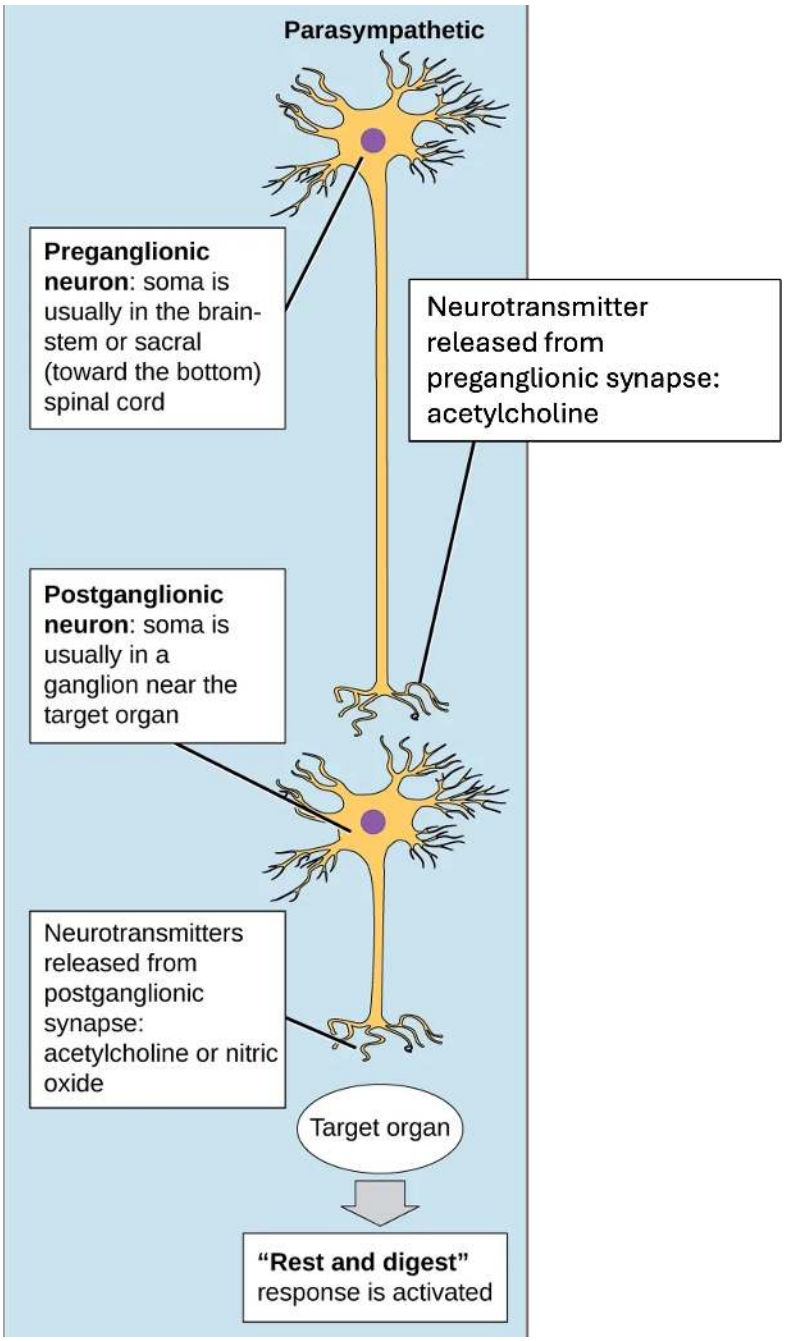

Parasympathetic
Preganglionic neuron: soma is usually in the brain-stem or sacral (toward the bottom) spinal cord
Neurotransmitter released from preganglionic synapse: acetylcholine
Postganglionic neuron: soma is usually in a ganglion near the target organ
Neurotransmitters released from postganglionic synapse: acetylcholine or nitric oxide
Target organ
"Rest and digest" response is activated

Figure 11.3.1 Parasympathetic Division of the ANS. *(Image and caption credit: "Autonomic Nervous System" by OpenStax is licensed under CC BY 4.0) / Cropped from original*

Parasympathetic preganglionic fibers primarily influence the heart, bronchi, and esophagus in the thoracic cavity and the stomach, liver, pancreas, gall bladder, 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. The responses by the parasympathetic division will often oppose those of the sympathetic division. These responses can be seen in Figure 11.3.2 below.

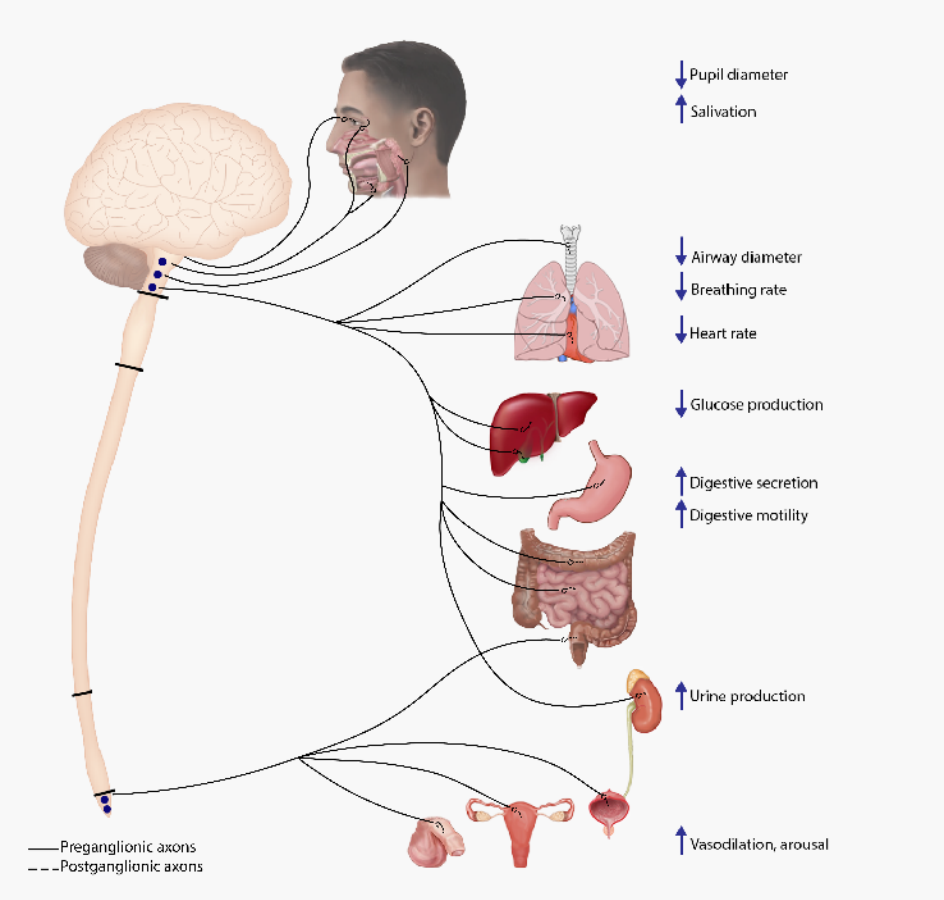


Figure 11.3.2 Parasympathetic Innervation: Neurons from brain-stem nuclei, or from the lateral horn of the sacral spinal cord, extend their preganglionic nerve fibers (shown in red) to terminal ganglia near the effector organs or to intramural ganglia within the walls of the effector organs. Postganglionic axons (shown in black) from these ganglionic neurons then project the short distance to target effectors *(Image and caption credit: "ANS - Parasympathetic Division Innervation" by Jennifer Lange is licensed under CC BY-NC-SA 4.0. Image incorporates originals from Functional Neuroanatomy, KnowledgeWorks, Patrick J. Lynch, and Ron Slagter.)*

The neurotransmitters used by the parasympathetic vs. sympathetic systems can be compared in the following table.

Table 11.3.1:Autonomic System Signaling Molecules

	Sympathetic	Parasympathetic
Preganglionic	Acetylcholine → nicotinic receptor	Acetylcholine → nicotinic receptor
Postganglionic	Norepinephrine → adrenergic receptors Acetylcholine → muscarinic receptor (associated with sweat glands)	Acetylcholine → muscarinic receptor

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11.4: Review Questions

Use the following questions to test your knowledge on the Autonomic Nervous System.

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CHAPTER OVERVIEW

12: The Endocrine System

12.1: An Overview of the Endocrine System
12.2: Hormones
12.3: The Pituitary Gland and Hypothalamus
12.4: Thyroid Gland and Parathyroid Glands
12.5: Adrenal Glands
12.6: Endocrine Pancreas
12.7: Review Questions

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12.1: An Overview of the Endocrine System

Learning Objectives

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

- Distinguish the types of intercellular communication, their importance, mechanisms, and effects
- Identify the major organs and tissues of the endocrine system and their location in the body

Communication is a process in which a sender transmits signals to one or more receivers to control and coordinate actions. In the human body, two major organ systems participate in relatively "long distance" communication: the nervous system and the endocrine system. Together, these two systems are primarily responsible for maintaining homeostasis in the body.

Neural and Endocrine Signaling

The nervous system uses two types of intercellular communication—electrical and chemical signaling—either by the direct action of an electrical potential, or in the latter case, through the action of chemical neurotransmitters such as serotonin or norepinephrine. Neurotransmitters act locally and rapidly. When an electrical signal in the form of an action potential arrives at the synaptic terminal, they diffuse across the synaptic cleft (the gap between a sending neuron and a receiving neuron or muscle cell). Once the neurotransmitters interact (bind) with receptors on the receiving (post-synaptic) cell, the receptor stimulation is transduced into a response such as continued electrical signaling or modification of cellular response. The target cell responds within milliseconds of receiving the chemical "message"; this response then ceases very quickly once the neural signaling ends. In this way, neural communication enables body functions that involve quick, brief actions, such as movement, sensation, and cognition. In contrast, **the endocrine system** uses just one method of communication: **chemical signaling**. These signals are sent by the endocrine organs, which secrete chemicals—the **hormone**—into the extracellular fluid. Hormones are transported primarily via the bloodstream throughout the body, where they bind to receptors on target cells, inducing a characteristic response. As a result, endocrine signaling requires more time than neural signaling to prompt a response in target cells, though the precise amount of time varies with different hormones. For example, the hormones released when you are confronted with a dangerous or frightening situation, called the fight-or-flight response, occur by the release of adrenal hormones—epinephrine and norepinephrine—within seconds. In contrast, it may take up to 48 hours for target cells to respond to certain reproductive hormones.

In addition, endocrine signaling is typically less specific than neural signaling. The same hormone may play a role in a variety of different physiological processes depending on the target cells involved. For example, the hormone oxytocin promotes uterine contractions in people in labor. It is also important in breastfeeding, and may be involved in the sexual response and in feelings of emotional attachment in humans.

In general, the nervous system involves quick responses to rapid changes in the external environment, and the endocrine system is usually slower acting—taking care of the internal environment of the body, maintaining homeostasis, and controlling reproduction (Table 12.1.1). So how does the fight-or-flight response that was mentioned earlier happen so quickly if hormones are usually slower acting? It is because the two systems are connected. It is the fast action of the nervous system in response to the danger in the environment that stimulates the adrenal glands to secrete their hormones. As a result, the nervous system can cause rapid endocrine responses to keep up with sudden changes in both the external and internal environments when necessary.

Table 12.1.1: Endocrine and Nervous Systems

	Endocrine system	Nervous system
Signaling mechanism(s)	Chemical	Chemical/electrical
Primary chemical signal	Hormones	Neurotransmitters
Distance traveled	Long or short	Always short
Response time	Fast or slow	Always fast
Environment targeted	Internal	Internal and external

Structures of the Endocrine System

The endocrine system consists of cells, tissues, and organs that secrete hormones as a primary or secondary function. The endocrine gland is the major player in this system. An **endocrine gland** secretes its hormones directly into the surrounding fluid, such as plasma in blood, which will transport the hormones throughout the body. Endocrine glands do not use ducts. This is in contrast to an exocrine gland which secretes its contents into ducts which then carry the contents to the target cells. Exocrine glands will be discussed further in the digestive system chapter. The endocrine system includes the pituitary, thyroid, parathyroid, adrenal, and pineal glands (Figure 12.1.1). Some of these glands have both endocrine and non-endocrine functions. For example, the pancreas contains cells that function in digestion (known as the **exocrine pancreas**) as well as cells that secrete the hormones insulin and glucagon (known as the **endocrine pancreas**), which regulate blood glucose levels. The hypothalamus, thymus, heart, kidneys, stomach, small intestine, liver, skin, ovaries, and testes are other organs that contain cells with endocrine function. Moreover, adipose tissue has long been known to produce hormones, and recent research has revealed that even bone tissue has endocrine functions.

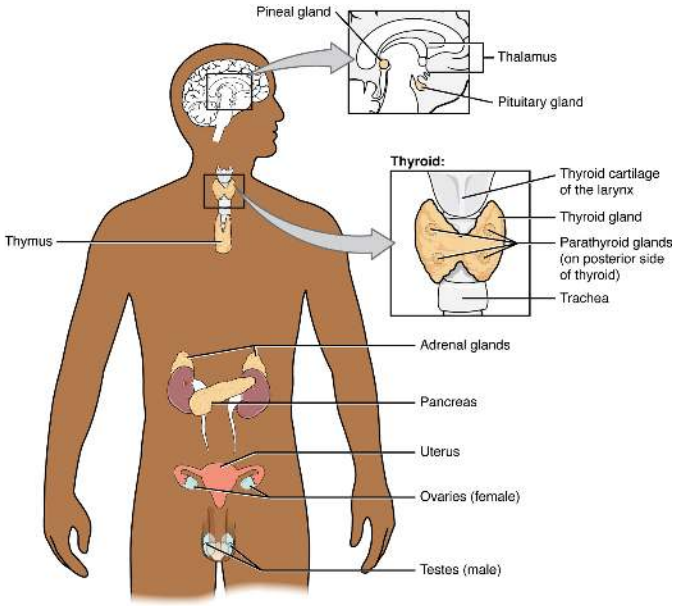


Figure 12.1.1 Endocrine System: Endocrine glands and cells are located throughout the body and play an important role in homeostasis.

Other Types of Chemical Signaling

In endocrine signaling, hormones secreted into the extracellular fluid diffuse into the blood or lymph, and can then travel great distances throughout the body. In contrast, autocrine signaling takes place within the same cell. An autocrine (auto- = "self") is a chemical that elicits a response in the same cell that secreted it. Interleukin-1, or IL-1, is a signaling molecule that plays an important role in inflammatory response. The cells that secrete IL-1 have receptors on their cell surface that bind these molecules, resulting in autocrine signaling.

Local intercellular communication is the province of the paracrine, also called a paracrine factor, which is a chemical that induces a response in neighboring cells. Although paracrines may enter the bloodstream, their concentration is generally too low to elicit a response from distant tissues. A familiar example to those with asthma is histamine, a paracrine that is released by immune cells in the bronchial tree. Histamine causes the smooth muscle cells of the bronchi to constrict, narrowing the airways. Another example is the neurotransmitters of the nervous system, which act only locally within the synaptic cleft.

Career Connection

Endocrinologist

Endocrinology is a specialty in the field of medicine that focuses on the treatment of endocrine system disorders. Endocrinologists—medical doctors who specialize in this field—are experts in treating diseases associated with hormonal

systems, ranging from thyroid disease to diabetes mellitus. Endocrine surgeons treat endocrine disease through the removal, or resection, of the affected endocrine gland.

Patients who are referred to endocrinologists may have signs and symptoms or blood test results that suggest excessive or impaired functioning of an endocrine gland or endocrine cells. The endocrinologist may order additional blood tests to determine whether the patient's hormonal levels are abnormal, or they may stimulate or suppress the function of the suspect endocrine gland and then have blood taken for analysis. Treatment varies according to the diagnosis. Some endocrine disorders, such as type 2 diabetes, may respond to lifestyle changes such as modest weight loss, adoption of a healthy diet, and regular physical activity. Other disorders may require medication, such as hormone replacement, and routine monitoring by the endocrinologist. These include disorders of the pituitary gland that can affect growth and disorders of the thyroid gland that can result in a variety of metabolic problems.

Some patients experience health problems as a result of the normal decline in hormones that can accompany aging. These patients can consult with an endocrinologist to weigh the risks and benefits of hormone replacement therapy intended to boost their natural levels of reproductive hormones.

In addition to treating patients, endocrinologists may be involved in research to improve the understanding of endocrine system disorders and develop new treatments for these diseases.

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12.2: Hormones

Learning Objectives

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

- Identify the three major classes of hormones on the basis of chemical structure
- Compare and contrast intracellular and cell membrane hormone receptors
- Identify several factors that influence a target cell's response
- Discuss the role of feedback loops and humoral, hormonal, and neural stimuli in hormone control

Although a given hormone may travel throughout the body in the bloodstream, it will affect the activity only of its target cells; it can only bind to cells that have receptors specifically for that hormone. Once the hormone binds to its specific receptor, a chain of events is initiated that leads to the target cell's response. Hormones play a critical role in the regulation of physiological processes because of the target cell responses they regulate. These responses contribute to human reproduction, growth and development of body tissues, metabolism, fluid, and electrolyte balance, sleep, and many other body functions. The major hormones of the human body and their effects are identified in Table 12.2.1.

Table 12.2.1: Endocrine Glands and Their Major Hormones

Endocrine gland	Associated hormones	Chemical class	Effect
Pituitary (anterior)	Growth hormone (GH)	Protein	Promotes growth of body tissues
Pituitary (anterior)	Prolactin (PRL)	Peptide	Promotes milk production
Pituitary (anterior)	Thyroid-stimulating hormone (TSH)	Glycoprotein	Stimulates thyroid hormone release
Pituitary (anterior)	Adrenocorticotropic hormone (ACTH)	Peptide	Stimulates hormone release by adrenal cortex
Pituitary (anterior)	Follicle-stimulating hormone (FSH)	Glycoprotein	Stimulates gamete production
Pituitary (anterior)	Luteinizing hormone (LH)	Glycoprotein	Stimulates androgen production by gonads
Pituitary (posterior)	Antidiuretic hormone (ADH)	Peptide	Stimulates water reabsorption by kidneys
Pituitary (posterior)	Oxytocin	Peptide	Stimulates uterine contractions during childbirth
Thyroid	Thyroxine (T_4), triiodothyronine (T_3)	Amine	Stimulate basal metabolic rate
Thyroid	Calcitonin	Peptide	Reduces blood Ca^{2+} levels
Parathyroid	Parathyroid hormone (PTH)	Peptide	Increases blood Ca^{2+} levels
Adrenal (cortex)	Aldosterone	Steroid	Increases blood Na^{+} levels
Adrenal (cortex)	Cortisol, corticosterone, cortisone	Steroid	Increase blood glucose levels
Adrenal (medulla)	Epinephrine, norepinephrine	Amine	Stimulate fight-or-flight response
Pineal	Melatonin	Amine	Regulates sleep cycles
Pancreas	Insulin	Protein	Reduces blood glucose levels

Endocrine gland	Associated hormones	Chemical class	Effect
Pancreas	Glucagon	Protein	Increases blood glucose levels
Testes	Testosterone	Steroid	Stimulates development of sex characteristics including a deeper voice, increased muscle mass, development of body hair, and sperm production
Ovaries	Estrogens and progesterone	Steroid	Stimulate development of sex characteristics including the development of adipose and breast tissue, and prepare the body for childbirth

Types of Hormones

The hormones of the human body can be divided into two major groups on the basis of their chemical structure. Hormones derived from amino acids include amines, peptides, and proteins. Those derived from lipids include steroids (Figure 12.2.1). These chemical groups affect a hormone's distribution, the type of receptors it binds to, and other aspects of its function.

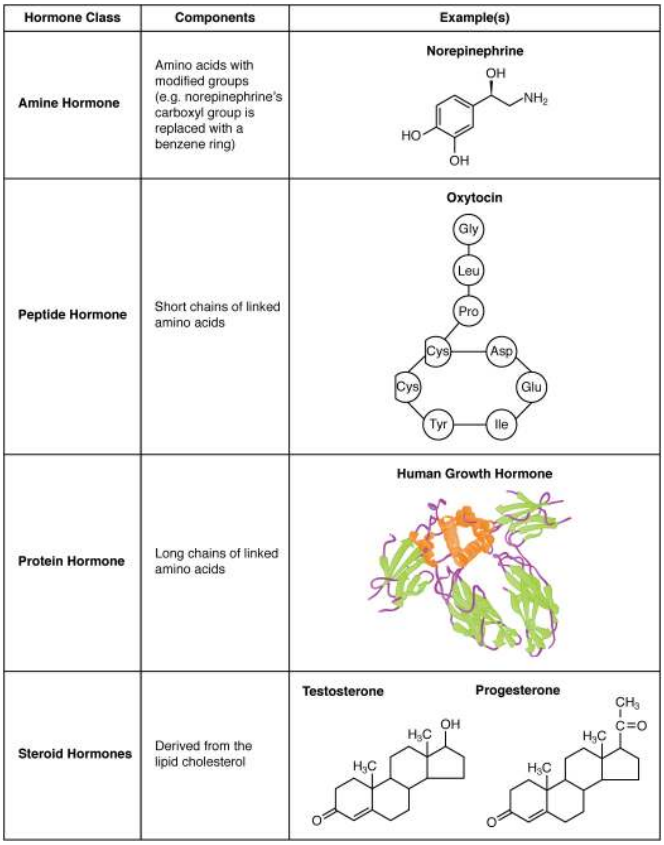


Figure 12.2.1: Amine, Peptide, Protein, and Steroid Hormone Structure

Amine, Peptide and Protein Hormones

Hormones derived from the modification of amino acids are referred to as **amine hormones**. **Peptide and protein hormones** consist of multiple amino acids that link to form an amino acid chain. Protein hormones consist of longer chains of amino acids than peptide hormones. Examples of peptide hormones include antidiuretic hormone (ADH), a pituitary hormone important in fluid balance and an example of a protein hormones is growth hormone, produced by the pituitary gland.

Amine hormones are synthesized from the amino acids tryptophan or tyrosine. An example of a hormone derived from tryptophan is melatonin, which is secreted by the pineal gland and helps regulate circadian rhythm. Tyrosine derivatives include the metabolism-regulating thyroid hormones. Examples of peptide hormones include antidiuretic hormone (ADH), a pituitary hormone important in fluid balance and an example of a protein hormones is growth hormone, produced by the pituitary gland.

Most amine and peptide/protein hormones are **hydrophilic** and thus are water-soluble, however, the thyroid hormones are an exception. T4 (thyroxine) and T3 (triiodothyronine) are amine hormones of the thyroid gland that are hydrophobic. Hydrophilic hormones are readily transported through the blood due to their water-soluble nature.

Steroid Hormones

The primary hormones derived from lipids are steroids. **Steroid hormones** are derived from the lipid cholesterol. For example, the reproductive hormones testosterone and the estrogens—which are produced by the gonads (testes and ovaries)—are steroid hormones. The adrenal glands produce the steroid hormone aldosterone, which is involved in osmoregulation, and cortisol, which plays a role in metabolism.

Like cholesterol, steroid hormones are not soluble in water (they are **hydrophobic**). Because blood is water-based, lipid-derived hormones must travel to their target cell bound to a transport protein.

Pathways of Hormone Action

The message a hormone sends is received by a hormone receptor, a protein located either inside the cell or within the cell membrane. The receptor will process the message by initiating other signaling events or cellular mechanisms that result in the target cell's response. Hormone receptors recognize molecules with specific shapes and side groups, and respond only to those hormones that are recognized. The same type of receptor may be located on cells in different body tissues, and trigger somewhat different responses. Thus, the response triggered by a hormone depends not only on the hormone, but also on the target cell.

Once the target cell receives the hormone signal, it can respond in a variety of ways. The response may include the stimulation of protein synthesis, activation or deactivation of enzymes, alteration in the permeability of the cell membrane, altered rates of mitosis and cell growth, and stimulation of the secretion of products. Moreover, a single hormone may be capable of inducing different responses in a given cell.

Pathways Involving Intracellular Hormone Receptors

Intracellular (intra = inside, cellular = cell) hormone receptors are located inside the cell. Hormones that bind to this type of receptor must be able to cross the cell membrane. Steroid hormones are derived from cholesterol and therefore can readily diffuse through the lipid bilayer of the cell membrane to reach the intracellular receptor (Figure 12.2.2). Thyroid hormones cross the cell membrane by a specific carrier-mediated mechanism that is energy and Na^+ dependent.

The location of steroid and thyroid hormone binding differs slightly: a steroid hormone may bind to its receptor within the cytosol or within the nucleus. In either case, this binding generates a hormone-receptor complex that binds to a particular segment of the cell's DNA in the nucleus. In contrast, thyroid hormones directly bind to receptors already bound to DNA. For both steroid and thyroid hormones, binding of the hormone-receptor complex with DNA triggers transcription of a target gene to messenger RNA (mRNA), which moves to the cytosol and directs protein synthesis by ribosomes.

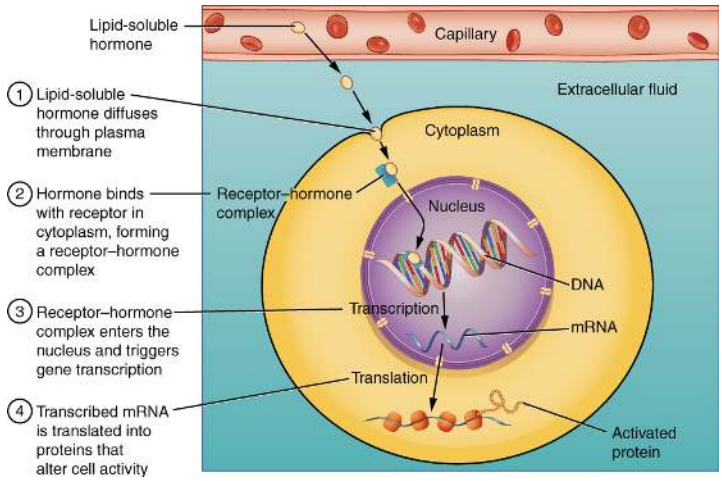


Figure 12.2.2: Binding of Lipid-Soluble Hormones A steroid hormone directly initiates the production of proteins within a target cell. Steroid hormones easily diffuse through the cell membrane. The hormone binds to its receptor in the cytosol, forming a receptor–hormone complex. The receptor–hormone complex then enters the nucleus and binds to the target gene on the DNA. Transcription of the gene creates a messenger RNA that is translated into the desired protein within the cytoplasm.

Pathways Involving Cell Membrane Hormone Receptors

Hydrophilic, or water-soluble, hormones are unable to diffuse through the lipid bilayer of the cell membrane and must therefore pass on their message to a receptor located at the surface of the cell (cell membrane). Except for thyroid hormones, which are lipid-soluble, all amino acid–derived hormones bind to cell membrane receptors that are located, at least in part, on the extracellular (outside) surface of the cell membrane. Therefore, they do not directly affect the transcription of target genes, but instead initiate a signaling cascade that is carried out by a molecule called a second messenger. In this case, the hormone is called a first messenger. The second messenger interacts with proteins within the cell that ultimately activate the targeted cellular response.

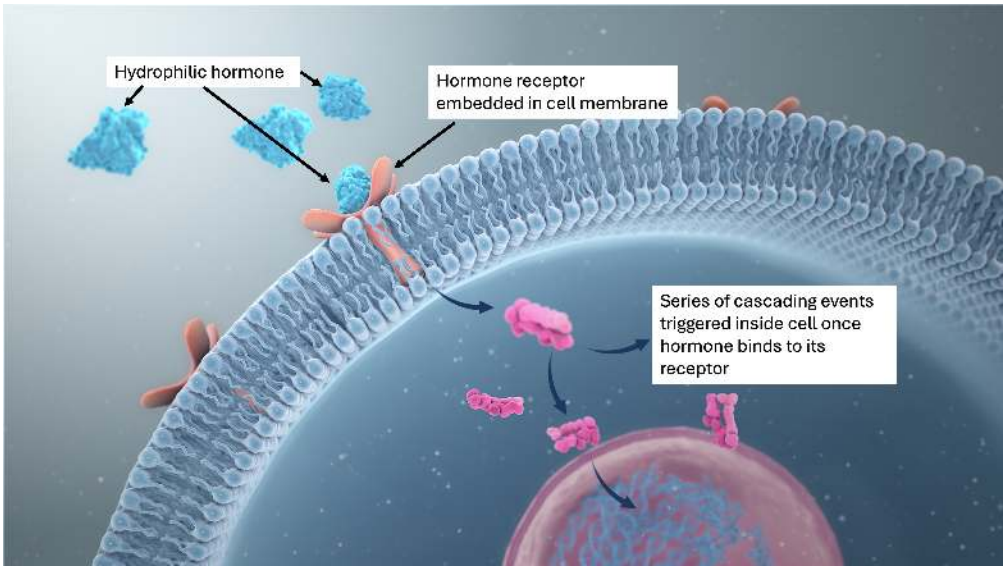


Figure 12.2.3 Hydrophilic Hormones: Since hydrophilic hormones cannot cross the cell membrane, they must bind to receptors located on the cell surface. Once the hydrophilic hormone binds to its receptor, this initiates a series of cascading events inside the cell that will then lead to the target action such as protein synthesis, activation of enzymes, etc. *(Image credit: "Signal Transduction" by Harmony Folse is licensed under CC BY-NC-SA 4.0, modification of original by Scientific Animations.)*

Factors Affecting Target Cell Response

You will recall that target cells must have receptors specific to a given hormone if that hormone is to trigger a response. But several other factors influence the target cell response. For example, the presence of a significant level of a hormone circulating in the

bloodstream can cause its target cells to decrease their number of receptors for that hormone. This process is called **downregulation**, and it allows cells to become less reactive to the excessive hormone levels. When the level of a hormone is chronically reduced, target cells engage in **upregulation** to increase their number of receptors. This process allows cells to be more sensitive to the hormone that is present. Cells can also alter the sensitivity of the receptors themselves to various hormones.

Regulation of Hormone Secretion

To prevent abnormal hormone levels and a potential disease state, hormone levels must be tightly controlled. The body maintains this control by balancing hormone production and degradation. Feedback loops govern the initiation and maintenance of most hormone secretion in response to various stimuli.

Role of Feedback Loops

The contribution of feedback loops to homeostasis will only be briefly reviewed here. Positive feedback loops are characterized by the release of additional hormone in response to an original hormone release. The release of oxytocin during childbirth is a positive feedback loop. The initial release of oxytocin begins to signal the uterine muscles to contract, which pushes the fetus toward the cervix, causing it to stretch. This, in turn, signals the pituitary gland to release more oxytocin, causing labor contractions to intensify. The release of oxytocin decreases after the birth of the child.

The more common method of hormone regulation is the **negative feedback loop**. Negative feedback is characterized by the inhibition of further secretion of a hormone in response to adequate levels of that hormone. This allows blood levels of the hormone to be regulated within a narrow range. An example of a negative feedback loop is the release of glucocorticoid hormones (such as cortisol) from the adrenal glands, as directed by the hypothalamus and pituitary gland. As glucocorticoid concentrations in the blood rise, the hypothalamus and pituitary gland reduce their signaling to the adrenal glands to prevent additional glucocorticoid secretion (Figure 12.2.4).

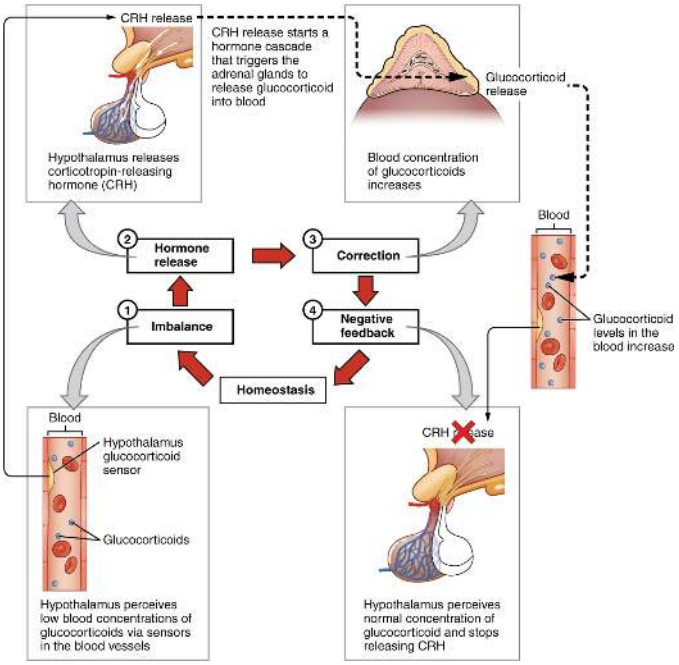


Figure 12.2.4 Negative Feedback Loop: The release of adrenal glucocorticoids is stimulated by the release of hormones from the hypothalamus and pituitary gland. This signaling is inhibited when glucocorticoid levels become elevated by causing negative signals to the pituitary gland and hypothalamus.

Role of Endocrine Gland Stimuli

Reflexes triggered by both chemical and neural stimuli control endocrine activity. These reflexes may be simple, involving only one hormone response, or they may be more complex and involve many hormones, as is the case with the hypothalamic control of various anterior pituitary–controlled hormones.

Humoral stimuli are changes in blood levels of non-hormone chemicals, such as nutrients or ions, which cause the release or inhibition of a hormone to, in turn, maintain homeostasis. For example, osmoreceptors in the hypothalamus detect changes in blood osmolarity (the concentration of solutes in the blood plasma). If blood osmolarity is too high, meaning that the blood is not dilute enough, osmoreceptors signal the hypothalamus to release antidiuretic hormone (ADH). ADH causes the kidneys to reabsorb more water and reduce the volume of urine produced. This reabsorption causes a reduction of the osmolarity of the blood, returning more water to the blood, thus diluting the blood to the appropriate level. The regulation of blood glucose is another example. High blood glucose levels cause the release of insulin from the pancreas, which increases glucose uptake by cells and liver storage of glucose as glycogen.

An endocrine gland may also secrete a hormone in response to the presence of another hormone produced by a different endocrine gland. Such **hormonal stimuli** often involve the hypothalamus, which produces releasing and inhibiting hormones that control the secretion of a variety of pituitary hormones.

In addition to these chemical signals, hormones can also be released in response to **neural stimuli**. A common example of neural stimuli is the activation of the fight-or-flight response by the sympathetic nervous system. When an individual perceives danger, sympathetic neurons signal the adrenal glands to secrete norepinephrine and epinephrine. The two hormones dilate blood vessels, increase the heart and respiratory rate, and suppress the digestive and immune systems. These responses boost the body's transport of oxygen to the brain and muscles, thereby improving the body's ability to fight or flee.

Everyday Connection

Bisphenol A and Endocrine Disruption

You may have heard news reports about the effects of a chemical called bisphenol A (BPA) in various types of food packaging. BPA is used in the manufacturing of hard plastics and epoxy resins. Common food-related items that may contain BPA include the lining of aluminum cans, plastic food-storage containers, drinking cups, as well as baby bottles and "sippy" cups. Other uses of BPA include medical equipment, dental fillings, and the lining of water pipes.

Research suggests that BPA is an endocrine disruptor, meaning that it negatively interferes with the endocrine system, particularly during the prenatal and postnatal development period. In particular, BPA mimics the hormonal effects of estrogens and has the opposite effect—that of androgens. The U.S. Food and Drug Administration (FDA) notes in their statement about BPA safety that although traditional toxicology studies have supported the safety of low levels of exposure to BPA, recent studies using novel approaches to test for subtle effects have led to some concern about the potential effects of BPA on the brain, behavior, and prostate gland in fetuses, infants, and young children. The FDA is currently facilitating decreased use of BPA in food-related materials. Many US companies have voluntarily removed BPA from baby bottles, "sippy" cups, and the linings of infant formula cans, and most plastic reusable water bottles sold today boast that they are "BPA free." In contrast, both Canada and the European Union have completely banned the use of BPA in baby products.

The potential harmful effects of BPA have been studied in both animal models and humans and include a large variety of health effects, such as developmental delay and disease. For example, prenatal exposure to BPA during the first trimester of human pregnancy may be associated with wheezing and aggressive behavior during childhood. Adults exposed to high levels of BPA may experience altered thyroid signaling and male sexual dysfunction. BPA exposure during the prenatal or postnatal period of development in animal models has been observed to cause neurological delays, changes in brain structure and function, sexual dysfunction, asthma, and increased risk for multiple cancers. In vitro studies have also shown that BPA exposure causes molecular changes that initiate the development of cancers of the breast, prostate, and brain. Although these studies have implicated BPA in numerous ill health effects, some experts caution that some of these studies may be flawed and that more research needs to be done. In the meantime, the FDA recommends that consumers take precautions to limit their exposure to BPA. In addition to purchasing foods in packaging free of BPA, consumers should avoid carrying or storing foods or liquids in bottles with the recycling code 3 or 7. Foods and liquids should not be microwave-heated in any form of plastic: use paper, glass, or ceramics instead.

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12.3: The Pituitary Gland and Hypothalamus

Learning Objectives

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

- Explain the interrelationships of the anatomy and functions of the hypothalamus and the posterior and anterior lobes of the pituitary gland
- Identify the two hormones released from the posterior pituitary, their target cells, and their principal actions
- Identify the six hormones produced by the anterior lobe of the pituitary gland, their target cells, their principal actions, and their regulation by the hypothalamus

The hypothalamus–pituitary complex can be thought of as the "command center" of the endocrine system. This complex secretes several hormones that directly produce responses in target tissues, as well as hormones that regulate the synthesis and secretion of hormones of other glands. In addition, the hypothalamus–pituitary complex coordinates the messages of the endocrine and nervous systems. In many cases, a stimulus received by the nervous system must pass through the hypothalamus–pituitary complex to be translated into hormones that can initiate a response.

The hypothalamus is a structure of the diencephalon of the brain located anterior and inferior to the thalamus (Figure 12.3.1). It has both neural and endocrine functions, producing and secreting many hormones. In addition, the hypothalamus is anatomically and functionally related to the pituitary gland (or hypophysis), a bean-sized organ suspended from it by a stem called the infundibulum (or pituitary stalk). The pituitary gland is cradled within the sphenoid bone of the skull. It consists of two lobes that arise from distinct parts of embryonic tissue: the **posterior pituitary** (neurohypophysis) is neural tissue, whereas the **anterior pituitary** (also known as the adenohypophysis) is glandular tissue. The hormones secreted by the posterior and anterior pituitary are summarized in Table 12.3.1.

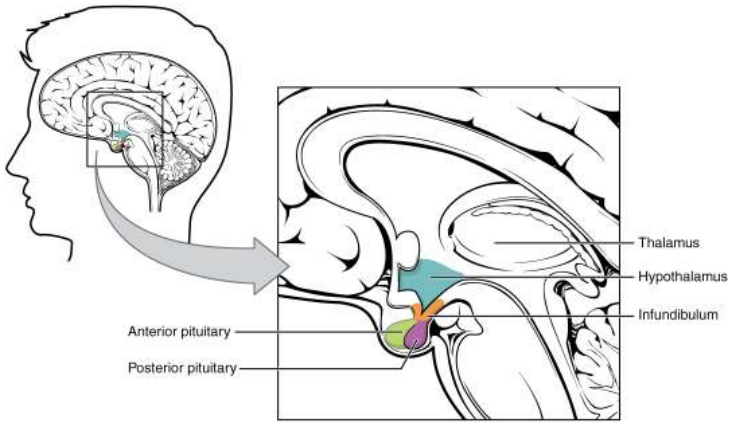


Figure 12.3.1: Hypothalamus–Pituitary Complex The hypothalamus region lies inferior and anterior to the thalamus. It connects to the pituitary gland by the stalk-like infundibulum. The pituitary gland consists of an anterior and posterior lobe, with each lobe secreting different hormones in response to signals from the hypothalamus.

Table 12.3.1: The hormones secreted by the posterior and anterior pituitary

Pituitary lobe	Associated hormones	Chemical class	Effect
Anterior	Growth hormone (GH)	Protein	Promotes growth of body tissues
Anterior	Prolactin (PRL)	Peptide	Promotes milk production from mammary glands
Anterior	Thyroid-stimulating hormone (TSH)	Glycoprotein	Stimulates thyroid hormone release from thyroid

Pituitary lobe	Associated hormones	Chemical class	Effect
Anterior	Adrenocorticotropic hormone (ACTH)	Peptide	Stimulates hormone release by adrenal cortex
Anterior	Follicle-stimulating hormone (FSH)	Glycoprotein	Stimulates gamete production in gonads
Anterior	Luteinizing hormone (LH)	Glycoprotein	Stimulates androgen production by gonads
Posterior	Antidiuretic hormone (ADH)	Peptide	Stimulates water reabsorption by kidneys
Posterior	Oxytocin	Peptide	Stimulates uterine contractions during childbirth

Posterior Pituitary

The posterior pituitary is actually an extension of neurons from the hypothalamus. The cell bodies of these neurons rest in the hypothalamus, but their axons descend as the hypothalamic–hypophyseal tract within the infundibulum, and end in axon terminals that comprise the posterior pituitary (Figure 12.3.2).

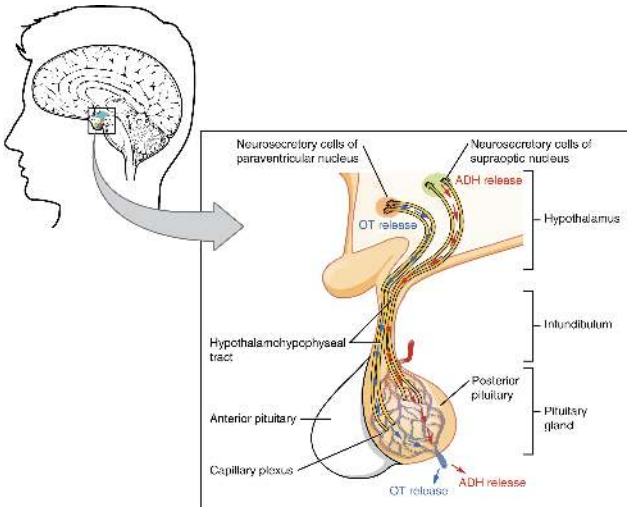


Figure 12.3.2: Posterior Pituitary. The paraventricular and supraoptic regions are regions in the hypothalamus where neurons that then extend into the posterior pituitary originate. Neurosecretory cells in the hypothalamus release oxytocin (OT) or ADH into the posterior lobe of the pituitary gland. These hormones are stored or released into the blood via the capillary plexus.

The posterior pituitary gland does not produce hormones, but rather stores and secretes hormones produced by the hypothalamus. The paraventricular nuclei produce the hormone oxytocin, whereas the supraoptic nuclei produce ADH. These hormones travel along the axons into storage sites in the axon terminals of the posterior pituitary. In response to signals from the same hypothalamic neurons, the hormones are released from the axon terminals into the bloodstream.

Antidiuretic Hormone (ADH)

The solute concentration of the blood, or blood osmolarity, may change in response to the consumption of certain foods and fluids, as well as in response to disease, injury, medications, or other factors. Blood osmolarity is constantly monitored by osmoreceptors —specialized cells within the hypothalamus that are particularly sensitive to the concentration of sodium ions and other solutes.

In response to high blood osmolarity, which can occur during dehydration or following a very salty meal, the osmoreceptors signal the posterior pituitary to release antidiuretic hormone (ADH). The target cells of ADH are located in the tubular cells of the kidneys. Its effect is to increase water reabsorption. The more water reabsorbed from the filtrate in the kidney tubules, the greater the amount of water that is returned to the blood and the less that is excreted in the urine. A greater concentration of water results in a reduced concentration of solutes in the blood. ADH is also known as vasopressin because, in very high concentrations, it causes

constriction of blood vessels, which increases blood pressure by increasing peripheral resistance. The release of ADH is controlled by a negative feedback loop. As blood osmolarity decreases, the hypothalamic osmoreceptors sense the change and prompt a corresponding decrease in the secretion of ADH. As a result, less water is reabsorbed from the urine filtrate.

Interestingly, drugs can affect the secretion of ADH. For example, alcohol consumption inhibits the release of ADH, resulting in increased urine production that can eventually lead to dehydration and a hangover. A disease called diabetes insipidus is characterized by chronic underproduction of ADH that causes chronic dehydration. Because little ADH is produced and secreted, not enough water is reabsorbed by the kidneys. Although patients feel thirsty, and increase their fluid consumption, this doesn't effectively decrease the solute concentration in their blood because ADH levels are not high enough to trigger water reabsorption in the kidneys. Electrolyte imbalances can occur in severe cases of diabetes insipidus.

Anterior Pituitary

Recall that the posterior pituitary does not synthesize hormones, but merely stores them. In contrast, **the anterior pituitary does manufacture hormones.** However, the secretion of hormones from the anterior pituitary is regulated by two classes of hormones. These hormones—secreted by the hypothalamus—are the **releasing hormones** that stimulate the secretion of hormones from the anterior pituitary and the **inhibiting hormones** that inhibit secretion.

Hypothalamic hormones are secreted by neurons, but enter the anterior pituitary through blood vessels (Figure 12.3.3). Within the infundibulum is a bridge of capillaries that connects the hypothalamus to the anterior pituitary. This network, called the **hypophyseal portal system**, allows hypothalamic hormones to be transported to the anterior pituitary without first entering the systemic circulation (that is, the circulation to the rest of the body).

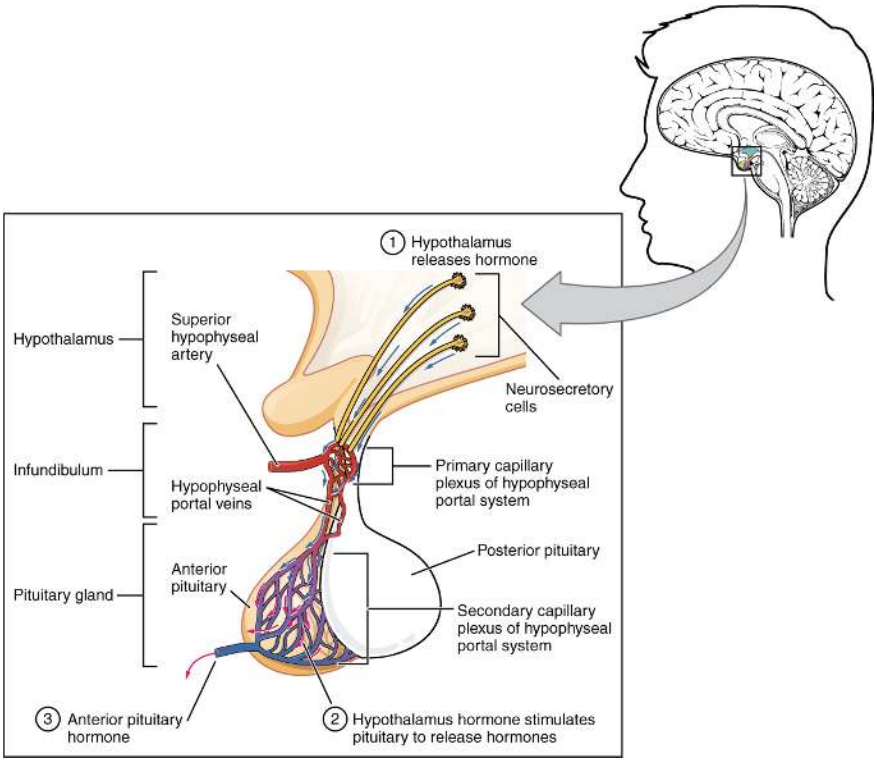


Figure 12.3.3: Anterior Pituitary The anterior pituitary manufactures seven hormones. The hypothalamus produces separate hormones that stimulate or inhibit hormone production in the anterior pituitary. Hormones from the hypothalamus reach the anterior pituitary via the hypophyseal portal system.

The anterior pituitary produces seven hormones. These are the growth hormone (GH), thyroid-stimulating hormone (TSH), adrenocorticotropic hormone (ACTH), follicle-stimulating hormone (FSH), luteinizing hormone (LH), beta endorphin, and prolactin. Of the hormones of the anterior pituitary, TSH, ACTH, FSH, and LH are collectively referred to as tropic hormones (trope- = "turning") because they turn on or off the function of other endocrine glands. Another way to think of tropic hormones are that they are hormones that affect the release of other hormones from other glands.

Tiers of Control

The hypothalamus and anterior pituitary gland control the release of hormones from other glands via **tier control**. There are three tiers of control which ultimately lead to the release of a target hormone from its gland. A stimuli will triggers the hypothalamus to release a hormone.

The tiers of control function as follows:

1. At the **first tier of control**, we find the hypothalamus. In response to a stimuli, the hypothalamus secretes a hormone to the second tier of control, the anterior pituitary gland.
2. At the **second tier of control**, the anterior pituitary gland responds to the hypothalamic hormone by secreting a hormone to the third tier of control, the target gland.
3. At the **third tier of control**, the target gland binds the hormone from the anterior pituitary gland. The target gland will then secrete it's specific hormone that will then have a variety of effects on the body to maintain homeostasis.

Growth Hormone

The endocrine system regulates the growth of the human body, protein synthesis, and cellular replication. A major hormone involved in this process is **growth hormone (GH)**, also called somatotropin—a protein hormone produced and secreted by the anterior pituitary gland. Its primary function is anabolic; it promotes protein synthesis and tissue building through direct and indirect mechanisms (Figure 12.3.4). GH levels are controlled by the release of growth hormone releasing hormone (**GHRH**) and growth hormone inhibiting hormone (**GHIH**), also known as somatostatin, from the hypothalamus.

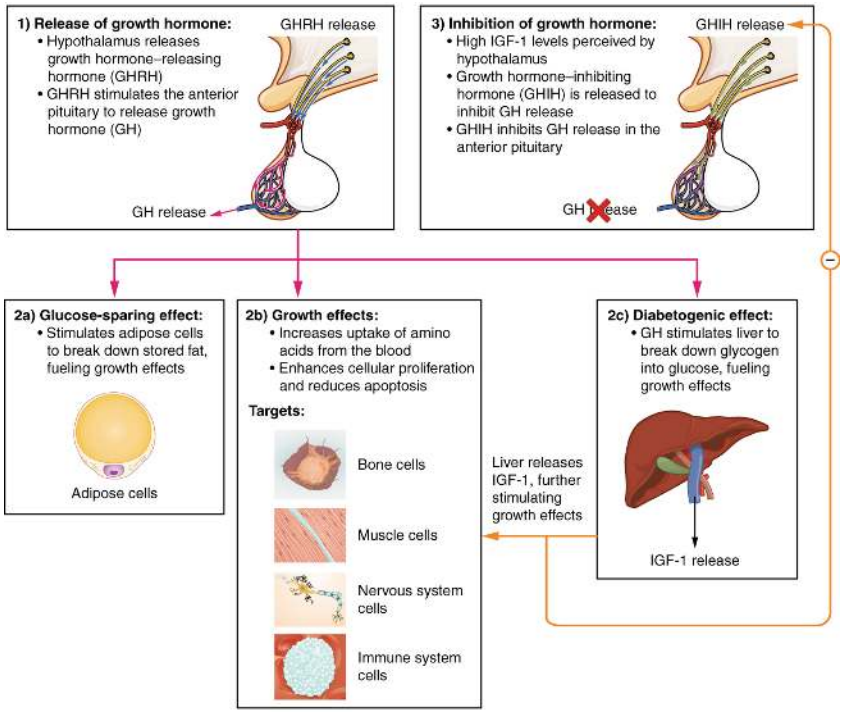


Figure 12.3.4: Hormonal Regulation of Growth Growth hormone (GH) directly accelerates the rate of protein synthesis in skeletal muscle and bones. Insulin-like growth factor 1 (IGF-1) is activated by growth hormone and indirectly supports the formation of new proteins in muscle cells and bone.

A glucose-sparing effect occurs when GH stimulates lipolysis, or the breakdown of adipose tissue, releasing fatty acids into the blood. As a result, many tissues switch from glucose to fatty acids as their main energy source, which means that less glucose is taken up from the bloodstream (hence, glucose *sparing*).

GH also initiates the diabetogenic effect in which GH stimulates the liver to break down glycogen to glucose, which is then deposited into the blood. The name “diabetogenic” is derived from the similarity in elevated blood glucose levels observed between individuals with untreated diabetes mellitus and individuals experiencing GH excess. Blood glucose levels rise as the result of a combination of glucose-sparing and diabetogenic effects.

GH indirectly mediates growth and protein synthesis by triggering the liver and other tissues to produce a group of proteins called **insulin-like growth factors** (IGFs). These proteins enhance cellular proliferation and inhibit apoptosis, or programmed cell death. IGFs stimulate cells to increase their uptake of amino acids from the blood for protein synthesis. Skeletal muscle and cartilage cells are particularly sensitive to stimulation from IGFs.

Dysfunction of the endocrine system's control of growth can result in several disorders. For example, **gigantism** is a disorder in children that is caused by the secretion of abnormally large amounts of GH, resulting in excessive growth. The name gigantism is given because individuals are typically very tall. A similar condition in adults is **acromegaly**, a disorder that results in the growth of bones in the face, hands, and feet in response to excessive levels of GH in individuals who have stopped growing. Those with acromegaly do not grow in height. Both people with gigantism and people with acromegaly are at risk of heart failure due to the enlargement of the heart. Abnormally low levels of GH in children can cause growth impairment—a disorder called pituitary dwarfism (also known as growth hormone deficiency).

Thyroid-Stimulating Hormone

The activity of the thyroid gland is regulated by thyroid-stimulating hormone (**TSH**), also called thyrotropin. TSH is released from the anterior pituitary in response to thyrotropin-releasing hormone (**TRH**) from the hypothalamus. As discussed shortly in the chapter on the thyroid gland, it triggers the secretion of thyroid hormones by the thyroid gland. In a classic negative feedback loop, elevated levels of thyroid hormones in the bloodstream then trigger a drop in production of TRH and subsequently TSH.

Adrenocorticotropic Hormone

The adrenocorticotropic hormone (**ACTH**), also called corticotropin, stimulates the **adrenal cortex** to secrete corticosteroid hormones such as **cortisol**.

The release of ACTH is regulated by the corticotropin-releasing hormone (**CRH**) from the hypothalamus in response to normal physiologic rhythms. A variety of stressors can also influence its release, and the role of ACTH in the stress response is discussed later in this chapter.

Follicle-Stimulating Hormone and Luteinizing Hormone

The endocrine glands secrete a variety of hormones that control the development and regulation of the reproductive system (these glands include the anterior pituitary, the adrenal cortex, and the gonads—the testes and the ovaries). Much of the development of the reproductive system occurs during puberty and is marked by the development of sex-specific characteristics in adolescents. Puberty is initiated by gonadotropin-releasing hormone (GnRH), a hormone produced and secreted by the hypothalamus. GnRH stimulates the anterior pituitary to secrete gonadotropins—hormones that regulate the function of the gonads. The levels of GnRH are regulated through a negative feedback loop; high levels of reproductive hormones inhibit the release of GnRH. Throughout life, gonadotropins regulate reproductive function and, in the case of females, the onset and cessation of reproductive capacity.

The gonadotropins include two glycoprotein hormones: follicle-stimulating hormone (FSH) stimulates the production and maturation of sex cells, or gametes, including ova and sperm. FSH also promotes follicular growth; these follicles then release estrogens in ovaries. Luteinizing hormone (LH) triggers ovulation, as well as the production of estrogens and progesterone by the ovaries. LH stimulates production of testosterone by the testes.

Prolactin

As its name implies, prolactin (PRL) promotes lactation (milk production). During pregnancy, it contributes to development of the mammary glands, and after birth, it stimulates the mammary glands to produce breast milk. However, the effects of prolactin depend heavily upon the permissive effects of estrogens, progesterone, and other hormones. And as noted earlier, the let-down of milk occurs in response to stimulation from oxytocin.

In non-pregnant females, prolactin secretion is inhibited by prolactin-inhibiting hormone (PIH), which is actually the neurotransmitter dopamine, and is released from neurons in the hypothalamus. Only during pregnancy do prolactin levels rise in response to prolactin-releasing hormone (PRH) from the hypothalamus.

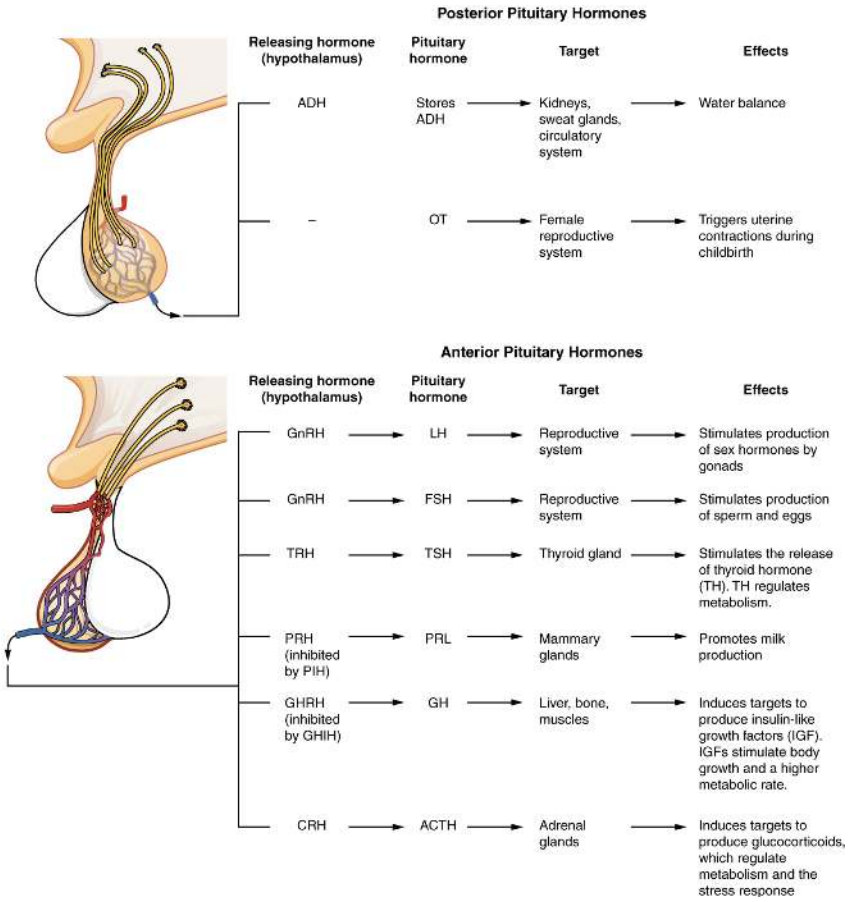


Figure 12.3.5 Major Pituitary Hormones Major pituitary hormones and their target organs.

Interactive Link

https://med.libretexts.org/@go/page/128674



Visit this link to watch an animation showing the role of the hypothalamus and the pituitary gland. Which hormone is released by the pituitary to stimulate the thyroid gland?

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12.4: Thyroid Gland and Parathyroid Glands

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

- Describe the location and anatomy of the thyroid gland
- Identify the hormones produced by the follicular cells and the parafollicular cells of the thyroid
- Describe the location and structure of the parathyroid glands
- Describe the hormonal control of blood calcium levels

Thyroid Gland

The **thyroid gland**, a butterfly-shaped organ, is located anterior to the trachea, just inferior to the larynx (Figure 12.4.1). The medial region, called the isthmus, is flanked by wing-shaped left and right lobes. Each of the thyroid lobes has a pair of parathyroid glands embedded on its posterior surface. The tissue of the thyroid gland is composed mostly of thyroid follicles lined with simple cuboidal epithelium (Figure 12.4.2). The **follicles** are made up of a central cavity filled with a sticky fluid called **colloid**. Surrounded by a wall of epithelial follicle cells, the colloid is the center of thyroid hormone production, and that production is dependent on the essential and unique component of thyroid hormones: iodine.

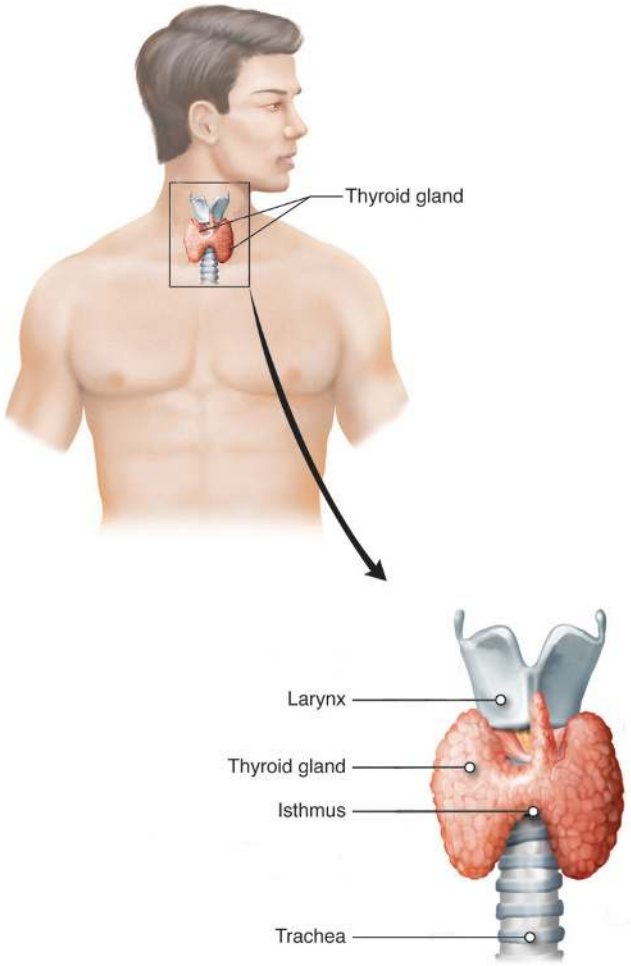


Figure 12.4.1: Thyroid Gland. The thyroid gland is located in the neck where it wraps around the anterior of the trachea just inferior to the thyroid cartilage of the larynx. *(Image Credit: "Thyroid Gland Location" by Gabrielle Spurlock is licensed under CC BY-NC-SA 4.0, modification of original by "KnowledgeWorks - Drawing Thyroid gland and its vascularisation - English labels".)*

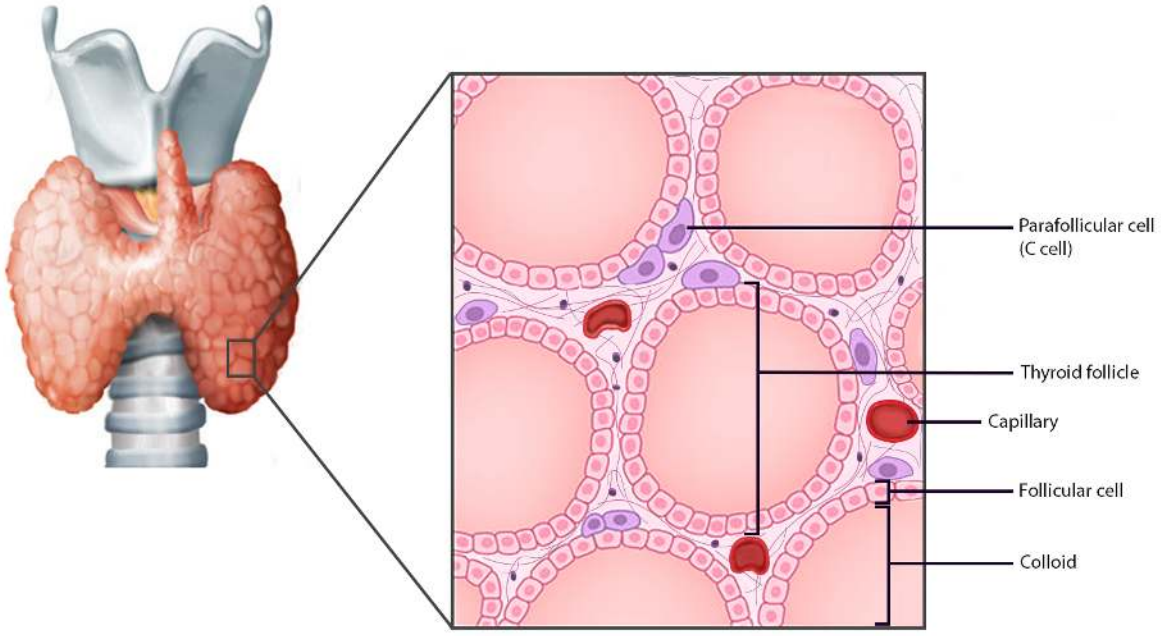


Figure 12.4.2: Thyroid Follicles. Each spherical thyroid follicle contains an external layer of epithelial follicular cells surrounding the colloid. Parafollicular cells are scattered in the connective tissue surrounding the follicles. *(Image Credit: "Thyroid Follicles" by Jennifer Lange is licensed under CC BY-NC-SA 4.0. Includes modification of original by "KnowledgeWorks - Drawing Thyroid gland and its vascularisation - English labels".)*

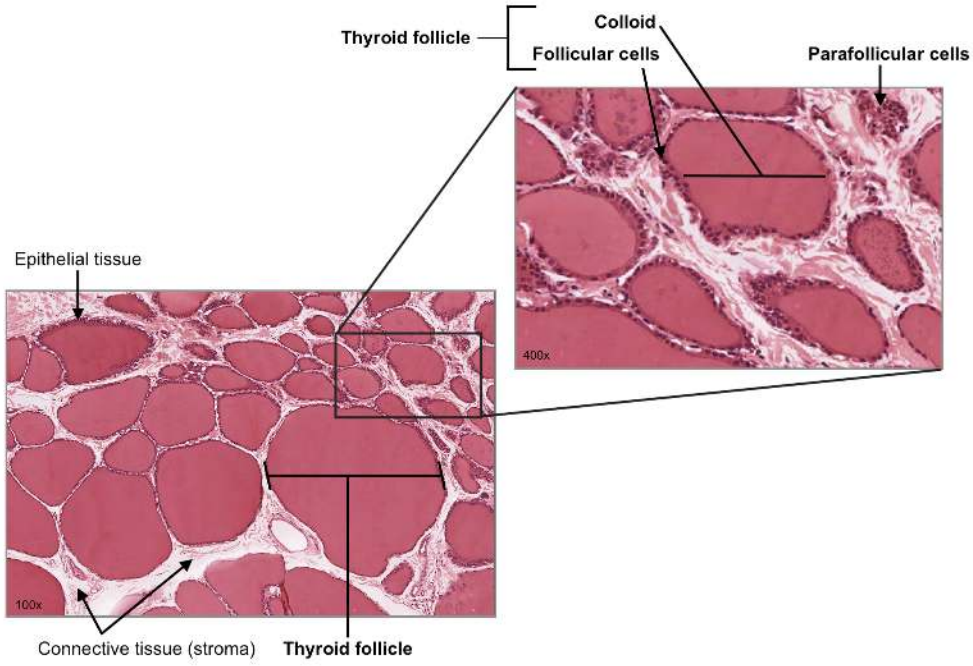


Figure 12.4.3: Thyroid Gland Histology. Visibly, the thyroid gland is dominated by the colloid of the follicles. Higher magnification is needed to clearly see the follicular cells and the parafollicular cells. *(Image credit: "Thyroid Gland Histology" by Jennifer Lange is licensed under CC BY-NC-SA 4.0. Micrograph from Digital Histology is licensed under CC BY-NC-SA 4.0.)*

Thyroid Hormones

Thyroid hormones are produced in the colloid when atoms of the mineral iodine attach to a glycoprotein called thyroglobulin that is secreted into the colloid by the follicle cells. This combination of iodine atoms and thyroglobulin results in the thyroid hormones **triiodothyronine** (T_3) and **thyroxine** (T_4). The 3 and 4 in the names of these hormones refers to how many iodine atoms are present in the hormone.

The release of T_3 and T_4 from the thyroid gland is regulated by hormones from the hypothalamus and anterior pituitary gland.

The tiers of control for release of T_3 and T_4 from the thyroid gland are as follows:

1. The **first tier of control** involves the hypothalamus secreting a hormone to the anterior pituitary gland. In response to a stimulus such as decreasing body temperature or decreased levels of T_3 and T_4, the hypothalamus will secrete the hormone **thyrotropin-releasing hormone (TRH)** to the anterior pituitary gland.
2. At the **second tier of control**, when TRH binds to the anterior pituitary gland, the anterior pituitary gland will respond by secreting **thyroid-stimulating hormone (TSH)** to the thyroid gland.
3. At the **third tier of control**, TSH will bind the thyroid gland. In response to TSH, the thyroid gland has a variety of effects on the body which include:
    - Increased synthesis and release of T_3 and T_4
    - Increased metabolic rate
    - Growth and development of the thyroid gland

Once levels of T_3 and T_4 in the body have increased to an appropriate level, a negative feedback mechanism is turned on to decrease synthesis of T_3 and T_4 so that their levels do not become excessively high. In response to increased levels of T_3 and T_4, the hypothalamus stops secreting TRH, which in turn stops secretion of TSH from the anterior pituitary gland. Without TSH, the thyroid gland will stop synthesizing and releasing T_3 and T_4. T_3 and T_4 levels will drop back down to normal.

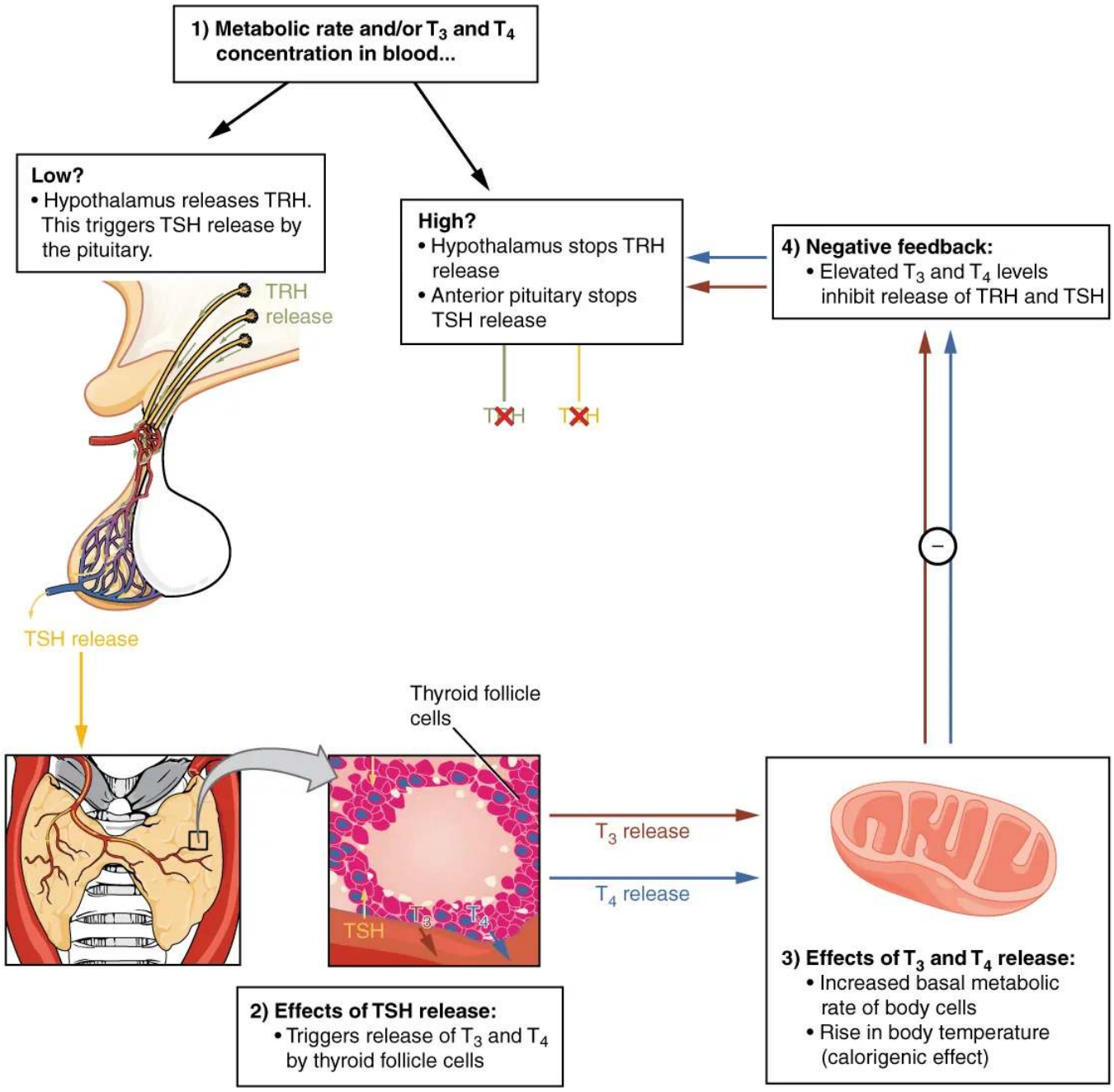


Figure 12.4.4

Regulation of Thyroid Hormones: A classic negative feedback loop controls the regulation of thyroid hormone levels.

DISORDERS OF THE...

Endocrine System: Iodine Deficiency, Hypothyroidism, and Hyperthyroidism

As discussed above, dietary iodine is required for the synthesis of T_3 and T_4. But for much of the world's population, foods do not provide adequate levels of this mineral, because the amount varies according to the level in the soil in which the food was grown, as well as the irrigation and fertilizers used. Marine fish and shrimp tend to have high levels because they concentrate iodine from seawater, but many people in landlocked regions lack access to seafood. Thus, the primary source of dietary iodine in many countries is iodized salt. Fortification of salt with iodine began in the United States in 1924, and international efforts to iodize salt in the world's poorest nations continue today.

Dietary iodine deficiency can result in the impaired ability to synthesize T_3 and T_4, leading to a variety of severe disorders. When T_3 and T_4 cannot be produced, TSH is secreted in increasing amounts. As a result of this hyperstimulation, thyroglobulin accumulates in the thyroid gland follicles, increasing their deposits of colloid. The accumulation of colloid increases the overall size of the thyroid gland, a condition called a goiter (Figure 12.4.4). A goiter is only a visible indication of the deficiency. Other iodine deficiency disorders include impaired growth and development, decreased fertility, and prenatal and infant death. Moreover, iodine deficiency is the primary cause of preventable intellectual disability worldwide. Neonatal hypothyroidism (cretinism) is characterized by cognitive deficits, short stature, and sometimes deafness and muteness in children and adults born to mothers who were iodine-deficient during pregnancy.



Figure 12.4.5: Goiter. A goiter is the abnormal enlargement of the thyroid gland. (*Image credit: "Goiter" by Almazi is licensed under CC BY 4.0*)

In the absence of iodine deficiency, inflammation of the thyroid gland is the more common cause of low blood levels of thyroid hormones. Called hypothyroidism, the condition is characterized by a low metabolic rate, weight gain, cold extremities, constipation, reduced libido, menstrual irregularities, and intellectual disability.

In contrast, hyperthyroidism—an abnormally elevated blood level of thyroid hormones—is often caused by a pituitary or thyroid tumor. In Graves' disease, the hyperthyroid state results from an autoimmune reaction in which antibodies overstimulate the follicle cells of the thyroid gland. Hyperthyroidism can lead to an increased metabolic rate, excessive body heat and sweating, diarrhea, weight loss, tremors, and increased heart rate. The person's eyes may bulge (called exophthalmos) as antibodies produce inflammation in the soft tissues of the orbits.

Calcitonin

The thyroid gland also secretes a hormone called **calcitonin** that is produced by the parafollicular cells (also called clear cells or C cells) that stud the tissue between distinct follicles (Figure 12.4.2 and Figure 12.4.3). Calcitonin is released in response to a rise in blood calcium levels.

The hormones secreted by the thyroid gland are summarized in Table 12.4.1.

Parathyroid Glands

The **parathyroid glands** are tiny, round structures usually found embedded in the posterior surface of the thyroid gland (Figure 12.4.6). A thick connective tissue capsule separates the glands from the thyroid tissue. Most people have four parathyroid glands, but occasionally there are more in tissues of the neck or chest.

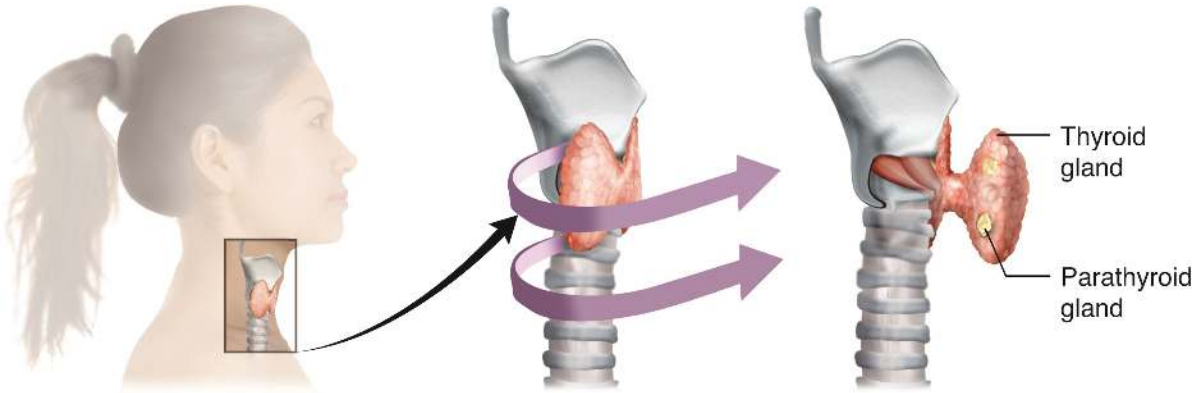


Figure 12.4.6: The Parathyroid Glands. Typically four parathyroid glands are embedded in the posterior surface of the thyroid gland alongside the superior portion of the trachea, two on the left and two on the right, with the superior set just inferior to the cricoid cartilage of the larynx. *(Image credit: "KnowledgeWorks - Drawing Location of the parathyroid glands - English labels" by KnowledgeWorks Global Ltd. is licensed under CC BY.)*

The primary functional cells of the parathyroid glands are the chief cells. These epithelial cells produce and secrete **parathyroid hormone (PTH)**, a major hormone involved in the regulation of blood calcium levels. The effects of PTH on blood calcium levels were previously discussed in 6.4: Bone Remodeling and Calcium Homeostasis. When blood calcium levels drop too low, PTH is released from the parathyroid glands into the bloodstream. Parathyroid hormone encourages the release of stored calcium from the bones and stimulates the kidneys to reabsorb calcium. In bones, PTH inhibits osteoblast activity while stimulating osteoclast activity, resulting in calcium being released from bone matrix into the bloodstream. In the kidneys, PTH stimulates an increase in calcium reabsorption into the bloodstream and also stimulates the release of calcitriol (not to be confused with calcitonin). Calcitriol targets the intestines to stimulate increased absorption of calcium from food. The hormone secreted by the parathyroid glands is summarized in Table 12.4.1.

DISORDERS OF THE...

Endocrine System: Hyperparathyroidism and Hypoparathyroidism

Abnormally high activity of the parathyroid gland can cause **hyperparathyroidism**, a disorder caused by an overproduction of PTH that results in excessive calcium reabsorption from bone. Hyperparathyroidism can significantly decrease bone density, leading to spontaneous fractures or deformities. As blood calcium levels rise, cell membrane permeability to sodium is decreased, and the responsiveness of the nervous system is reduced. At the same time, calcium deposits may collect in the body's tissues and organs, impairing their functioning.

In contrast, abnormally low blood calcium levels may be caused by parathyroid hormone deficiency, called **hypoparathyroidism**, which may develop following injury or surgery involving the thyroid gland. Low blood calcium increases membrane permeability to sodium, resulting in muscle twitching, cramping, spasms, or convulsions. Severe deficits can paralyze muscles, including those involved in breathing, and can be fatal.

Table 12.4.1: Thyroid and Parathyroid Hormones

Associated hormones	Target(s)	Effect(s)	Associated Disorders
Thyroid Hormone: Thyroxine (T_4), triiodothyronine (T_3)	Most body cells	Stimulate basal metabolic rate	Hypothyroidism: goiter Hyperthyroidism: Graves disease
Calcitonin	Bones, kidneys	Reduces blood Ca^{+2} levels; increases Ca^{+2} deposition in bone	Hypersecretion: increased risk of some cancers; renal failure
Parathyroid Hormone	Bones, kidneys	Increases blood Ca^{+2} levels; decreases Ca^{+2} deposition in bone	Hypersecretion: increased risk of fractures, kidney stones, constipation; decreased mental activity and coma.

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12.5: Adrenal Glands

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

- Describe the location and structure of the adrenal glands
- Identify the hormones produced by the adrenal cortex and adrenal medulla, and summarize their target cells and effects

The **adrenal glands**, also known as the suprarenal glands, are wedges of glandular and neuroendocrine tissue adhering to the top of the kidneys by a fibrous capsule of dense connective tissue (Figure 12.5.1). The adrenal glands have a rich blood supply and experience one of the highest rates of blood flow in the body. Adrenal hormones are released into the circulation via the left and right suprarenal veins. The adrenal gland consists of an outer cortex and an inner medulla.

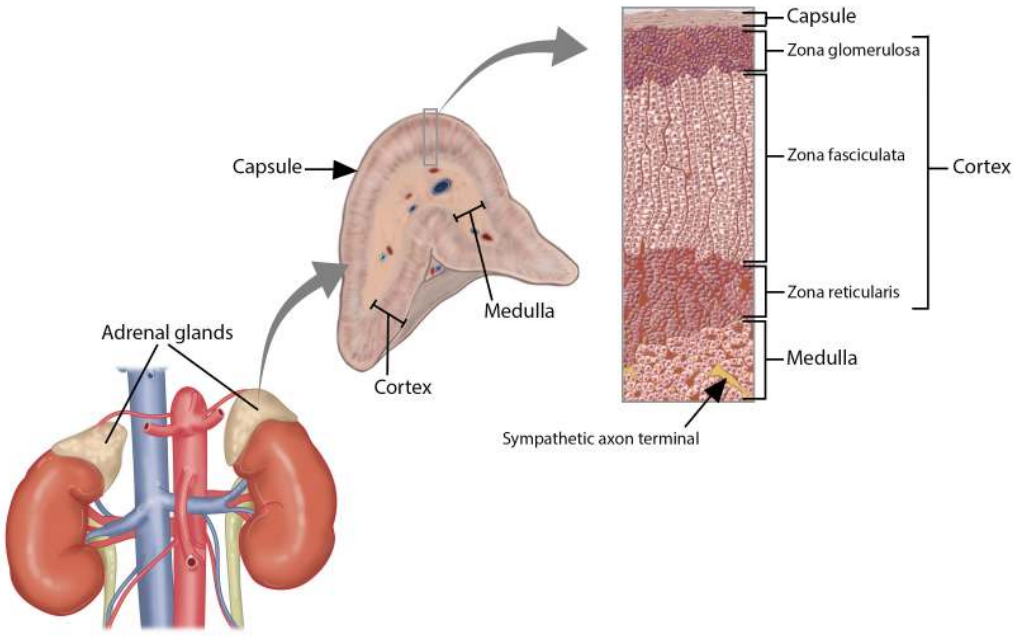


Figure 12.5.1: The Adrenal Glands. Both adrenal glands sit atop the kidneys and are composed of an outer cortex and an inner medulla, all surrounded by a connective tissue capsule. The cortex can be subdivided into additional zones. *(Image credit: "The Adrenal Glands" by Jennifer Lange is licensed under CC BY-NC-SA 4.0; includes section of "Slagter - Drawing Anatomy of the kidney, adrenal glands and bladder - no labels" by Ron Slagter, license: CC BY-NC-SA.)*

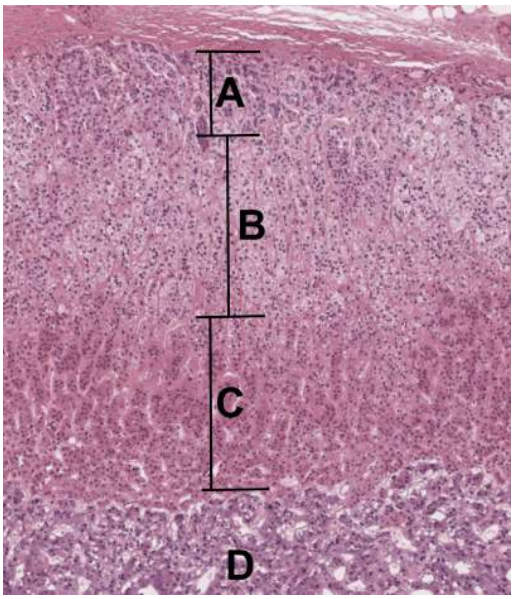


Figure 12.5.2:The Adrenal Gland slide. The adrenal gland is locacted on top of each kidney. The histolgy seen here shows the different parts of the gland that is responsible for the production of different types of hormones. A - Zona Glomerulosa, B - Zona Fasciculata, C - Zona Reticularis, and D - Medulla. (*Image credit: "Histology of Adrenal Gland" by Yancy Aquino is licensed under CC BY-NC-SA 4.0, slide provided by the Regents of the University of Michigan Medical School © 2022 under CC BY-NC-SA 3.0.*)

STRESS!

One of the major functions of the adrenal gland is to respond to stress. Stress can be either physical or psychological or both. Physical stresses include exposing the body to injury, walking outside in cold and wet conditions without a coat on, or malnutrition. Psychological stresses include the perception of a physical threat, a fight with a loved one, or just a bad day at school.

The body responds in different ways to short-term stress and long-term stress following a pattern known as the **general adaptation syndrome (GAS)**. Stage one of GAS is called the **alarm reaction**. This is short-term stress, the fight-or-flight response, mediated by the hormones epinephrine and norepinephrine from the adrenal medulla. Their function is to prepare the body for extreme physical exertion. Both epinephrine and norepinephrine signal the liver and skeletal muscle cells to convert glycogen into glucose, resulting in increased blood glucose levels. These hormones increase the heart rate, pulse, and blood pressure to prepare the body to fight the perceived threat or flee from it. In addition, the pathway dilates the airways, raising blood oxygen levels. It also prompts vasodilation, further increasing the oxygenation of important organs such as the lungs, brain, heart, and skeletal muscle. At the same time, it triggers vasoconstriction to blood vessels serving less essential organs such as the gastrointestinal tract, kidneys, and skin, and down regulates some components of the immune system. Other effects include a dry mouth, loss of appetite, pupil dilation, and a loss of peripheral vision.Once this stress is relieved, the body quickly returns to normal.

If the stress is not relieved quickly, the body adapts to the stress in the second stage called the **stage of resistance**. If a person is starving for example, the body may send signals to the gastrointestinal tract to maximize the absorption of nutrients from food.

If the stress continues for a longer term however, the body responds with symptoms quite different than the fight-or-flight response. During the **stage of exhaustion**, individuals may begin to suffer depression, the suppression of their immune response, severe fatigue, or even a fatal heart attack. These symptoms are mediated by the hormones of the adrenal cortex, especially cortisol.

The Adrenal Cortex

The adrenal cortex consists of multiple layers of lipid-storing cells that occur in three structurally distinct regions: the **zona glomerulosa**, the **zona fasciculata**, and the **zona reticularis**. Each region secretes its own set of steroid hormones important for the regulation of the long-term stress response, blood pressure and blood volume, nutrient uptake and storage, fluid and electrolyte balance, and inflammation.

Hormones of the Zona Glomerulosa

The most superficial region of the adrenal cortex is the zona glomerulosa, which produces a group of hormones collectively referred to as **mineralocorticoids** because of their effect on body minerals, especially sodium and potassium. These hormones are essential for fluid and electrolyte balance.

Aldosterone is the major mineralocorticoid. It is important in the regulation of the concentration of sodium (Na^+) and potassium (K^+) ions in urine, sweat, and saliva. For example, it is released in response to elevated blood K^+, low blood Na^+, low blood pressure, or low blood volume. In response, aldosterone increases the excretion of K^+ and the retention of Na^+, which in turn increases blood volume and blood pressure. Its secretion is prompted when CRH from the hypothalamus triggers ACTH release from the anterior pituitary.

The tiers of control for the release of aldosterone from the adrenal gland are as follows:

1. A stimulus such as decreased blood pH (blood becoming acidic), increased K^+ or low blood pressure triggers the **first tier of control.** In response to stimuli, the hypothalamus secretes corticotropin-releasing hormone (**CRH**) to the anterior pituitary gland.
2. At the **second tier of control**, when CRH binds to the anterior pituitary gland, the anterior pituitary gland will respond by secreting adrenocorticotropic hormone (ACTH) to the adrenal gland.
3. At the **third tier of control**, ACTH will bind the adrenal gland. In response to ACTH, the adrenal gland releases **aldosterone** which has the following effects on the body:
    - Regulates concentrations of K+, Na+ and H+ in the blood
    - Increases blood pressure through interacting with the renin-angiotensin-aldosterone system (RAAS) described below.

Aldosterone is also a key component of the renin-angiotensin-aldosterone system (RAAS) in which specialized cells of the kidneys secrete the enzyme renin in response to low blood volume or low blood pressure. Renin the triggers and enzymatic cascade that results in the production of angiotensin II, which has three major functions:

1. Initiating vasoconstriction of the arterioles, decreasing blood flow;
2. Stimulating kidney tubules to reabsorb NaCl and water, increasing blood volume;
3. Signaling the adrenal cortex to secrete aldosterone, the effects of which further contribute to fluid retention, restoring blood pressure and blood volume.

For individuals with hypertension, or high blood pressure, drugs are available that block the production of angiotensin II. These drugs, known as ACE inhibitors, block the enzyme that produces angiotensin II, thus mitigating the latter's ability to increase blood pressure.

Hormones of the Zona Fasciculata

The intermediate region of the adrenal cortex is the zona fasciculata, named as such because the cells form small fascicles (bundles) separated by tiny blood vessels. These cords of cells are oriented perpendicular to the surface of the organ. The cells of the zona fasciculata produce hormones called **glucocorticoids** because of their role in glucose metabolism. The most important of these is **cortisol**, some of which the liver converts to cortisone.

In response to long-term stressors, the **hypothalamic-pituitary-adrenal (HPA) axis** activates the tiers of control which are as follows:

1. At the first tier of control, in response to stressors, the hypothalamus secretes corticotropin-releasing hormone (**CRH**) to the anterior pituitary gland.
2. At the **second tier of control**, when CRH binds to the anterior pituitary gland, the anterior pituitary gland will respond by secreting adrenocorticotropic hormone (ACTH) to the adrenal gland.
3. At the **third tier of control**, ACTH will bind the adrenal gland. In response to ACTH, the adrenal gland releases **cortisol** which has the following effects on the body:

- Stimulates breakdown of glycogen to glucose to provide fuel for the body
- Releases fatty acids from adipose tissue for fuel
- Releases amino acids from muscle tissue for fuel
- Inhibits the inflammatory response

You are probably familiar with prescription and over-the-counter medications containing glucocorticoids, such as cortisone injections into inflamed joints, prednisone tablets and steroid-based inhalers used to manage severe asthma, and hydrocortisone creams applied to relieve itchy skin rashes. These drugs reflect another role of cortisol—the down regulation of the immune system, which inhibits the inflammatory response.

A negative feedback loop works to decrease cortisol levels once they have reached an appropriate level. Increased levels of cortisol signal the hypothalamus to stop secreting CRH which then leads to a decrease in secretion of ACTH from the anterior pituitary gland. With less ACTH, the adrenal gland will decrease its secretion of cortisol.

Hormones of the Zona Reticularis

The deepest region of the adrenal cortex is the zona reticularis, which produces small amounts of a class of steroid sex hormones called androgens. During puberty and most of adulthood, androgens are produced in the gonads. The androgens produced in the zona reticularis supplement the gonadal androgens. They are produced in response to ACTH from the anterior pituitary and are converted in the tissues to testosterone or estrogens. After menopause in those with ovaries, as the functions of the ovaries decline, the main source of estrogens becomes the androgens produced by the zona reticularis.

Table 12.5.1: Hormones of the Adrenal Glands

Adrenal gland region	Associated hormones	Effect
Adrenal cortex (Zona Glomerulosa)	Aldosterone	Increases blood Na^+ levels
Adrenal cortex (Zona Fasciculata)	Cortisol, corticosterone, cortisone	Increase blood glucose levels
Adrenal cortex (Zona Reticularis)	Androgens	Supplement gonadal androgens
Adrenal medulla	Epinephrine, norepinephrine	Stimulate fight-or-flight response

The Adrenal Medulla

The **adrenal medulla** is the central portion of the adrenal gland composed of **chromaffin cells**, which are modified postganglionic sympathetic neurons. The adrenal medulla develops from neural crest cells, which are also the origin of sympathetic ganglia. These cells secrete epinephrine and norepinephrine into the bloodstream and have the general effect of preparing the body for fight or flight. The adrenal medulla has features of both the neural and endocrine systems: it is made of modified neural tissue and its activity is regulated by a direct neural input, while the outputs are released into blood and act at distant sites by activating specific receptors. The actions of the medullary hormones are far more rapid and short-lived than those of most "classic" hormones.

DISORDERS OF THE...

Endocrine System: Disorders Involving the Adrenal Glands

Several disorders are caused by the dysregulation of the hormones produced by the adrenal glands. For example, Cushing's disease is a disorder characterized by high blood glucose levels and the accumulation of lipid deposits on the face and neck. It is caused by hypersecretion of cortisol. The most common source of Cushing's disease is a pituitary tumor that secretes cortisol or ACTH in abnormally high amounts. Other common signs of Cushing's disease include the development of a moon-shaped face, a buffalo hump on the back of the neck, rapid weight gain, and hair loss. Chronically elevated glucose levels are also associated with an elevated risk of developing type 2 diabetes. In addition to hyperglycemia, chronically elevated glucocorticoids compromise immunity, resistance to infection, and memory, and can result in rapid weight gain and hair loss.

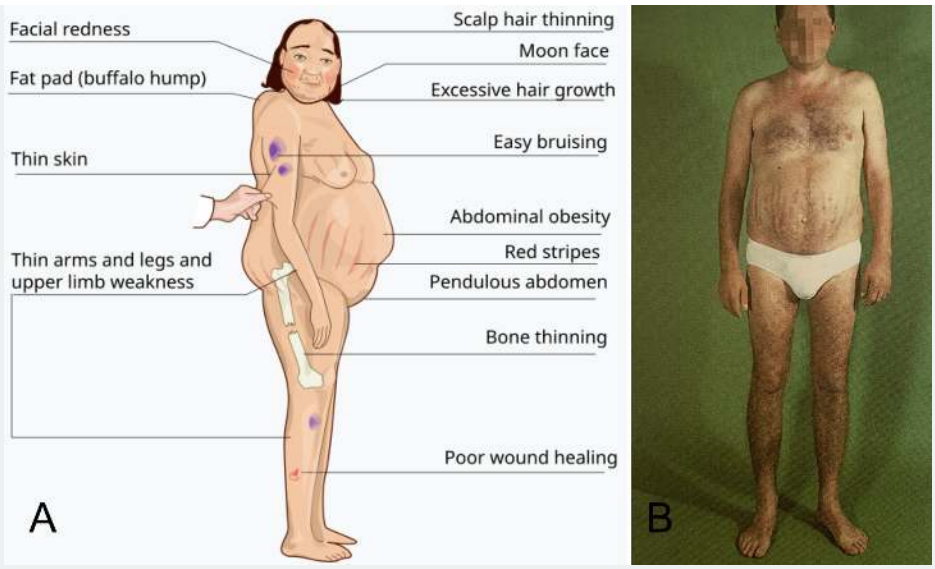


Figure 12.5.3: A. The different symptoms of a person with Cushing's syndrome. B. A picture of a person with Cushing's syndrome showing the prominent stretch marks on the abdomen. *(Image credit: "A. Cushing Syndrome Symptoms" and "B. Cushign Syndrome" by Yancy Aquino is licensed under CC BY-NC-SA 4.0, modification of original by OpenStax.)*

In contrast, the hyposecretion of corticosteroids can result in Addison's disease, a rare disorder that causes low blood glucose levels and low blood sodium levels. The signs and symptoms of Addison's disease are vague and are typical of other disorders as well, making diagnosis difficult. They may include general weakness, abdominal pain, weight loss, nausea, vomiting, sweating, and cravings for salty food.



Figure 12.5.4: Addison's Disease. A 69-year-old female with tiredness and a persistent tan. Facial appearance at presentation (left), showing pigmentation, and after treatment (right). *(Image credit: "Addison's Disease" by Yancy Aquino is licensed under CC BY-NC-SA 4.0, modification of original by OpenStax.)*

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12.6: Endocrine Pancreas

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

- Describe the location and structure of the pancreas, and the morphology and function of the pancreatic islets
- Compare and contrast the functions of insulin and glucagon

The **pancreas** is a long, slender retroperitoneal organ, most of which is located posterior to the bottom half of the stomach (Figure 12.6.1). It is bordered on its right by the retroperitoneal section of the duodenum and on its left by the spleen. The acinar cells of the pancreas line many short cul-de-sac-shaped areas connected directly to the pancreatic duct that drains transversely through the core of the pancreas to the duodenum nestled against its right side. Although it is primarily an exocrine gland, with its acinar cells secreting a variety of digestive enzymes that comprise pancreatic juice that will function outside the epithelial lining of the small intestine, the pancreas also has an endocrine function. Scattered around the cul-de-sacs of acinar cells throughout the pancreas are about a million **pancreatic islets**—clusters of cells formerly known as the islets of Langerhans— that secrete the hormones glucagon, insulin, somatostatin, and pancreatic polypeptide (PP).

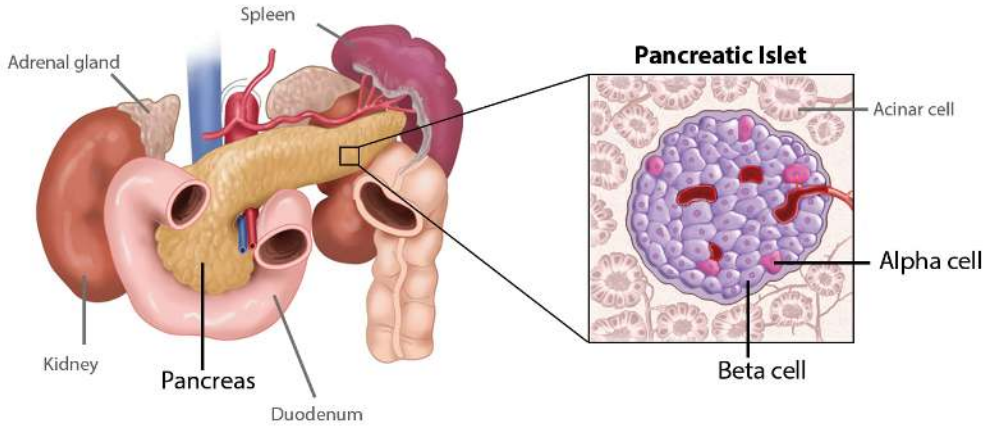


Figure 12.6.1: The Pancreas. The endocrine portion of the pancreas is small clusters of cells called pancreatic islets. Multiple hormones are secreted by the islets, with the two regulating blood glucose levels coming from the beta cells (insulin) and alpha cells (glucagon). *(Image credit: "Endocrine Pancreas" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, derivatives of original works "Leiden - Drawing pancreas and neighbouring organs - no labels" by Ron Slagter and "Endocrine Pancreas" by Cenveo.)*

Cells and Secretions of the Pancreatic Islets

Each pancreatic islet (Figure 12.6.1 and Figure 12.6.2) contains four types of cells whose secretions move into the bloodstream to travel to their target cells:

- The **alpha cell** produces the hormone glucagon and makes up approximately 20 percent of each islet. Glucagon plays an important role in blood glucose regulation; low blood glucose levels stimulate its release.
- The **beta cell** produces the hormone insulin and makes up approximately 75 percent of each islet. Elevated blood glucose levels stimulate the release of insulin.
- The **delta cell** accounts for four percent of the islet cells and secretes the peptide hormone somatostatin. Recall that somatostatin is also released by the hypothalamus (as GHIH), and the stomach and intestines also secrete it. An inhibiting hormone, pancreatic somatostatin inhibits the release of both glucagon and insulin.

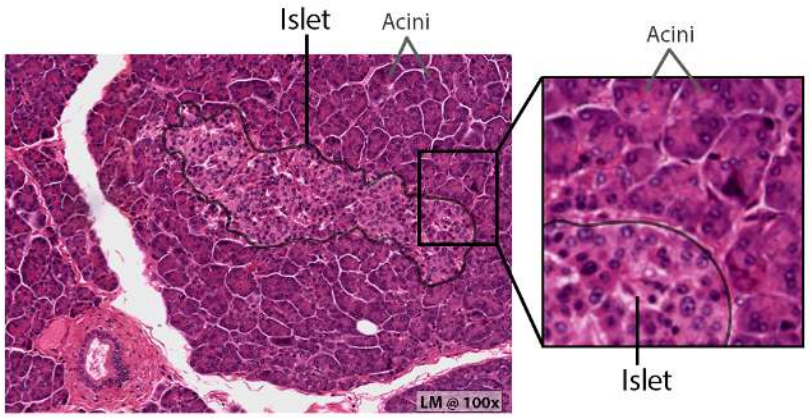


Figure 12.6.2: Histology of the Pancreas. On slides the pancreatic islets are seen as clusters of smaller, lighter staining cells that the surrounding blocks of acini (acinar cells). *(Image credit: "Histology of the Pancreas" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, slide provided by the Regents of the University of Michigan Medical School © 2022.)*

Regulation of Blood Glucose Levels by Insulin and Glucagon

Glucose is required for cellular respiration and is the preferred fuel for all body cells. The body derives glucose from the breakdown of the carbohydrate-containing foods and drinks we consume. Glucose not immediately taken up by cells for fuel can be stored by the liver and muscles as glycogen, or converted to triglycerides and stored in the adipose tissue. Hormones regulate both the storage and the utilization of glucose as required. Receptors located in the pancreas sense blood glucose levels, and subsequently the pancreatic cells secrete glucagon or insulin to maintain normal levels.

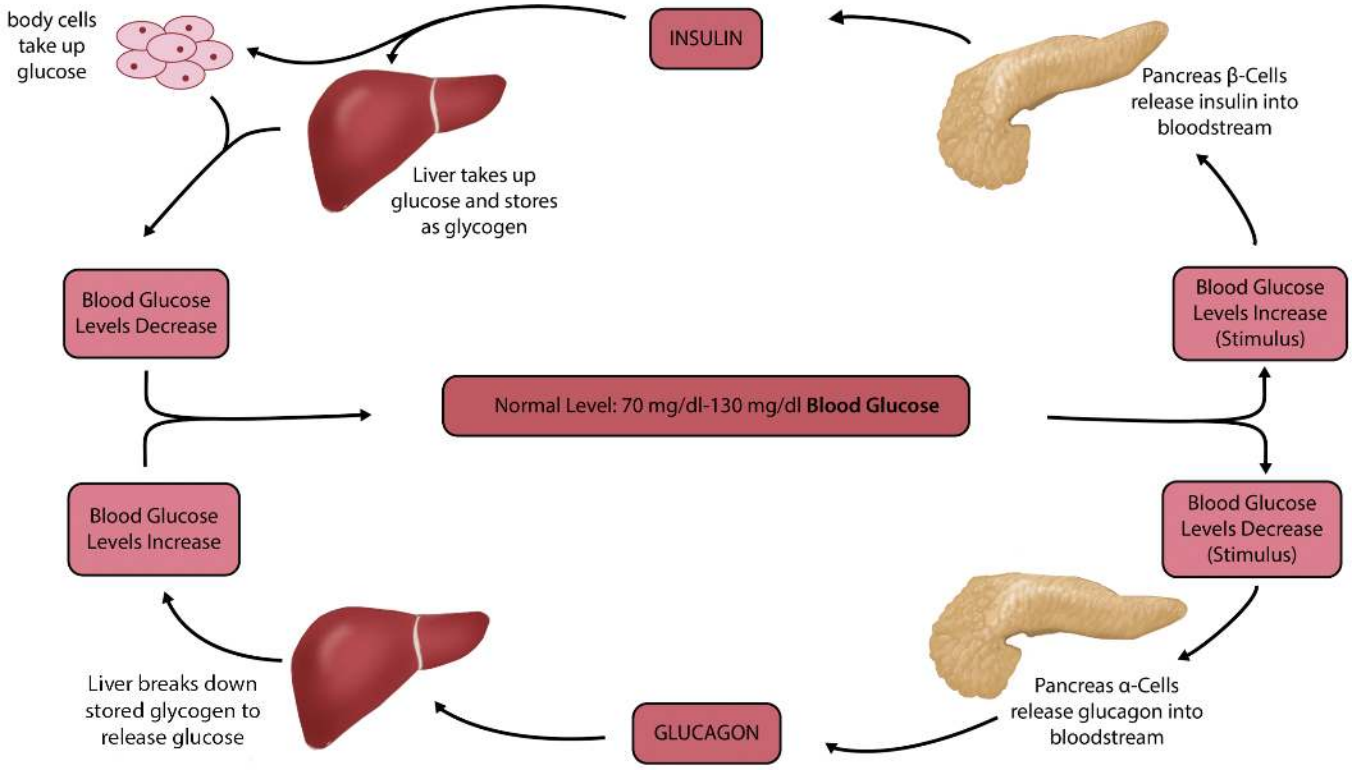


Figure 12.6.3: Glucose Homeostasis. Blood glucose levels are regulated by two pancreatic hormones that act antagonistically. *(Image credit: "Glucose Homeostasis" by Gabrielle Spurlock is licensed under CC BY-NC-SA 4.0. Pancreas image by Ron Slagter; liver image by Ron Slagter.)*

Table 12.6.1: Hormones of the Pancreas

Associated hormone (and the cells that secretes it)	Effect
Insulin (beta cells)	Reduces blood glucose levels
Glucagon (alpha cells)	Increases blood glucose levels
Somatostatin (delta cells)	Inhibits insulin and glucagon release

DISORDERS OF THE...

Endocrine System: Diabetes Mellitus

Dysfunction of insulin production and secretion, as well as the target cells' responsiveness to insulin, can lead to a condition called diabetes mellitus. An increasingly common disease, diabetes mellitus has been diagnosed in more than 18 million adults in the United States, and more than 200,000 children. It is estimated that up to 7 million more adults have the condition but have not been diagnosed. In addition, approximately 79 million people in the US are estimated to have pre-diabetes, a condition in which blood glucose levels are abnormally high, but not yet high enough to be classified as diabetes.

There are two main forms of diabetes mellitus. Type 1 diabetes is an autoimmune disease affecting the beta cells of the pancreas. Certain genes are recognized to increase susceptibility. The beta cells of people with type 1 diabetes do not produce insulin; thus, synthetic insulin must be administered by injection or infusion. This form of diabetes accounts for less than five percent of all diabetes cases.

Type 2 diabetes accounts for approximately 95 percent of all cases. It is acquired, and lifestyle factors such as poor diet, inactivity, and the presence of pre-diabetes greatly increase a person's risk. About 80 to 90 percent of people with type 2 diabetes are overweight or obese. In type 2 diabetes, cells become resistant to the effects of insulin. In response, the pancreas increases its insulin secretion, but over time, the beta cells become exhausted. In many cases, type 2 diabetes can be reversed by moderate weight loss, regular physical activity, and consumption of a healthy diet; however, if blood glucose levels cannot be controlled, the diabetic will eventually require insulin.

Two of the early manifestations of diabetes are excessive urination and excessive thirst. They demonstrate how the out-of-control levels of glucose in the blood affect kidney function. The kidneys are responsible for filtering glucose from the blood. Excessive blood glucose draws water into the urine, and as a result the person eliminates an abnormally large quantity of sweet urine. The use of body water to dilute the urine leaves the body dehydrated, and so the person is unusually and continually thirsty. The person may also experience persistent hunger because the body cells are unable to access the glucose in the bloodstream.

Over time, persistently high levels of glucose in the blood injure tissues throughout the body, especially those of the blood vessels and nerves. Inflammation and injury of the lining of arteries lead to atherosclerosis and an increased risk of heart attack and stroke. Damage to the microscopic blood vessels of the kidney impairs kidney function and can lead to kidney failure. Damage to blood vessels that serve the eyes can lead to blindness. Blood vessel damage also reduces circulation to the limbs, whereas nerve damage leads to a loss of sensation, called neuropathy, particularly in the hands and feet. Together, these changes increase the risk of injury, infection, and tissue death (necrosis), contributing to a high rate of toe, foot, and lower leg amputations in people with diabetes. Uncontrolled diabetes can also lead to a dangerous form of metabolic acidosis called ketoacidosis. Deprived of glucose, cells increasingly rely on fat stores for fuel. However, in a glucose-deficient state, the liver is forced to use an alternative lipid metabolism pathway that results in the increased production of ketone bodies (or ketones), which are acidic. The build-up of ketones in the blood causes ketoacidosis, which—if left untreated—may lead to a life-threatening "diabetic coma." Together, these complications make diabetes the seventh leading cause of death in the United States.

Diabetes is diagnosed when lab tests reveal that blood glucose levels are higher than normal, a condition called hyperglycemia. The treatment of diabetes depends on the type, the severity of the condition, and the ability of the patient to make lifestyle changes. As noted earlier, moderate weight loss, regular physical activity, and consumption of a healthful diet can reduce blood glucose levels. Some patients with type 2 diabetes may be unable to control their disease with these lifestyle changes, and will require medication. Historically, the first-line treatment of type 2 diabetes was insulin. Research advances have resulted in alternative options, including medications that enhance pancreatic function.

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12.7: Review Questions

Use the following questions to test your knowledge on the Endocrine System.

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CHAPTER OVERVIEW

13: The Cardiovascular System - Blood

Chapter Objectives

- Identify the primary functions of blood, its fluid and cellular components, and its physical characteristics
- Identify the most important proteins and other solutes present in blood plasma
- Describe the formation of the formed element components of blood
- Discuss the structure and function of red blood cells and hemoglobin
- Classify and characterize white blood cells
- Describe the structure of platelets and explain the process of hemostasis
- Explain the significance of AB and Rh blood groups in blood transfusions
- Discuss a variety of blood disorders

13.1: An Overview of Blood
13.2: Erythrocytes
13.3: Leukocytes and Platelets
13.4: Blood Typing
13.5: Review Questions

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13.1: An Overview of Blood

Learning Objectives

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

- Identify the primary functions of blood in transportation, defense, and maintenance of homeostasis
- Name the fluid component of blood and the three major types of formed elements, and identify their relative proportions in a blood sample
- Discuss the unique physical characteristics of blood
- Identify the composition of blood plasma, including its most important solutes and plasma proteins

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

Functions of Blood

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

Transportation

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

Defense

Many types of white blood cells, also called **leukocytes**, protect the body from external threats, such as disease-causing bacteria that have entered the bloodstream in a wound. Other WBCs seek out and destroy internal threats, such as cells with mutated DNA that could multiply to become cancerous, or body cells infected with viruses.

When damage to the vessels results in bleeding, blood platelets and certain proteins dissolved in the plasma interact to block the ruptured areas of the blood vessels involved. This protects the body from further blood loss. This process is called blood clotting and will be described later on in this chapter.

Maintenance of Homeostasis

Recall that body temperature is regulated via a classic negative-feedback loop. If you were exercising on a warm day, your rising core body temperature would trigger several homeostatic mechanisms, including increased transport of blood from your core to your body periphery, which is typically cooler. As blood passes through the vessels of the skin, heat would be dissipated to the environment, and the blood returning to your body core would be cooler. In contrast, on a cold day, blood is diverted away from the skin to maintain a warmer body core. In extreme cases, this may result in frostbite.

Blood also helps to maintain the chemical balance of the body. Proteins and other compounds in blood act as buffers, which thereby help to regulate the pH of body tissues. Blood also helps to regulate the water content of body cells.

Composition of Blood

You have probably had blood drawn from a superficial vein in your arm, which was then sent to a lab for analysis. Some of the most common blood tests—for instance, those measuring lipid or glucose levels in plasma—determine which substances are

present within blood and in what quantities. Other blood tests check for the composition of the blood itself, including the quantities and types of formed elements.

One such test, called a **hematocrit**, measures the percentage of RBCs, clinically known as **erythrocytes**, in a blood sample. It is performed by spinning the blood sample in a specialized centrifuge, a process that causes the heavier elements suspended within the blood sample to separate from the lightweight, liquid plasma (Figure 13.1.1). Because the heaviest elements in blood are the erythrocytes, these settle at the very bottom of the hematocrit tube. Located above the erythrocytes is a pale, thin layer composed of the remaining formed elements of blood. These are the WBCs, and the platelets, cell fragments also called **thrombocytes**. This layer is referred to as the buffy coat because of its color; it normally constitutes less than 1 percent of a blood sample. Above the buffy coat is the blood plasma, normally a pale, straw-colored fluid, which constitutes the remainder of the sample.

The volume of erythrocytes after centrifugation is also commonly referred to as **packed cell volume (PCV)**. In normal blood, about 45 percent of a sample is erythrocytes. The hematocrit of any one sample can vary significantly, however, about 36–50 percent, according to gender and other factors. Normal hematocrit values for females range from 37 to 47, with a mean value of 41; for males, hematocrit ranges from 42 to 52, with a mean of 47. The percentage of other formed elements, the WBCs and platelets, is extremely small so it is not normally considered with the hematocrit. So the mean plasma percentage is the percent of blood that is not erythrocytes: for females, it is approximately 59 (or 100 minus 41), and for males, it is approximately 53 (or 100 minus 47).

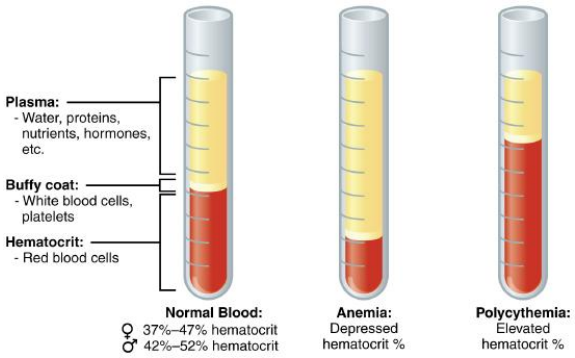


Figure 13.1.1: Composition of Blood The cellular elements of blood include a vast number of erythrocytes and comparatively fewer leukocytes and platelets. Plasma is the fluid in which the formed elements are suspended. A sample of blood spun in a centrifuge reveals that plasma is the lightest component. It floats at the top of the tube separated from the heaviest elements, the erythrocytes, by a buffy coat of leukocytes and platelets. Hematocrit is the percentage of the total sample that is comprised of erythrocytes. Depressed and elevated hematocrit levels are shown for comparison.

A hematocrit can be useful in helping to diagnose **anemia**. Anemia is a blood disorder in which there is a reduced ability of red blood cells to deliver oxygen to the body, due to either a lower number of red blood cells or reduced amounts of hemoglobin. Individuals with anemia typically experience fatigue, weakness, and trouble breathing. There are a variety of causes of anemia which can range from having an iron deficiency (hemoglobin requires iron to bind oxygen) to having a genetic mutation (sickle cell anemia is a genetic disorder). Anemia will be discussed in greater detail later in this chapter. When an individual with anemia has their blood analyzed through a hematocrit, it is expected that their hematocrit values will be lower than normal (<37% for adult females and <42% for adult males).

Characteristics of Blood

When you think about blood, the first characteristic that probably comes to mind is its color. Blood that has just taken up oxygen in the lungs is bright red, and blood that has released oxygen in the tissues is a more dusky red. This is because hemoglobin is a pigment that changes color, depending upon the degree of oxygen saturation.

Blood is viscous and somewhat sticky to the touch. It has a viscosity approximately five times greater than water. Viscosity is a measure of a fluid's thickness or resistance to flow, and is influenced by the presence of the plasma proteins and formed elements within the blood. The viscosity of blood has a dramatic impact on blood pressure and flow. Consider the difference in flow between water and honey. The more viscous honey would demonstrate a greater resistance to flow than the less viscous water. The same principle applies to blood.

The normal temperature of blood is slightly higher than normal body temperature—about 38 °C (or 100.4 °F), compared to 37 °C (or 98.6 °F) for an internal body temperature reading, although daily variations of 0.5 °C are normal. Although the surface of blood

vessels is relatively smooth, as blood flows through them, it experiences some friction and resistance, especially as vessels age and lose their elasticity, thereby producing heat. This accounts for its slightly higher temperature.

The pH of blood averages about 7.4; however, it can range from 7.35 to 7.45 in a healthy person. **Blood is therefore somewhat more basic** (alkaline) on a chemical scale than pure water, which has a pH of 7.0. Blood contains numerous buffers that actually help to regulate pH. The pH of blood must be tightly regulated as pH variations beyond the normal range can cause the proteins in blood to become **denatured**, affecting their normal functioning.

Blood constitutes approximately 8 percent of adult body weight. Adult males typically average about 5 to 6 liters of blood. Females average 4–5 liters.

Blood Plasma

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

Interactive Link

Visit this site for a list of normal levels established for many of the substances found in a sample of blood. Serum, one of the specimen types included, refers to a sample of plasma after clotting factors have been removed. What types of measurements are given for levels of glucose in the blood?

Plasma Proteins

About 7 percent of the volume of plasma—nearly all that is not water—is made of proteins. These include several plasma proteins (proteins that are unique to the plasma), plus a much smaller number of regulatory proteins, including enzymes and some hormones. The major components of plasma are summarized in Figure 13.1.2.

The three major groups of plasma proteins are as follows:

- Albumin is the most abundant of the plasma proteins. Manufactured by the liver, albumin molecules serve as binding proteins—transport vehicles for fatty acids and steroid hormones. Recall that lipids are hydrophobic; however, their binding to albumin enables their transport in the watery plasma. Albumin is also the most significant contributor to the osmotic pressure of blood; that is, it acts as a solute, drawing water into the blood from tissues, across blood vessel walls, and into the bloodstream. This in turn helps to maintain both blood volume and blood pressure. Albumin normally accounts for approximately 54 percent of the total plasma protein content, in clinical levels of 3.5–5.0 g/dL blood.
- The second most common plasma proteins are the globulins. A heterogeneous group, there are three main subgroups known as alpha, beta, and gamma globulins. The alpha and beta globulins transport iron, lipids, and the fat-soluble vitamins A, D, E, and K to the cells; like albumin, they also contribute to osmotic pressure. The gamma globulins are proteins involved in immunity and are better known as an **antibodies** or immunoglobulins. Although other plasma proteins are produced by the liver, immunoglobulins are produced by specialized leukocytes known as plasma cells. (Seek additional content for more information about immunoglobulins.) Globulins make up approximately 38 percent of the total plasma protein volume, in clinical levels of 1.0–1.5 g/dL blood.
- Fibrinogen is the third of the three major groups of plasma proteins. Like albumin and the alpha and beta globulins, fibrinogen is produced by the liver. It is essential for blood clotting, a process described later in this chapter. Fibrinogen accounts for about 7 percent of the total plasma protein volume, in clinical levels of 0.2–0.45 g/dL blood.

Other Plasma Solutes

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

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

Figure 13.1.2: Major Blood Components

Career Connection

Phlebotomy and Medical Lab Technology

Phlebotomists are professionals trained to draw blood (phleb- = “a blood vessel”; -tomy = “to cut”). When more than a few drops of blood are required, phlebotomists perform a venipuncture, typically of a surface vein in the arm. They perform a capillary stick on a finger, an earlobe, or the heel of an infant when only a small quantity of blood is required. An arterial stick is collected from an artery and used to analyze blood gases. After collection, the blood may be analyzed by medical laboratories or perhaps used for transfusions, donations, or research. While many allied health professionals practice phlebotomy, the American Society of Phlebotomy Technicians issues certificates to individuals passing a national examination, and some large labs and hospitals hire individuals expressly for their skill in phlebotomy.

Medical or clinical laboratories employ a variety of individuals in technical positions:

- Medical technologists (MT), also known as clinical laboratory technologists (CLT), typically hold a bachelor's degree and certification from an accredited training program. They perform a wide variety of tests on various body fluids, including blood. The information they provide is essential to the primary care providers in determining a diagnosis and in monitoring the course of a disease and response to treatment.
- Medical laboratory technicians (MLT) typically have an associate's degree but may perform duties similar to those of an MT.
- Medical laboratory assistants (MLA) spend the majority of their time processing samples and carrying out routine assignments within the lab. Clinical training is required, but a degree may not be essential to obtaining a position.

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13.2: Erythrocytes

Learning Objectives

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

- Describe the anatomy of erythrocytes
- Discuss the various steps in the lifecycle of an erythrocyte
- Explain the composition and function of hemoglobin

The erythrocyte, commonly known as a red blood cell (or RBC), is by far the most common formed element: A single drop of blood contains millions of erythrocytes and just thousands of leukocytes. Specifically, males have about 5.4 million erythrocytes per microliter (μL) of blood, and females have approximately 4.8 million per μL. In fact, erythrocytes are estimated to make up about 25 percent of the total cells in the body. As you can imagine, they are quite small cells, with a mean diameter of only about 7–8 micrometers (μm) (Figure 13.2.1). The primary functions of erythrocytes are to pick up inhaled oxygen from the lungs and transport it to the body's tissues, and to pick up some (about 24 percent) carbon dioxide waste at the tissues and transport it to the lungs for exhalation. Erythrocytes remain within the vascular network. Although leukocytes typically leave the blood vessels to perform their defensive functions, movement of erythrocytes from the blood vessels is abnormal.

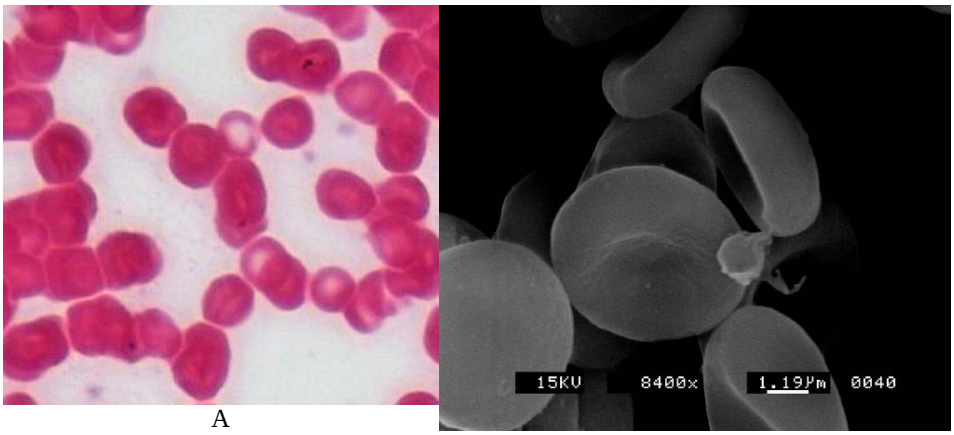
Formed element	Major subtypes	Numbers present per microliter (μL) and mean (range)	Appearance in a standard blood smear	Summary of functions	Comments
Erythrocytes (red blood cells)		5.2 million (4.4–6.0 million)	Flattened biconcave disk; no nucleus; pale red color	Transport oxygen and some carbon dioxide between tissues and lungs	Lifespan of approximately 120 days

Figure 13.2.1: Summary of Erythrocytes / Cropped from original

Shape and Structure of Erythrocytes

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

Erythrocytes are biconcave disks; that is, they are plump at their periphery and very thin in the center (Figure 13.2.2). Since they lack most organelles, there is more interior space for the presence of the hemoglobin molecules that, as you will see shortly, transport gases. The biconcave shape also provides a greater surface area across which gas exchange can occur, relative to its volume; a sphere of a similar diameter would have a lower surface area-to-volume ratio. In the capillaries, the oxygen carried by the erythrocytes can diffuse into the plasma and then through the capillary walls to reach the cells, whereas some of the carbon dioxide produced by the cells as a waste product diffuses into the capillaries to be picked up by the erythrocytes. Capillary beds are extremely narrow, slowing the passage of the erythrocytes and providing an extended opportunity for gas exchange to occur. However, the space within capillaries can be so minute that, despite their own small size, erythrocytes may have to fold in on themselves if they are to make their way through. Fortunately, their structural proteins are flexible, allowing them to bend over themselves to a surprising degree, then spring back again when they enter a wider vessel. In wider vessels, erythrocytes may stack up much like a roll of coins, forming a rouleaux, from the French word for "roll."



A B

Figure 13.2.2 Red Blood Cells: A) This image shows red blood cells viewed under a compound microscope at 400x total magnification. B) This image shows red blood cells viewed under a scanning electron microscope at 8400x total magnification. The biconcave shape of the RBCs can be seen. *(A: Image credit: "Connective Tissue" by* Berkshire Community College Bioscience Image Library, *licensed under CC0 1.0, via Wikimedia Commons) / Cropped from original (B) Image credit: "Red Blood Cells" by Jmarchn, licensed under CC BY-SA 3.0, via Wikimedia Commons)*

Hemoglobin

Hemoglobin is a large molecule made up of proteins and iron. It consists of four folded chains of a protein called globin, designated alpha 1 and 2, and beta 1 and 2 (Figure 13.2.3**a**). Each of these globin molecules is bound to a red pigment molecule called heme, which contains an ion of iron (Fe^{2+}) (Figure 13.2.3**b**).

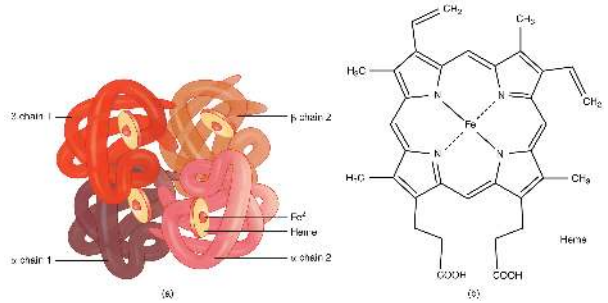


Figure 13.2.3: Hemoglobin (a) A molecule of hemoglobin contains four globin proteins, each of which is bound to one molecule of the iron-containing pigment heme. (b) A single erythrocyte can contain 300 million hemoglobin molecules, and thus more than 1 billion oxygen molecules.

Each iron ion in the heme can bind to one oxygen molecule; therefore, each hemoglobin molecule can transport four oxygen molecules. An individual erythrocyte may contain about 300 million hemoglobin molecules, and therefore can bind to and transport up to 1.2 billion oxygen molecules (Figure 13.2.3).

In the lungs, hemoglobin picks up oxygen, which binds to the iron ions, forming oxyhemoglobin. The bright red, oxygenated hemoglobin travels to the body tissues, where it releases some of the oxygen molecules, becoming darker red deoxyhemoglobin, sometimes referred to as reduced hemoglobin. Oxygen release depends on the need for oxygen in the surrounding tissues, so hemoglobin rarely if ever leaves all of its oxygen behind. In the capillaries, carbon dioxide enters the bloodstream. About 76 percent dissolves in the plasma, and the remainder forming bicarbonate ion. About 23–24 percent of it binds to the amino acids in hemoglobin, forming a molecule known as carbaminohemoglobin. From the capillaries, the hemoglobin carries carbon dioxide back to the lungs, where it releases it for exchange of oxygen.

Changes in the levels of RBCs can have significant effects on the body's ability to effectively deliver oxygen to the tissues. Ineffective hematopoiesis results in insufficient numbers of RBCs and results in one of several forms of **anemia**. An overproduction of RBCs produces a condition called **polycythemia**. The primary drawback with polycythemia is not a failure to

directly deliver enough oxygen to the tissues, but rather the increased viscosity of the blood, which makes it more difficult for the heart to circulate the blood.

In patients with insufficient hemoglobin, the tissues may not receive sufficient oxygen, resulting in another form of anemia. In determining oxygenation of tissues, the value of greatest interest in healthcare is the **percent saturation**; that is, the percentage of hemoglobin sites occupied by oxygen in a patient's blood. Clinically this value is commonly referred to simply as "percent sat."

Percent saturation is normally monitored using a device known as a **pulse oximeter**, which is applied to a thin part of the body, typically the tip of the patient's finger. The device works by sending two different wavelengths of light (one red, the other infrared) through the finger and measuring the light with a photodetector as it exits. Hemoglobin absorbs light differentially depending upon its saturation with oxygen. The machine calibrates the amount of light received by the photodetector against the amount absorbed by the partially oxygenated hemoglobin and presents the data as percent saturation. Normal pulse oximeter readings range from 95–100 percent. Lower percentages reflect **hypoxemia**, or low blood oxygen. The term hypoxia is more generic and simply refers to low oxygen levels.

The kidneys filter about 180 liters (~380 pints) of blood in an average adult each day, or about 20 percent of the total resting volume, and thus have many receptors that determine oxygen saturation. In hypoxemia, there will be be low oxygen concentration in the tissue fluid of the kidney. In response, cells called fibroblasts within the kidney secrete a protein called erythropoietin (EPO). EPO then signals to red bone marrow to increase erythrocyte production, which in turn, increases oxygen levels. This is another example of a negative feedback loop used by the body to maintain homeostasis. When oxygen levels fall, EPO is secreted to red bone marrow to increase RBC production and thus increase oxygen levels. Once oxygen levels return to normal, EPO production decreases.

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

Disorders of Erythrocytes

The size, shape, and number of erythrocytes, and the number of hemoglobin molecules can have a major impact on a person's health. When the number of RBCs or hemoglobin is deficient, the general condition is called **anemia**. There are more than 400 types of anemia and more than 3.5 million Americans suffer from this condition. Anemia can be broken down into three major groups:

1. Anemia caused by blood loss
2. Anemia caused by faulty or decreased RBC production
3. Anemia caused by excessive destruction of RBCs.

Clinicians often use two groupings in diagnosis: The kinetic approach focuses on evaluating the production, destruction, and removal of RBCs, whereas the morphological approach examines the RBCs themselves, paying particular emphasis to their size. A common test is the **mean corpuscle volume (MCV)**, which measures size. The effects of the various anemias are widespread, because reduced numbers of RBCs or hemoglobin will result in lower levels of oxygen being delivered to body tissues. Since oxygen is required for tissue functioning, anemia produces fatigue, lethargy, and an increased risk for infection. An oxygen deficit in the brain impairs the ability to think clearly, and may prompt headaches and irritability. Lack of oxygen leaves the patient short of breath, even as the heart and lungs work harder in response to the deficit.

Blood loss anemias are fairly straightforward. In addition to bleeding from wounds or other lesions, these forms of anemia may be due to ulcers, hemorrhoids, inflammation of the stomach (gastritis), and some cancers of the gastrointestinal tract. The excessive use of aspirin or other nonsteroidal anti-inflammatory drugs such as ibuprofen can trigger ulceration and gastritis. Excessive menstruation and loss of blood during childbirth are also potential causes.

Anemias caused by faulty or decreased RBC production include sickle cell anemia, iron deficiency anemia, vitamin deficiency anemia, and diseases of the bone marrow and stem cells.

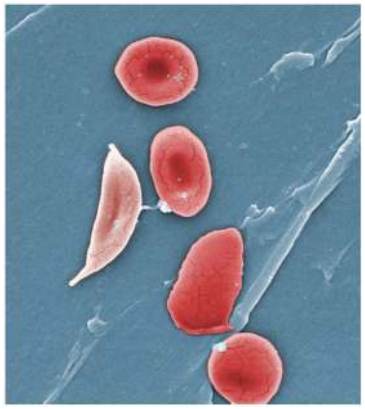


Figure 13.2.5 Sickle Cells Sickle cell anemia is caused by a mutation in one of the hemoglobin genes. Erythrocytes produce an abnormal type of hemoglobin, which causes the cell to take on a sickle or crescent shape. (credit: Janice Haney Carr)

In contrast to anemia, an elevated RBC count is called polycythemia and is detected in a patient's elevated hematocrit. It can occur transiently in a person who is dehydrated; when water intake is inadequate or water losses are excessive, the plasma volume falls. As a result, the hematocrit rises. For reasons mentioned earlier, a mild form of polycythemia is chronic but normal in people living at high altitudes. Some elite athletes train at high elevations specifically to induce this phenomenon. Finally, a type of bone marrow disease called polycythemia vera (from the Greek vera = "true") causes an excessive production of immature erythrocytes. Polycythemia vera can dangerously elevate the viscosity of blood, raising blood pressure and making it more difficult for the heart to pump blood throughout the body. It is a relatively rare disease that occurs more often in males than in females, and is more likely to be present in elderly patients those over 60 years of age.

Types of Anemia

- A characteristic change in the shape of erythrocytes is seen in sickle cell disease (also referred to as sickle cell anemia). A genetic disorder, it is caused by production of an abnormal type of hemoglobin, called hemoglobin S, which delivers less oxygen to tissues and causes erythrocytes to assume a sickle (or crescent) shape, especially at low oxygen concentrations (Figure 13.2.5). These abnormally shaped cells can then become lodged in narrow capillaries because they are unable to fold in on themselves to squeeze through, blocking blood flow to tissues and causing a variety of serious problems from painful joints to delayed growth and even blindness and cerebrovascular accidents (strokes). Sickle cell anemia is a genetic condition particularly found in individuals of African descent.
- Iron deficiency anemia is the most common type and results when the amount of available iron is insufficient to allow production of sufficient heme. This condition can occur in individuals with a deficiency of iron in the diet and is especially common in teens and children as well as in vegans and vegetarians. Additionally, iron deficiency anemia may be caused by either an inability to absorb and transport iron or slow, chronic bleeding.
- Vitamin-deficient anemias generally involve insufficient vitamin B12 and folate.
    - Megaloblastic anemia involves a deficiency of vitamin B12 and/or folate, and often involves diets deficient in these essential nutrients. Lack of meat or a viable alternate source, and overcooking or eating insufficient amounts of vegetables may lead to a lack of folate.
    - Pernicious anemia is caused by poor absorption of vitamin B12 and is often seen in patients with Crohn's disease (a severe intestinal disorder often treated by surgery), surgical removal of the intestines or stomach (common in some weight loss surgeries), intestinal parasites, and AIDS.
    - Pregnancies, some medications, excessive alcohol consumption, and some diseases such as celiac disease are also associated with vitamin deficiencies. It is essential to provide sufficient folic acid during the early stages of pregnancy to reduce the risk of neurological defects, including spina bifida, a failure of the neural tube to close.
- Assorted disease processes can also interfere with the production and formation of RBCs and hemoglobin. If myeloid stem cells are defective or replaced by cancer cells, there will be insufficient quantities of RBCs produced.

- Aplastic anemia is the condition in which there are deficient numbers of RBC stem cells. Aplastic anemia is often inherited, or it may be triggered by radiation, medication, chemotherapy, or infection.
- Thalassemia is an inherited condition typically occurring in individuals from the Middle East, the Mediterranean, African, and Southeast Asia, in which maturation of the RBCs does not proceed normally. The most severe form is called Cooley's anemia.
- Lead exposure from industrial sources or even dust from paint chips of iron-containing paints or pottery that has not been properly glazed may also lead to destruction of the red marrow.

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

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13.3: Leukocytes and Platelets

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

- Describe the general characteristics of leukocytes
- Classify leukocytes according to their lineage, their main structural features, and their primary functions
- Identify the lineage, basic structure, and function of platelets
- Describe the general steps of the blood clotting process

Leukocytes

The **leukocyte**, commonly known as a white blood cell (or WBC), is a major component of the body's defenses against disease. Leukocytes protect the body against invading microorganisms and body cells with mutated DNA, and they clean up debris. You may find it helpful to reference Figure 13.3.11 at the bottom of this section to keep track of the various leukocytes.

Characteristics of Leukocytes

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

One of the most distinctive characteristics of leukocytes is their movement. Whereas erythrocytes spend their days circulating within the blood vessels, leukocytes routinely leave the bloodstream to perform their defensive functions in the body's tissues. For leukocytes, the vascular network is often simply a highway they travel and soon exit to reach their true destination. When they arrive, they may differentiate further and be given distinct names, such as macrophage or microglia, depending on their function. As shown in Figure 13.3.1, they leave the capillaries—the smallest blood vessels—or other small vessels through a process known as **emigration** (from the Latin for "removal") or **diapedesis** (dia- = "through"; -pedan = "to leap") in which they squeeze through adjacent cells in a blood vessel wall.

Once they have exited the capillaries, some leukocytes will take up residence in lymphatic tissue, bone marrow, the spleen, the thymus, or other organs. Others will move about through the tissue spaces very much like amoebae, continuously extending their plasma membranes, sometimes wandering freely, and sometimes moving toward the direction in which they are drawn by chemical signals. This attracting of leukocytes occurs because of **positive chemotaxis** (literally "movement in response to chemicals"), a phenomenon in which injured or infected cells and nearby leukocytes emit the equivalent of a chemical "911" call, attracting more leukocytes to the site. In clinical medicine, the differential counts of the types and percentages of leukocytes present are often key indicators in making a diagnosis and selecting a treatment.

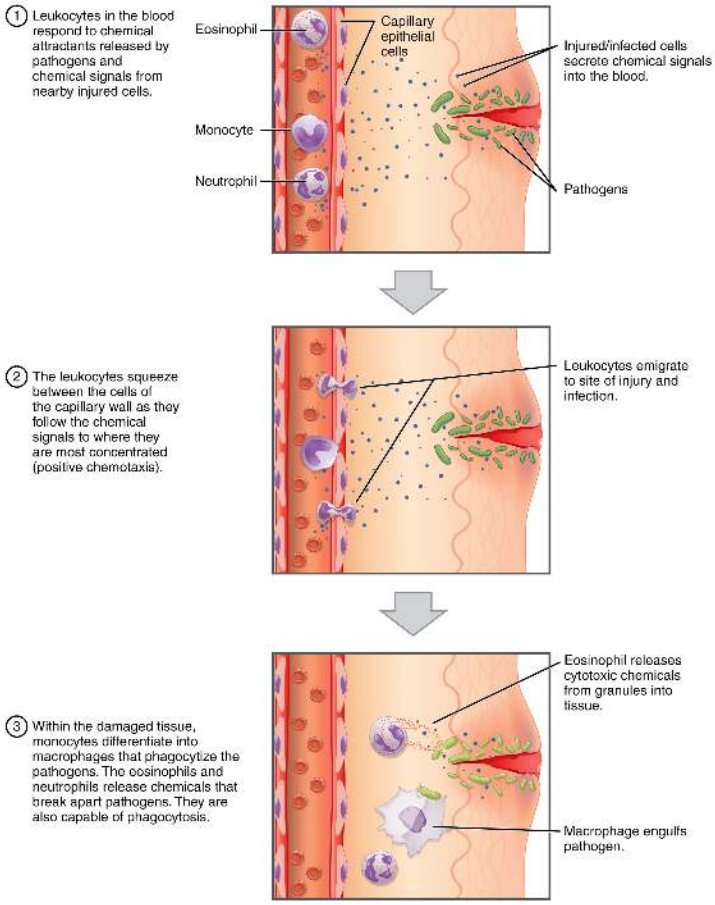


Figure 13.3.1: Emigration or Diapedesis. Injured and/or infected cells secrete chemical signals into the blood. Leukocytes in the blood respond to chemical attractants released by pathogens and chemical signals from nearby injured cells. The leukocytes emigrate or squeeze between the cells of the capillary wall as they follow the chemical signals to where they are most concentrated (positive chemotaxis). Within the damaged tissue, monocytes differentiate into macrophages that phagocytize the pathogens. The eosinophils and neutrophils release cytotoxic chemicals that break apart pathogens from granules into the tissue. They are also capable of phagocytosis. exit the blood vessel and then move through the connective tissue of the dermis toward the site of a wound. Some leukocytes, such as the eosinophil and neutrophil, are characterized as granular leukocytes. They release chemicals from their granules that destroy pathogens; they are also capable of phagocytosis. The monocyte differentiates into a macrophage that then phagocytizes the pathogens. (Image credit: "Emigration" by OpenStax is licensed under CC BY 3.0)

Classification of Leukocytes

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

- **Granular leukocytes** (granulocytes) contain abundant granules within the cytoplasm. They include neutrophils, eosinophils, and basophils (you can view their lineage from myeloid stem cells in Figure 16.5.1 Hemopoietic System of Bone Marrow).
- While granules are not totally lacking in **agranular leukocytes** (agranulocytes), they are far fewer and less obvious. Agranular leukocytes include monocytes, which also arise from myeloid stem cells and mature into macrophages that are phagocytic, and lymphocytes, which arise from the lymphoid stem cell line.

Granular Leukocytes

We will consider the granular leukocytes (granulocytes) in order from most common to least common. All of these are produced in the red bone marrow and have a short lifespan of hours to days. They typically have a lobed nucleus and are classified according to which type of stain best highlights their granules (Figure 13.3.2).

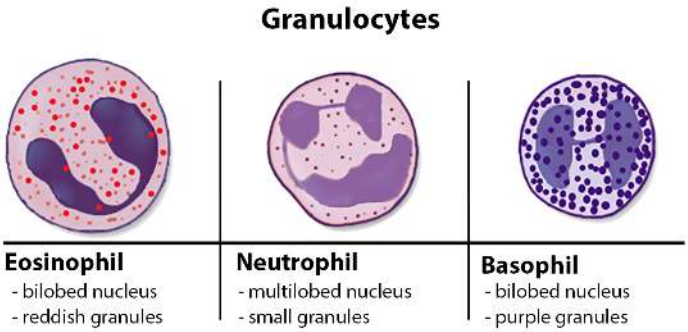


Figure 13.3.2: Granulocytes. A neutrophil has small granules that stain light lilac and a nucleus with two to five lobes. An eosinophil's granules are slightly larger and stain reddish-orange, and its nucleus has two lobes. A basophil has large granules that stain dark blue to purple and a two-lobed nucleus. *(Image credit: "Granulocytes" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original by OpenStax.)*

The most common of all the leukocytes, **neutrophils** (Figure 13.3.3) will normally comprise 50–70 percent of the total leukocyte count. They are 10–12 μm in diameter, significantly larger than erythrocytes. They are called neutrophils because their granules show up most clearly with stains that are chemically neutral (neither acidic nor basic). The granules are numerous but quite fine and normally appear light lilac. The nucleus has a distinct lobed appearance and may have two to five lobes, the number increasing with the age of the cell. Older neutrophils have increasing numbers of lobes and are often referred to as **polymorphonuclear** (a nucleus with many forms), or simply "polys." Younger and immature neutrophils begin to develop lobes and are known as "bands."

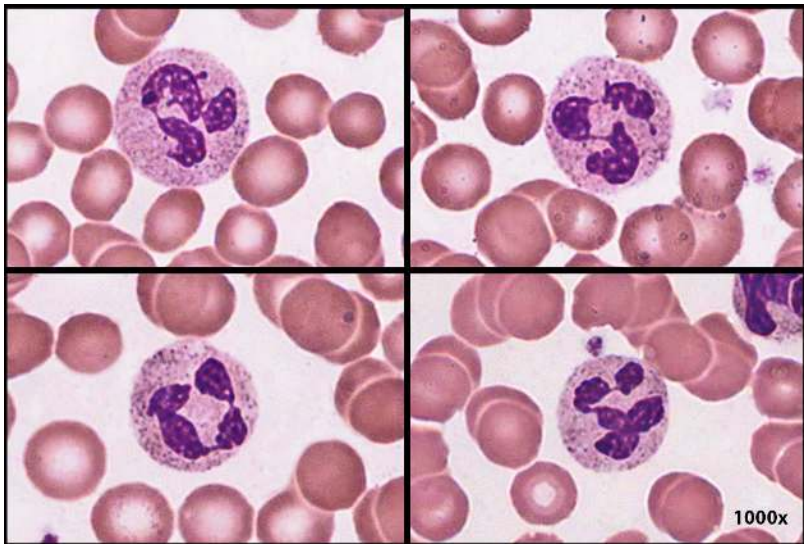


Figure 13.3.3: Neutrophils. Visually neutrophils are about twice the size of RBCs and have a nucleus with 3-5 lobes that can have a variety of appearances. *(Image credit: "Neutrophil" micrographs by Virginia Commonwealth University are licensed under CC BY-NC-SA 4.0)*

Neutrophils are rapid responders to the site of infection and are efficient phagocytes with a preference for bacteria. Their granules include vesicles filled with substances that help them neutralize infectious agents: **lysozyme**, an enzyme capable of lysing, or breaking down, bacterial cell walls; oxidants such as hydrogen peroxide; and **defensins**, proteins that bind to and puncture bacterial and fungal plasma membranes so that the cell contents leak out. Abnormally high counts of neutrophils indicate infection and/or inflammation, particularly triggered by bacteria, but are also found in burn patients and others experiencing unusual stress. A burn injury increases the proliferation of neutrophils in order to fight off infection that can result from the destruction of the barrier of the skin. Low counts may be caused by drug toxicity and other disorders, and may increase an individual's susceptibility to infection.

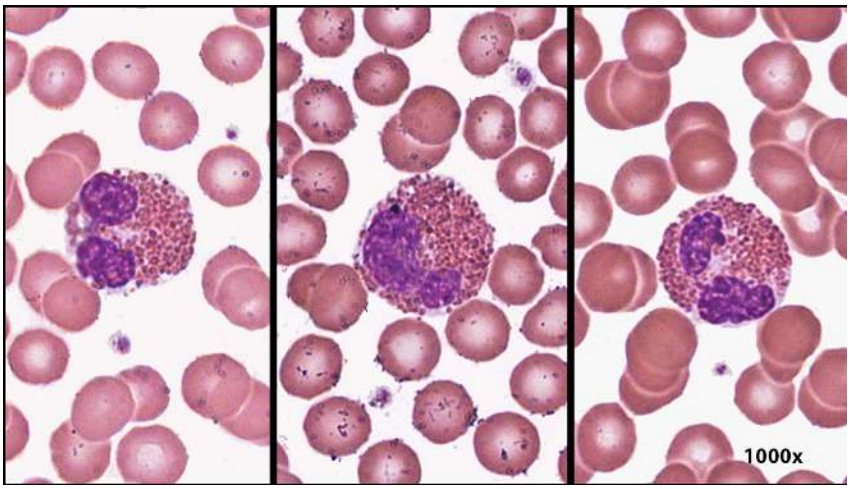


Figure 13.3.4: Eosinophils. Visually eosinophils are about twice the size of RBCs, have a nucleus with 2 lobes and have abundant reddish granules that are easy to see. *(Image credit: "Eosinophil" micrographs by Virginia Commonwealth University are licensed under CC BY-NC-SA 4.0.)*

Eosinophils typically represent 2–4 percent of the total leukocyte count. They are also 10–12 μm in diameter. The granules of eosinophils stain best with an acidic stain known as eosin (Figure 13.3.4). The nucleus of the eosinophil will typically have two lobes and, if stained properly, the granules will have a distinct red to orange color.

The granules of eosinophils include vesicles filled with antihistamine molecules, which counteract the activities of histamines, inflammatory chemicals produced by basophils and mast cells. Some eosinophil granules contain molecules toxic to parasitic worms, which can enter the body through the integument, or when an individual consumes raw or undercooked fish or meat. Eosinophils are also capable of phagocytosis and are particularly effective at disposing of antigen-antibody complexes. Antibodies are immunoglobulin proteins produced by certain lymphocytes that carry out several functional aspects of the specific immune response. Antibodies are designed to match-up to a specific molecule, typically a protein called an antigen, on the surface of an invading pathogen such as a parasitic worm, bacterium, or viral particle. Antibodies can also match up with a ubiquitous molecule (such as one on the surface of a pollen granule) and cause an allergic reaction. In this case the antigen is called an allergen, but antibody-antigen complexes are formed during the body's response to the presence of the allergen as if it were the antigen of an invading pathogen. Because it is the function of the eosinophils to use phagocytosis to clear out the debris associated with antibody-antigen complexes, high counts of eosinophils are typical of patients experiencing allergies and some autoimmune diseases, but eosinophils can also be elevated in the case of parasitic worm infestations. Low counts may be due to drug toxicity and stress.

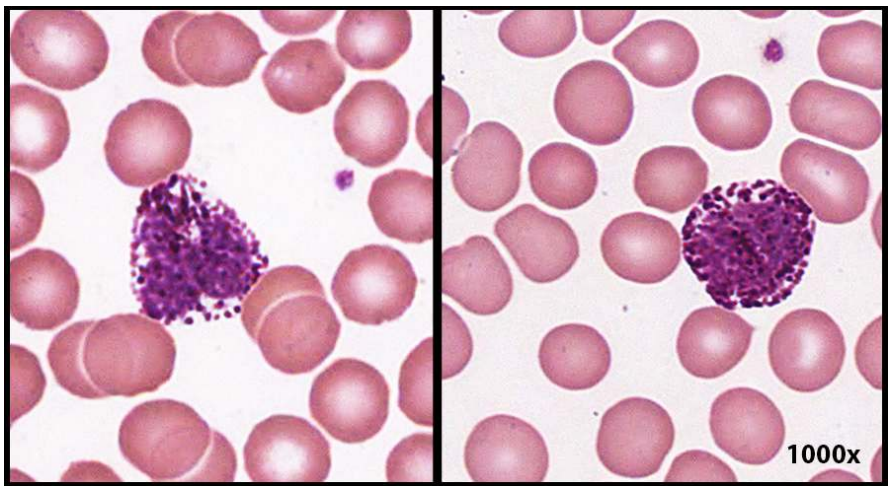


Figure 13.3.5: Basophils. Visually basophils are about twice the size of RBCs, have a nucleus with 2 lobes and have abundant dark blue or dark purple granules that are easy to see and often obscure the nucleus. *(Image credit: "Basophil" micrographs by Virginia Commonwealth University are licensed under CC BY-NC-SA 4.0.)*

Basophils are the least common leukocytes, typically comprising less than one percent of the total leukocyte count. They are slightly smaller than neutrophils and eosinophils at 8–10 μm in diameter. The granules of basophils stain best with basic (alkaline)

stains. Basophils contain large granules that pick up a dark blue stain and are so common they may make it difficult to see the two-lobed nucleus (Figure 13.3.5).

In general, basophils intensify the inflammatory response. They share this trait with mast cells of connective tissue proper. In the past, mast cells were considered to be basophils that left the circulation. However, this appears not to be the case, as the two cell types develop from different lineages.

The granules of basophils release histamines, which contribute to inflammation, and heparin, which opposes blood clotting. High counts of basophils are associated with allergies, parasitic infections, and hypothyroidism. Low counts are associated with pregnancy, stress, and hyperthyroidism.

Agranular Leukocytes

Agranular leukocytes (agranulocytes) contain smaller, less-visible granules in their cytoplasm than do granular leukocytes. The nucleus is simple in shape, sometimes with an indentation but without distinct lobes. There are two major types of agranulocytes: lymphocytes and monocytes (Figure 13.3.6).

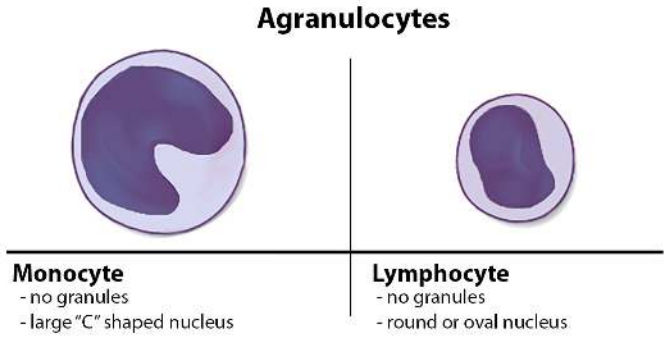


Figure 13.3.6: Agranulocytes. The cytoplasm of agranulocytes appears smooth. A monocyte is the largest WBC. It has a large nucleus shaped like a bean or a "C" and abundant cytoplasm. A lymphocyte, when un-activated, is the smallest WBC. Its nucleus is round or oval in shape and it occupies most of the interior of the cell. *(Image credit: "Agranulocytes" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original by OpenStax.)*

Lymphocytes are the only formed element of blood that arises from lymphoid stem cells. Although they form initially in the red bone marrow, much of their subsequent development and reproduction occurs in the lymphatic tissues. Lymphocytes are the second most common type of leukocyte, accounting for about 20–30 percent of all leukocytes, and are an essential part of the immune response. The size range of lymphocytes is quite extensive, with some authorities recognizing two size classes and others three. Typically, the large cells are 10–14 μm and have a smaller nucleus-to-cytoplasm ratio (Figure 13.3.7). The smaller cells are typically 6–9 μm with a larger volume of nucleus to cytoplasm, creating a “halo” effect. A few cells may fall outside these ranges, at 14–17 μm. This finding has led to the three size range classification.

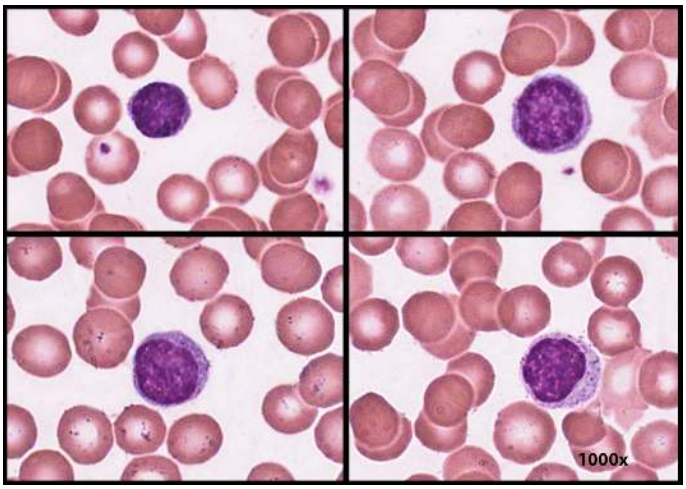


Figure 13.3.7: Lymphocytes. Lymphocytes are the smallest leukocytes and typically have a round or oval nucleus with a small ring of cytoplasm. They come in a variety of sizes, but none have abundant cytoplasm compared to the size of the nucleus. *(Image credit: "Lymphocyte" micrographs by Virginia Commonwealth University are licensed under CC BY-NC-SA 4.0.)*

The three major groups of lymphocytes include natural killer cells, B cells, and T cells. **Natural killer (NK) cells** are capable of recognizing cells that do not express “self” proteins on their plasma membrane or that contain foreign or abnormal markers. These “non-self” cells include abnormal body cells such as cancer cells, cells infected with a virus, and other cells with atypical surface proteins. Thus, they provide generalized, nonspecific immunity. The larger lymphocytes are typically NK cells.

B cells and T cells, also called **B lymphocytes** and **T lymphocytes**, play prominent roles in defending the body against specific pathogens (disease-causing microorganisms) and are involved in specific immunity. One form of B cells (plasma cells) produces the antibodies or immunoglobulins that bind to specific foreign or abnormal components of plasma membranes. This is also referred to as humoral (body fluid) immunity, since antibodies are proteins dissolved in body fluids. T cells provide cellular-level immunity by physically attacking foreign or diseased cells. A **memory cell** is a variety of both B and T cells that forms after exposure to a pathogen and mounts rapid responses upon subsequent exposures. Unlike other leukocytes, memory cells may live for many years. B cells undergo a maturation process in the bone marrow (B for bone marrow), whereas T cells undergo maturation in the thymus (T for thymus). This site of the maturation process gives rise to the name B and T cells. Smaller lymphocytes are either B or T cells; they cannot be differentiated in a normal blood smear.

Abnormally high lymphocyte counts are characteristic of viral infections as well as some types of cancer. Abnormally low lymphocyte counts are characteristic of prolonged (chronic) illness or immunosuppression, including that caused by HIV infection and drug therapies that often involve steroids.

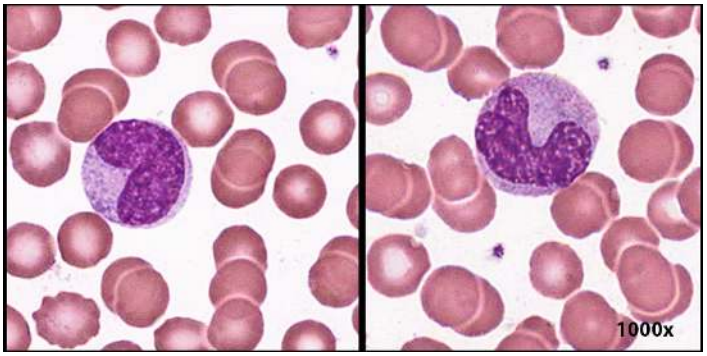


Figure 13.3.8: Monocytes. Monocytes are the largest leukocytes and typically have an indented nucleus ("C" or "U" shaped) with a volume of cytoplasm that is on par with the size of the nucleus. *(Image credit: "Monocyte" micrographs by Virginia Commonwealth University are licensed under CC BY-NC-SA 4.0.)*

Monocytes originate from myeloid stem cells and they normally represent 2–8 percent of the total leukocyte count. They are typically easily recognized by their large size of 12–20 μm and indented or horseshoe-shaped nuclei Figure 13.3.8. Macrophages are monocytes that have left the circulation and further differentiated; macrophages are larger than monocytes and feature many extensions of the plasma membrane spread evenly around their periphery to increase their surface area. Macrophages phagocytize debris, foreign pathogens, worn-out erythrocytes, and many other dead, worn out, or damaged cells. Macrophages also release antimicrobial defensins and chemotactic chemicals that attract other leukocytes to the site of an infection. Some macrophages reside permanently in specific locations of the body, whereas others wander primarily through the matrix of connective tissues patrolling for abnormal cells.

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

Lifecycle of Leukocytes

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

DISORDERS OF THE....

Leukocytes

Leukopenia is a condition in which too few leukocytes are produced. If this condition is pronounced, the individual may be unable to ward off disease. Excessive leukocyte proliferation is known as **leukocytosis**. Although leukocyte counts are high,

the cells themselves are often nonfunctional, leaving the individual at increased risk for disease.

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

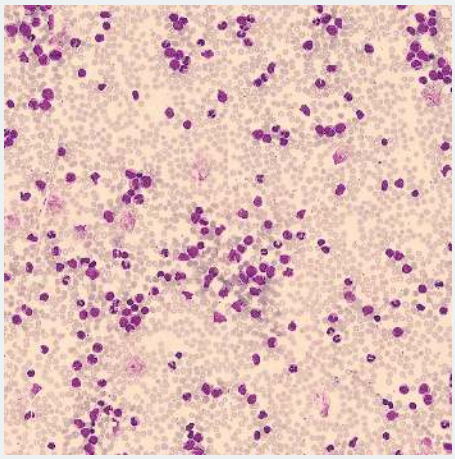


Figure 13.3.9: Chronic Myelogenous Leukemia. Notice the overabundance of white blood cells in this blood smear. *(Image credit: "CML Accelerated Phase" by El*Falal via Wikimedia Commons is licensed under CC BY-SA 4.0 International.)*

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

Platelets

Platelets are essential for the formation of blood clots to prevent blood loss in the event of damage to a blood vessel wall.

Characteristics and Functions of Platelets

You may occasionally see platelets referred to as **thrombocytes**, but because this name suggests they are a type of cell, it is misleading. A platelet is not a cell but rather a fragment of the cytoplasm of a cell called a **megakaryocyte** that is surrounded by a plasma membrane. Megakaryocytes are descended from myeloid stem cells and are large, typically 50–100 μm in diameter, and contain an enlarged, lobed nucleus (Figure 13.3.10). These remain within red bone marrow tissue and ultimately form platelet-precursor extensions that extend through the walls of bone marrow capillaries to release into the circulation thousands of cytoplasmic fragments, each enclosed by a bit of plasma membrane. These enclosed fragments are platelets. Each megakaryocyte releases 2,000–3,000 platelets during its lifespan. Following platelet release, megakaryocyte remnants, which are little more than a cell nucleus, are consumed by macrophages.

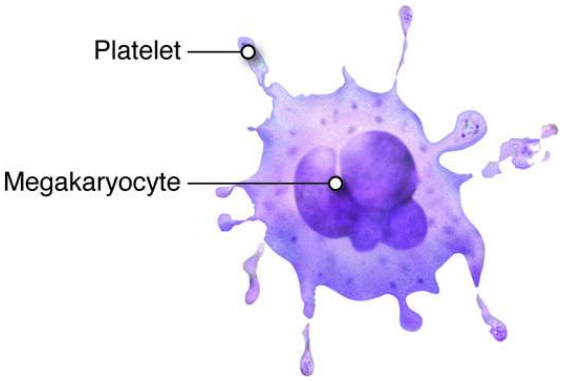


Figure 13.3.10: Megakaryocyte and Platelets. A platelet is a fragment of a cell. When activated, its plasma membrane gains surface area with many hairlike extensions and becomes sticky. *(Image credit: "Megakaryocyte and Platelets" by Cenveo is licensed under CC BY 3.0.)*

Platelets are relatively small, 2–4 μm in diameter, but numerous, with typically 150,000–160,000 per μL of blood. After entering the circulation, approximately one-third migrate to the spleen for storage for later release in response to any rupture in a blood vessel. They then become activated to perform their primary function, which is to limit blood loss. Activated platelets develop hair-like extensions to increase their surface area and become sticky. Platelets remain only about 10 days, then are phagocytized by macrophages.

Formed element	Major subtypes	Numbers present per microliter (μL) and mean (range)	Appearance in a standard blood smear	Summary of functions	Comments
Leukocytes (white blood cells)		7000 (5000–10,000)	Obvious dark-staining nucleus	All function in body defenses	Exit capillaries and move into tissues; lifespan of usually a few hours or days
	Granulocytes including neutrophils, eosinophils, and basophils	4360 (1800–9950)	Abundant granules in cytoplasm; nucleus normally lobed	Nonspecific (innate) resistance to disease	Classified according to membrane-bound granules in cytoplasm
	Neutrophils 	4150 (1800–7300)	Nuclear lobes increase with age; pale lilac granules	Phagocytic; particularly effective against bacteria. Release cytotoxic chemicals from granules	Most common leukocyte; lifespan of minutes to days
	Eosinophils 	165 (0–700)	Nucleus generally two-lobed; bright red-orange granules	Phagocytic cells; particularly effective with antigen- antibody complexes. Release antihistamines. Increase in allergies and parasitic infections	Lifespan of minutes to days
	Basophils 	44 (0–150)	Nucleus generally two-lobed but difficult to see due to presence of heavy, dense, dark purple granules	Promotes inflammation	Least common leukocyte; lifespan unknown
	Agranulocytes including lymphocytes and monocytes	2640 (1700–4950)	Lack abundant granules in cytoplasm; have a simple-shaped nucleus that may be indented	Body defenses	Group consists of two major cell types from different lineages
	Lymphocytes 	2185 (1500–4000)	Spherical cells with a single often large nucleus occupying much of the cell's volume; stains purple; seen in large (natural killer cells) and small (B and T cells) variants	Primarily specific (adaptive) immunity: T cells directly attack other cells (cellular immunity); B cells release antibodies (humoral immunity); natural killer cells are similar to T cells but nonspecific	Initial cells originate in bone marrow, but secondary production occurs in lymphatic tissue; several distinct subtypes; memory cells form after exposure to a pathogen and rapidly increase responses to subsequent exposure; lifespan of many years
	Monocytes 	455 (200–950)	Largest leukocyte with an indented or horseshoe-shaped nucleus	Very effective phagocytic cells engulfing pathogens or worn out cells; also serve as antigen-presenting cells (APCs) for other components of the immune system	Produced in red bone marrow; referred to as macrophages after leaving circulation
Platelets 		350,000 (150,000–500,000)	Cellular fragments surrounded by a plasma membrane and containing granules; purple stain	Hemostasis plus release growth factors for repair and healing of tissue	Formed from megakaryocytes that remain in the red bone marrow and shed platelets into circulation

Figure 13.3.11 Summary of leukocytes and platelets. / *"(Image Credit: Summary of Formed Elements in Blood" by OpenStax is licensed under CC BY 4.0) / Cropped from Original*

Hemostasis and Blood Clotting

Platelets are critical to **hemostasis**, the stoppage of blood flow following damage to a vessel. The process of hemostasis involves three steps: vascular spasm, platelet plug formation, and **coagulation** (formation of a blood clot).

During vascular spasm, smooth muscle in the wall of the damaged vessel responds to signal chemicals and pain receptors detecting the damage by constricting to restrict blood flow through the damaged area (the body's own way of applying pressure to the bleeding wound). Exposure of the connective tissue around the blood vessel begins to attract platelets to the wound side. The **platelet plug** is a temporary attempt to seal the damaged vessel wall. It forms when activated platelets clump and attach to the damaged area of the vessel wall. As the platelets form this initial plug, they also release signaling chemicals to initiate a cascade of events that allows the more durable and long-lasting blood clot to form. Platelets and injured tissues release a clotting factor called **prothrombin activator**, which converts **prothrombin** to **thrombin**. **Thrombin** converts **fibrinogen** to **fibrin threads.** Ca^{2+} ions are also necessary for the formation of these clotting factors. Once fibrin threads have formed, they act like a mesh that traps platelets and red blood cells in place, allowing for the tissue to repair itself and seal the wound.

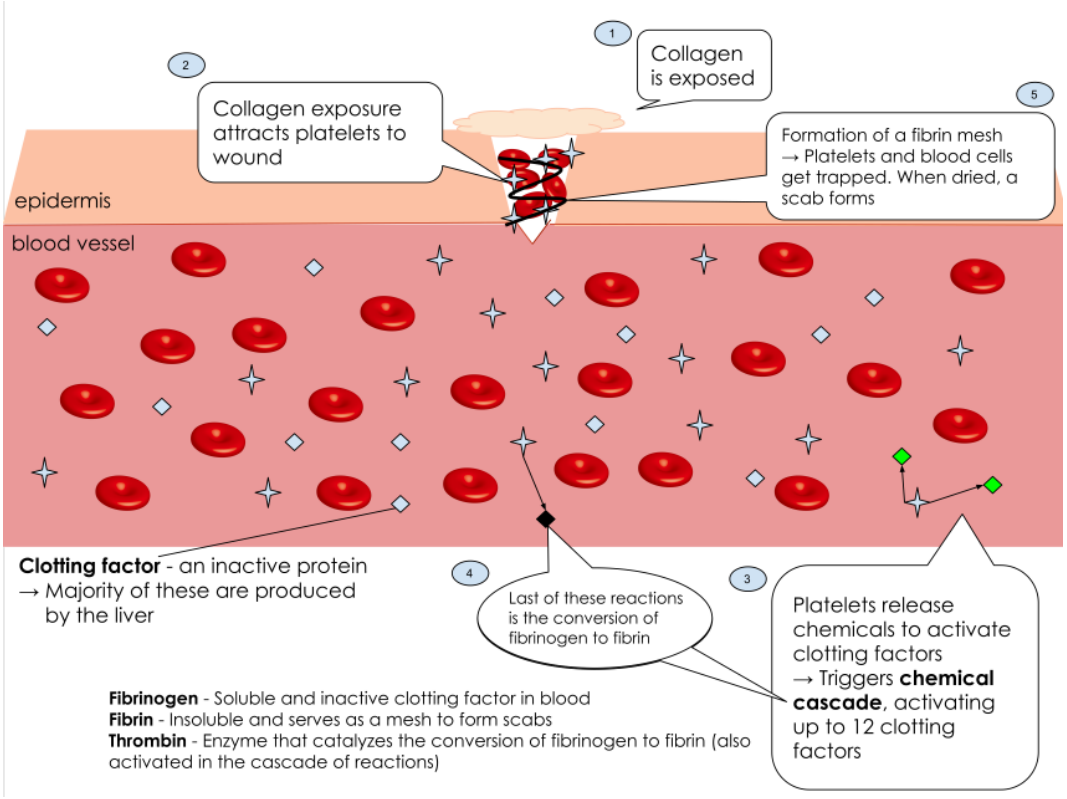


Figure 13.3.12 General steps of blood clot formation. Note: Not all clotting factors are explicitly pointed out; blue clotting factors are inactive, green are active, and black is the activated fibrinogen. *(Image credit: "Blood clot formation" by Victdomi is licensed under CC BY-SA 3.0, via Wikimedia Commons)*

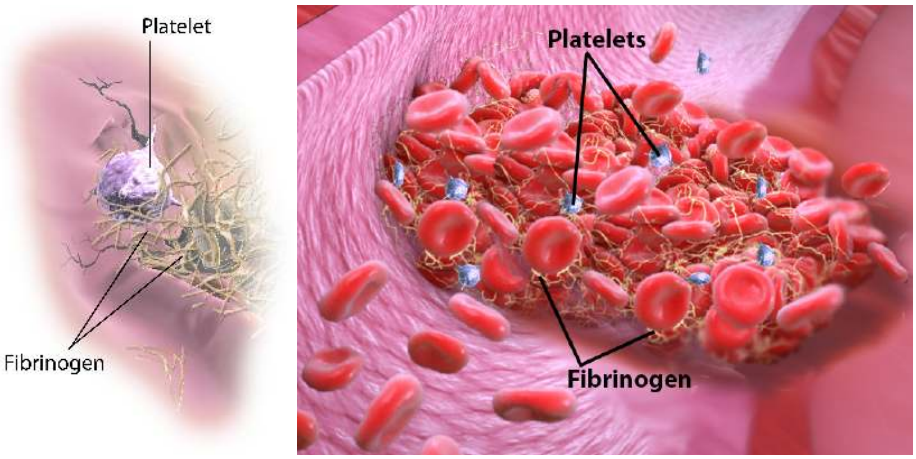


Figure 13.3.13: Blood Clot. A blood clot forms when a vessel wall is damaged. Inactive platelets and fibrinogen circulate in blood and both are activated if a vessel wall is damaged. Activated platelets grow in surface area and stick together, while fibrin becomes fibrous, creating a net-like mesh that sticks to the platelets and traps erythrocytes in the clot as well. *(Image Credits: "Blood Clot" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of originals by Scientific Animations and the National Science Foundation.)*

DISORDERS OF THE....

Platelets

Thrombocytosis is a condition in which there are too many platelets. This may trigger formation of unwanted blood clots (thrombosis), a potentially fatal disorder.

If there is an insufficient number of platelets, called **thrombocytopenia**, blood may not clot properly and excessive bleeding may result. **Hemophilia** is a group of genetic disorders also marked by excessive bleeding, but caused by inadequate production of one or more clotting factors, resulting in failure of the blood to properly clot.

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13.4: Blood Typing

Learning Objectives

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

- Describe the two basic physiological consequences of transfusion of incompatible blood
- Compare and contrast ABO and Rh blood groups
- Identify which blood groups may be safely transfused into patients with different ABO types
- Discuss the pathophysiology of hemolytic disease of the newborn

Blood transfusions in humans were risky procedures until the discovery of the major human blood groups by Karl Landsteiner, an Austrian biologist and physician, in 1900. Until that point, physicians did not understand that death sometimes followed blood transfusions, when the type of donor blood infused into the patient was incompatible with the patient's own blood. Blood groups are determined by the presence or absence of specific marker molecules on the plasma membranes of erythrocytes. With their discovery, it became possible for the first time to match patient-donor blood types and prevent transfusion reactions and deaths.

Antigens, Antibodies, and Transfusion Reactions

Antigens are substances that the body does not recognize as belonging to the "self" and that therefore trigger a defensive response from the leukocytes of the immune system. Here, we will focus on the role of immunity in blood transfusion reactions. With RBCs in particular, you may see the antigens referred to as isoantigens or agglutinogens (surface antigens) and the antibodies referred to as isoantibodies or agglutinins. In this chapter, we will use the more common terms antigens and antibodies.

Antigens are generally large proteins, but may include other classes of organic molecules, including carbohydrates, lipids, and nucleic acids. Following an infusion of incompatible blood, erythrocytes with foreign antigens appear in the bloodstream and trigger an immune response. Proteins called antibodies (immunoglobulins), which are produced by certain B lymphocytes called plasma cells, attach to the antigens on the plasma membranes of the infused erythrocytes and cause them to adhere to one another.

- When the antibodies attach to the foreign antigens, they cause the foreign erythrocytes to clump up together. This process is called agglutination.
- The clumps of erythrocytes block small blood vessels throughout the body, depriving tissues of oxygen and nutrients.
- As the erythrocyte clumps are degraded, in a process called hemolysis, their hemoglobin is released into the bloodstream. This hemoglobin travels to the kidneys, which are responsible for filtration of the blood. However, the load of hemoglobin released can easily overwhelm the kidney's capacity to clear it, and the patient can quickly develop kidney failure.

More than 50 antigens have been identified on erythrocyte membranes, but the most significant in terms of their potential harm to patients are classified in two groups: the ABO blood group and the Rh blood group.

The ABO Blood Group

Although the ABO blood group name consists of three letters, ABO blood typing designates the presence or absence of just two antigens, A and B, on the surface of RBCs. Both antigens are glycoproteins, meaning they are proteins linked to a sugar molecule and are found embedded within the cell membrane of these cells. People whose erythrocytes have A antigens on their erythrocyte membrane surfaces are designated blood type A, and those whose erythrocytes have B antigens are blood type B. People can also have both A and B antigens on their erythrocytes, in which case they are blood type AB. People with neither A nor B antigens are designated blood type O. ABO blood types are genetically determined.

The body must be exposed to a foreign antigen before an antibody can be produced. ABO blood group antigens are found in foods and microbes throughout nature. Thus, the human immune system is exposed to A and B antigens at an early age and antibodies are formed naturally. Individuals with type A blood—without any prior exposure to incompatible blood—have naturally-formed antibodies to the B antigen. These anti-B antibodies are found circulating in their blood plasma. These antibodies will cause agglutination and hemolysis if they ever encounter erythrocytes with B antigens. Similarly, an individual with type B blood has naturally-formed anti-A antibodies. Individuals with type AB blood, which has both antigens, do not have naturally-formed antibodies to either of these. People with type O blood lack antigens A and B on their erythrocytes, but both anti-A and anti-B antibodies circulate in their blood plasma.

Rh Blood Groups

The Rh blood group is classified according to the presence or absence of a second erythrocyte antigen identified as Rh. (It was first discovered in a type of primate known as a rhesus macaque, which is often used in research, because its blood is similar to that of humans.) Although dozens of Rh antigens have been identified, only one, designated D, is clinically important. Those who have the Rh D antigen present on their erythrocytes—about 85 percent of Americans—are described as Rh positive (Rh^+) and those who lack it are Rh negative (Rh^-). Note that the Rh group is distinct from the ABO group, so any individual, no matter their ABO blood type, may have or lack this Rh antigen. When identifying a patient's blood type, the Rh group is designated by adding the word positive or negative to the ABO type. For example, A positive (A^+) means ABO group A blood with the Rh antigen present, and AB negative (AB^-) means ABO group AB blood without the Rh antigen.

Table 13.4.1 summarizes the distribution of the ABO and Rh blood types within the United States.

Table 13.4.1: Summary of ABO and Rh Blood Types within the United States

Blood Type	Asian	Black non-Hispanic	Hispanic	North American Indian	White non-Hispanic
A^+	27.3	24.0	28.7	31.3	33.0
A^-	0.5	1.9	2.4	3.8	6.8
B^+	25.0	18.4	9.2	7.0	9.1
B^-	0.4	1.3	0.7	0.9	1.8
AB^+	7.0	4.0	2.3	2.2	3.4
AB^-	0.1	0.3	0.2	0.3	0.7
O^+	39.0	46.6	52.6	50.0	37.2
O^-	0.7	3.6	3.9	4.7	8.0

In contrast to the ABO group antibodies, which are pre-formed (meaning they are formed without exposure to an incompatible blood type), antibodies to the Rh antigen are produced only in Rh^- individuals after exposure to the antigen. This process, called sensitization, occurs following a transfusion with Rh-incompatible blood or, more commonly, with the birth of an Rh^+ baby to an Rh^- person. Problems are rare in a first pregnancy, since the baby's Rh^+ cells rarely cross the placenta (the organ of gas and nutrient exchange between the fetus and the pregnant person). However, during or immediately after birth, the Rh^- parent can be exposed to the baby's Rh^+ cells (Figure 13.4.1). Research has shown that this occurs in about 13−14 percent of such pregnancies. After exposure, the immune system of the person who has given birth begins to generate anti-Rh antibodies. If this same person should then become pregnant with another Rh^+ baby, the Rh antibodies they have produced can cross the placenta into the fetal bloodstream and destroy the fetal RBCs. This condition, known as h**emolytic disease of the newborn (HDN)** or erythroblastosis fetalis, may cause anemia in mild cases, but the agglutination and hemolysis can be so severe that without treatment the fetus may die in the womb or shortly after birth.

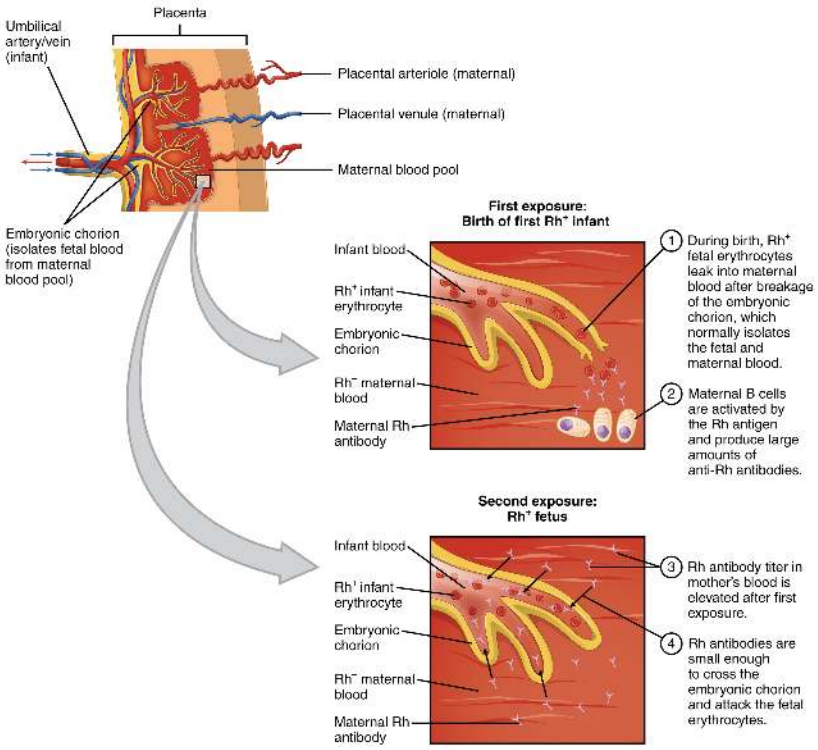


Figure 13.4.1:Hemolytic Disease of the Newborn. The first exposure of an Rh^- person to Rh^+ erythrocytes during pregnancy induces sensitization. Anti-Rh antibodies begin to circulate in the pregnant person's bloodstream. A second exposure occurs with a subsequent pregnancy with an Rh^+ fetus in the uterus. During that subsequent pregnancy, the pregnant person's anti-Rh antibodies may cross the placenta and enter the fetal bloodstream, causing agglutination and hemolysis of fetal erythrocytes.

A drug known as RhoGAM, short for Rh immune globulin, can temporarily prevent the development of Rh antibodies in the Rh^- parent, thereby averting this potentially serious disease for the fetus. RhoGAM antibodies destroy any fetal Rh^+ erythrocytes that may cross the placental barrier. RhoGAM is normally administered to Rh^- pregnant people during weeks 26−28 of pregnancy and within 72 hours following birth. It has proven remarkably effective in decreasing the incidence of HDN. Earlier we noted that the incidence of HDN in an Rh^+ subsequent pregnancy to an Rh^- person is about 13–14 percent without preventive treatment. Since the introduction of RhoGAM in 1968, the incidence has dropped to about 0.1 percent in the United States.

Determining ABO Blood Types

Clinicians are able to determine a patient’s blood type quickly and easily using commercially prepared antibodies. An unknown blood sample is allocated into separate wells. Into one well a small amount of anti-A antibody is added, and to another a small

amount of anti-B antibody. If the antigen is present, the antibodies will cause visible agglutination of the cells (Figure 13.4.2). The blood should also be tested for Rh antibodies.

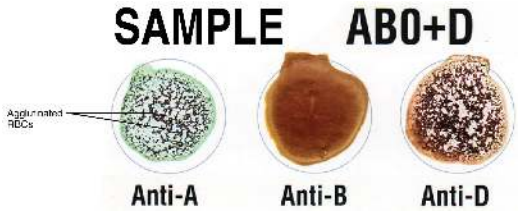


Figure 13.4.2: Cross Matching Blood Types This sample of a commercially produced “bedside” card enables quick typing of both a recipient’s and donor’s blood before transfusion. The card contains three reaction sites or wells. One is coated with an anti-A antibody, one with an anti-B antibody, and one with an anti-D antibody (tests for the presence of Rh factor D). Mixing a drop of blood and saline into each well enables the blood to interact with a preparation of type-specific antibodies, also called anti-seras. Agglutination of RBCs in a given site indicates a positive identification of the blood antigens, in this case A and Rh antigens for blood type A^+. For the purpose of transfusion, the donor’s and recipient’s blood types must match.

ABO Transfusion Protocols

To avoid transfusion reactions, it is best to transfuse only matching blood types; that is, a type B^+ recipient should ideally receive blood only from a type B^+ donor and so on. That said, in emergency situations, when acute hemorrhage threatens the patient’s life, there may not be time for cross matching to identify blood type. In these cases, blood from a **universal donor**—an individual with type O^- blood—may be transfused. Although it is always preferable to cross match a patient’s blood before transfusing, in a true life-threatening emergency situation, this is not always possible, and these procedures may be implemented.

A patient with blood type AB^+ is known as the **universal recipient**. This patient can theoretically receive any type of blood, because the patient’s own blood—having both A and B antigens on the erythrocyte surface—does not produce anti-A or anti-B antibodies. In addition, an Rh^+ patient can receive both Rh^+ and Rh^- blood. Figure 13.4.3 summarizes the blood types and compatibilities.

At the scene of multiple-vehicle accidents, military engagements, and natural or human-caused disasters, many victims may suffer simultaneously from acute hemorrhage, yet type O blood may not be immediately available. In these circumstances, medics may at least try to replace some of the volume of blood that has been lost. This is done by intravenous administration of a saline solution that provides fluids and electrolytes in proportions equivalent to those of normal blood plasma. Research is ongoing to develop a safe and effective artificial blood that would carry out the oxygen-carrying function of blood without the RBCs, enabling transfusions in the field without concern for incompatibility. These blood substitutes normally contain hemoglobin- as well as perfluorocarbon-based oxygen carriers.

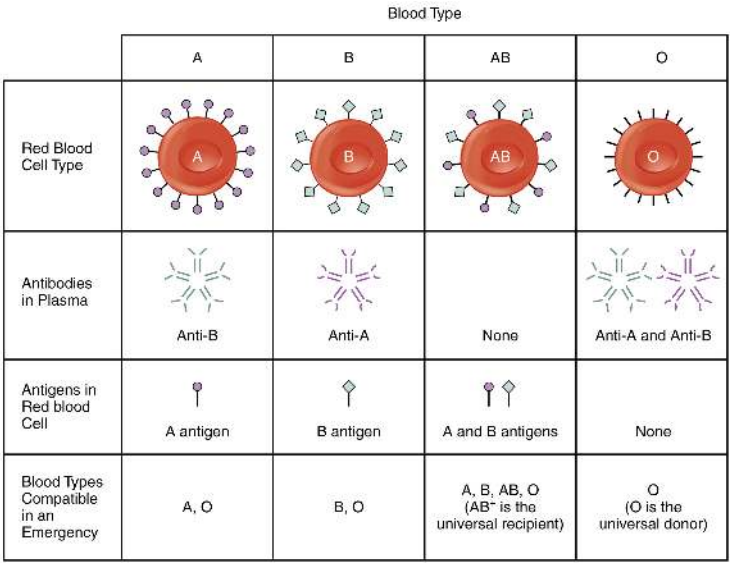


Figure 13.4.3: ABO Blood Group This chart summarizes the characteristics of the blood types in the ABO blood group. See the text for more on the concept of a universal donor or recipient.

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13.5: Review Questions

Use the following questions to test your knowledge on Blood.

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CHAPTER OVERVIEW

14: The Cardiovascular System - Heart and Blood Vessels

14.1: Heart Anatomy
14.2: Cardiac Muscle and Electrical Activity
14.3: Cardiac Cycle
14.4: Structure and Function of Blood Vessels
14.5: Blood Flow, Blood Pressure, and Resistance
14.6: Review Questions

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14.1: Heart Anatomy

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

- Describe the location and position of the heart within the body cavity
- Describe the internal and external anatomy of the heart
- Identify the tissue layers of the heart and pericardium
- Compare systemic circulation to pulmonary circulation
- Trace the pathway of oxygenated and deoxygenated blood through the chambers of the heart

The vital importance of the heart is obvious. If one assumes an average rate of contraction of 75 contractions per minute, a human heart would contract approximately 108,000 times in one day, more than 39 million times in one year, and nearly 3 billion times during a 75-year lifespan. Each of the major pumping chambers of the heart ejects approximately 70 mL of blood per contraction in a resting adult. This would be equal to 5.25 liters of fluid per minute and approximately 14,000 liters per day. Over one year, that would equal 10,000,000 liters or 2.6 million gallons of blood sent through roughly 60,000 miles of vessels.

Location and Position of the Heart

The human heart is located within the thoracic cavity, medially between the lungs in the region known as the mediastinum. The mediastinum also includes the portions of the major blood vessels, the trachea, and the esophagus that are positioned between the lungs medially. Figure 14.1.1 shows the position of the heart within the thoracic cavity. Within the mediastinum, the heart is separated from the other mediastinal structures and is held in place by a tough wrapping known as the pericardium, or pericardial sac. The sac also limits the range of motion of the heart as it beats. The double layered pericardial sac creates a thin space surrounding the heart called the **pericardial cavity** that is filled with serous fluid to prevent friction as the heart beats.

The dorsal surface of the heart lies near the bodies of the vertebrae and its anterior surface sits deep to the sternum and costal cartilages. The great veins, the superior and inferior venae cavae, and the great arteries, the aorta and pulmonary trunk, are attached to the superior surface of the heart, called the base. The base of the heart is located at the level of the third costal cartilage, as seen in Figure 14.1.1. The inferior tip of the heart, the apex, lies just to the left of the sternum between the junction of the fourth and fifth ribs near their articulation with the costal cartilages. The heart is also rotated slightly around its vertical axis such that the more of the right side of the heart is visible in an anterior view while more of the left side is visible in a posterior view. It is important to remember the position and orientation of the heart when placing a stethoscope on the chest of a patient and listening for heart sounds, and also when looking at images taken from a midsagittal perspective. The slight deviation of the apex to the left is reflected in a depression in the medial surface of the inferior lobe of the left lung, called the **cardiac notch**.

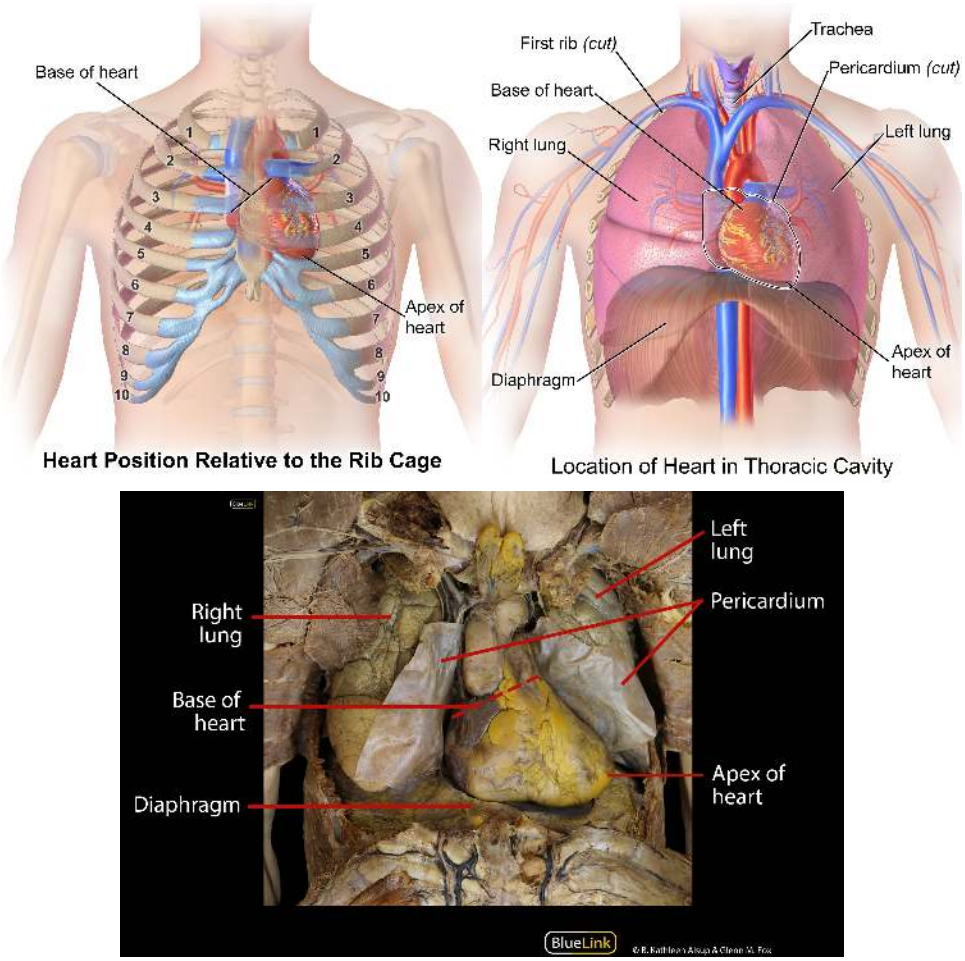


Figure 14.1.1: Location of Heart in the Thorax. The heart is located within the thoracic cavity, medially between the lungs in the mediastinum. It is about the size of a fist, is broad at the top, and tapers toward the base. (Caption from OpenStax) *(Image credits: "Blausen 0467 - Heart position relative to the rib cage - English labels" by Blausen.com staff (2014), license: CC BY. Source: "Medical gallery of Blausen Medical 2014" https://en.wikiversity.org/wiki/Wiki...n_Medical_2014 "Blausen 0458 - Heart position in the thoracic cavity - English labels" by Blausen.com staff (2014), license: CC BY. Source: "Medical gallery of Blausen Medical 2014" https://en.wikiversity.org/wiki/Wiki...n_Medical_2014. "Cadaver Heart" by BlueLink is licensed under CC BY-NC 4.0 with notification of the original authors.)*

EVERYDAY CONNECTION

CPR

The position of the heart in the torso between the vertebrae and sternum (see Figure 14.1.2 for the position of the heart within the thorax) allows for individuals to apply an emergency technique known as cardiopulmonary resuscitation (CPR) if the heart of a patient should stop. If one hand is placed over the other in the middle of the chest about two finger-widths superior to the xiphoid process (Figure 14.1.2), it is possible to manually compress the blood within the heart enough to push some of the blood within it into the pulmonary and systemic circuits. This is particularly critical for the brain, as irreversible damage and death of neurons occur within minutes of loss of blood flow. Current standards call for compression of the chest at least 5 cm deep and at a rate of 100 compressions per minute, a rate equal to the beat in “Staying Alive,” recorded in 1977 by the Bee Gees. If you are unfamiliar with this song, a version is available on www.youtube.com. At this stage, the emphasis is on performing high-quality chest compressions, rather than providing artificial respiration. CPR is generally performed until the patient regains spontaneous contraction or is declared dead by an experienced healthcare professional.

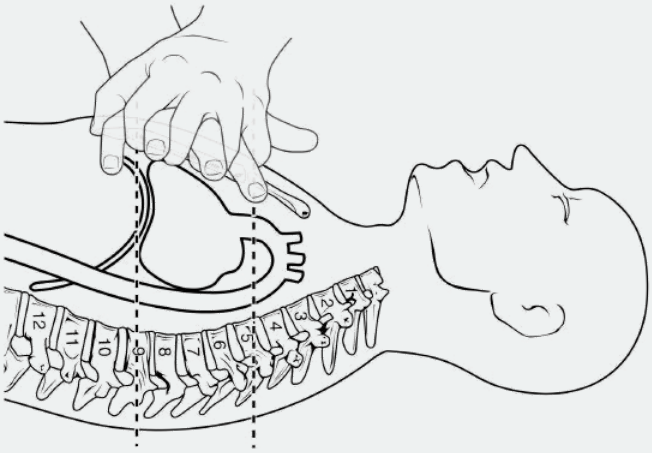


Figure 14.1.2: CPR Technique. If the heart should stop, CPR can maintain the flow of blood until the heart resumes beating. By applying pressure to the sternum, the blood within the heart will be squeezed out of the heart and into the circulation. Proper positioning of the hands on the sternum to perform CPR would be between the lines at T4 and T9, or directly superior to two finger-widths above the xiphoid process. (Image credit: "CPR Technique" by OpenStax College is licensed under CC BY 3.0)

When performed by untrained or overzealous individuals, CPR can result in broken ribs or a broken sternum, and can inflict additional severe damage on the patient. It is also possible, if the hands are placed too low on the sternum, to manually drive the xiphoid process into the liver, a consequence that may prove fatal for the patient. Proper training is essential. This proven life-sustaining technique is so valuable that virtually all medical personnel as well as concerned members of the public should be certified and routinely re-certified in its application. CPR courses are offered at a variety of locations, including colleges, hospitals, the American Red Cross, and some commercial companies. They normally include practice of the compression technique on a mannequin.

The shape of the heart is similar to a pinecone, rather broad at the superior surface (the **base,** on the posterior side) and tapering to the **apex** (Figure 14.1.1). The apex of the heart is inferior and to the left while the base of the heart is superior and posterior.

A typical heart is approximately the size of your fist: 12 cm (5 in) in length, 8 cm (3.5 in) wide, and 6 cm (2.5 in) in thickness. Heart size is dependent on body size, the typical range is 250 to 350 grams (about 1/2 to 3/4 of a pound). The heart of a well-trained athlete, especially one specializing in aerobic sports, can be considerably larger than this. Cardiac muscle responds to exercise in a manner similar to that of skeletal muscle. That is, exercise results in the addition of protein myofilaments that increase the size of the individual cells without increasing their numbers, a concept called hypertrophy. Hearts of athletes can pump blood more effectively at lower rates than those of non-athletes. Enlarged hearts are not always a result of exercise; they can result from pathologies, such as **hypertrophic cardiomyopathy**. The cause of an abnormally enlarged heart muscle is unknown, but hearts with this condition often have mutation(s) in one of the proteins of the sarcomere, such as myosin or troponin (Popa-Fotea *et al*, 2019). The condition can be inherited, is often undiagnosed and can cause sudden death in apparently otherwise healthy young people.

Pulmonary and Systemic Circuits

There are two distinct but linked circuits in the human blood circulation called the pulmonary and systemic circuits. Although both circuits transport blood and everything it carries, we can initially view the circuits from the point of view of gases. The **pulmonary circuit** transports blood to and from the lungs, where it picks up oxygen and delivers carbon dioxide for exhalation. The **systemic circuit** transports **oxygenated blood** to virtually all of the tissues of the body and returns relatively deoxygenated blood and carbon dioxide to the heart to be sent back to the pulmonary circulation.

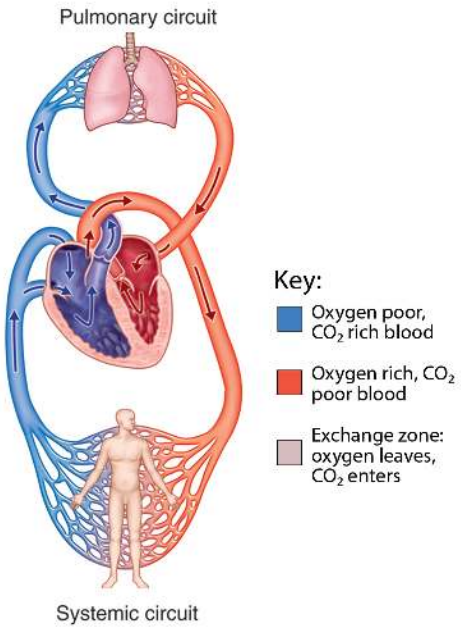


Figure 14.1.3: Cardiovascular System Circuits. The pulmonary circuit moves blood from the right side of the heart to the lungs and back to the heart. The systemic circuit moves blood from the left side of the heart to the head and body and returns it to the right side of the heart to repeat the cycle. The arrows indicate the direction of blood flow, and the colors show the relative levels of oxygen concentration. (Caption from OpenStax) *(Image Credit: "Systemic and Pulmonary Circuits" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original by Open Learning Initiative.)*

Pericardium and the Heart Wall

The heart is contained within the pericardium. This serous membrane attaches to the large blood vessels superior to the heart and to the diaphragm and helps to anchor the heart in place within the thoracic cavity. The wall of the heart is composed of three layers of unequal thickness. From superficial to deep, these are the epicardium, the myocardium, and the endocardium (see Figure 14.1.4). The outermost layer of the wall of the heart is also the innermost layer of the pericardium, the epicardium, or the visceral pericardium discussed earlier.

The multi-layered membrane that directly surrounds the heart and defines the pericardial cavity is called the **pericardium** or **pericardial sac**. It also surrounds the “roots” of the major vessels, or the areas of closest proximity to the heart. The pericardium, which literally translates as “around the heart,” consists of two distinct sublayers: the sturdy outer **fibrous pericardium** and the inner **serous pericardium**. The fibrous pericardium is made of tough, dense irregular connective tissue that protects the heart and maintains its position in the thorax while also limiting the heart's motion during the heartbeat. The more delicate serous pericardium consists of two layers: the **parietal pericardium**, which is fused to the fibrous pericardium, and an inner **visceral pericardium**, or **epicardium**, which is fused to the heart and is part of the heart wall. The pericardial cavity, filled with lubricating serous fluid, lies between the epicardium and the parietal pericardium. The serous layers of the pericardium consist of a simple squamous epithelium anchored by a layer of areolar connective tissue. The areolar connective tissue connects the parietal pericardium to the fibrous pericardium and it connects the epicardium to the myocardium. The epithelial tissue secretes the lubricating serous fluid that fills the pericardial cavity and reduces friction as the heart contracts. Adipose connective tissue can also be found in the epicardium, particularly in the areas where blood vessels run along the heart's surface. Figure 14.1.4 illustrates the pericardial membrane and the layers of the heart.

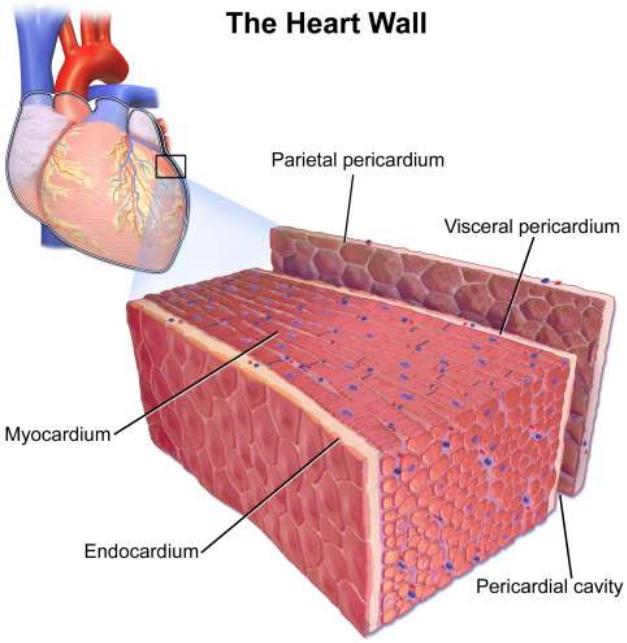


Figure 14.1.4:Pericardial Membranes and Layers of the Heart Wall. The pericardial membrane that surrounds the heart consists of three layers and the pericardial cavity. The heart wall also consists of three layers. The pericardial membrane and the heart wall share the epicardium. (Caption from OpenStax) *(Image credit: "Heart Wall" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original by Blausen.com staff (2014).)*

The middle and thickest layer is the **myocardium.** Composed primarily of cardiac muscle, with small amounts of endomysium, the contractile force of the myocardium propels blood forward through the pulmonary and systemic circuits. As with skeletal muscle, the amount of force generated increases with increasing numbers of myofibers.

The myocardium is built upon a framework of dense connective tissue called the cardiac skeleton (covered in detail later in this section). It is the contraction of the myocardium that pumps blood through the heart and into the major arteries. The muscle pattern is elegant and complex, as the muscle cells swirl and spiral to form the chambers of the heart. To create this complex 3D structure, cardiac muscle cells approximately follow a figure 8 pattern around the atria and around the roots of the great vessels. Deeper ventricular muscles also form a figure 8 around the two ventricles and proceed toward the apex. More superficial layers of ventricular muscle wrap around both ventricles. This complex swirling pattern allows the heart to pump blood more effectively by decreasing the size of each interior chamber during contraction. Figure 14.1.5 illustrates the arrangement of muscle cells.

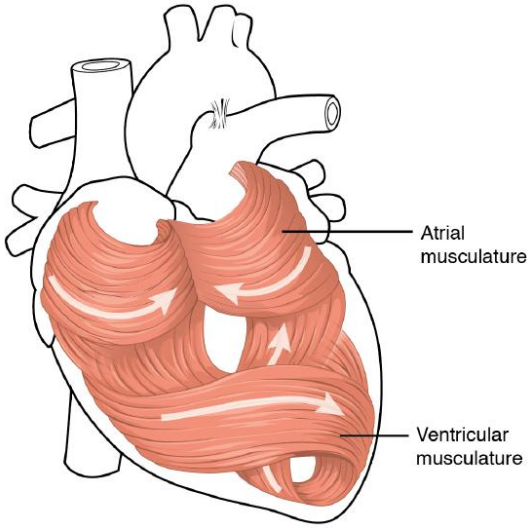


Figure 14.1.5: Cardiac Musculature. The swirling pattern of cardiac muscle tissue contributes significantly to the heart's ability to pump blood effectively. *(Image credit: "Heart Musculature" by OpenStax is licensed under CC BY 3.0.)*

Although the ventricles on the right and left sides pump the same amount of blood per contraction, the muscle of the left ventricle is much thicker and better developed than that of the right ventricle. In order to overcome the high resistance required to pump blood into the long systemic circuit, the left ventricle must generate a great amount of pressure. The right ventricle does not need to generate as much pressure, since the pulmonary circuit is shorter and provides less resistance. Figure 14.1.6 illustrates the differences in muscular thickness needed for each of the ventricles.

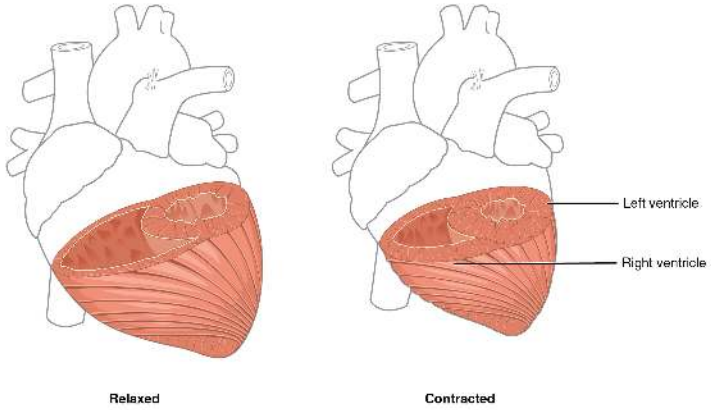


Figure 14.1.6: Differences in Ventricular Muscle Thickness. The myocardium in the left ventricle is significantly thicker than that of the right ventricle. In both relaxed and contracting states, also note the differences in the relative size of the lumens, the region inside each ventricle where the blood is contained. *(Image credit: "Ventricular Muscle Thickness" by OpenStax is licensed under CC BY 3.0.)*

The innermost layer of the heart wall, the **endocardium**, is joined to the myocardium with a thin layer of areolar connective tissue. The endocardium lines the chambers where the blood circulates and covers the heart valves. It is made of simple squamous epithelium called **endothelium**, which is continuous with the endothelial lining of the blood vessels (Figure 14.1.4).

DISORDERS OF THE...

Heart: Cardiac Tamponade

If excess fluid builds within the pericardial space, it can lead to a condition called cardiac tamponade, or pericardial tamponade. With each contraction of the heart, more fluid—in most instances, blood—accumulates within the pericardial cavity. In order to fill with blood for the next contraction, the heart must relax. However, the excess fluid in the pericardial cavity puts pressure on the heart and prevents full relaxation, so the chambers within the heart contain slightly less blood as they begin each heart cycle. Over time, less and less blood is ejected from the heart. If the fluid builds up slowly, as in hypothyroidism, the pericardial cavity may be able to expand gradually to accommodate this extra volume. Some cases of fluid in excess of one liter within the pericardial cavity have been reported. Rapid accumulation of as little as 100 mL of fluid following trauma may trigger cardiac tamponade. Other common causes include myocardial rupture, pericarditis, cancer, or even cardiac surgery. Removal of this excess fluid requires insertion of drainage tubes into the pericardial cavity. Premature removal of these drainage tubes, for example, following cardiac surgery, or clot formation within these tubes are causes of this condition. Untreated, cardiac tamponade can lead to death.

Surface Features of the Heart

The heart is composed of four hollow chambers: two atria and two ventricles. The thin walled **right and left atria** are the two superior chambers. While both atria are visible from the anterior, the majority of the left atrium is seen on the posterior aspect ((Figure 14.1.7). Each atrium has a superficial flap-like extension called an **auricle** because its shape resembles the external ear of a human (Figure 14.1.8). You may also hear them referred to as atrial appendages. The auricles can increase the atrial capacity at times of exertion by filling with blood and, thus, relieving high atrial pressure. The two ventricles are inferior to the atria and they form the largest portion of the heart. Their walls are significantly thicker than those of the atria as a large amount of muscle mass is needed to push the blood into the arteries. The **right ventricle** makes up the right side and much of the anterior portion of the heart, while the **left ventricle** makes up the left side and much of the posterior portion of the heart (Figure 14.1.6).

Also prominent along the superficial surfaces of the heart is a series of fat-filled grooves, each of which is known as a **sulcus** (plural = sulci), containing major coronary blood vessels. The deepest is the **coronary sulcus,** which encircles the heart between

the atria and ventricles. Located between the left and right ventricles are two shallower sulci: the **anterior interventricular sulcus** is visible on the anterior surface of the heart (Figure 14.1.8.*A*), whereas the **posterior interventricular sulcus** is visible on the posterior surface of the heart (Figure 14.1.8.*B*).

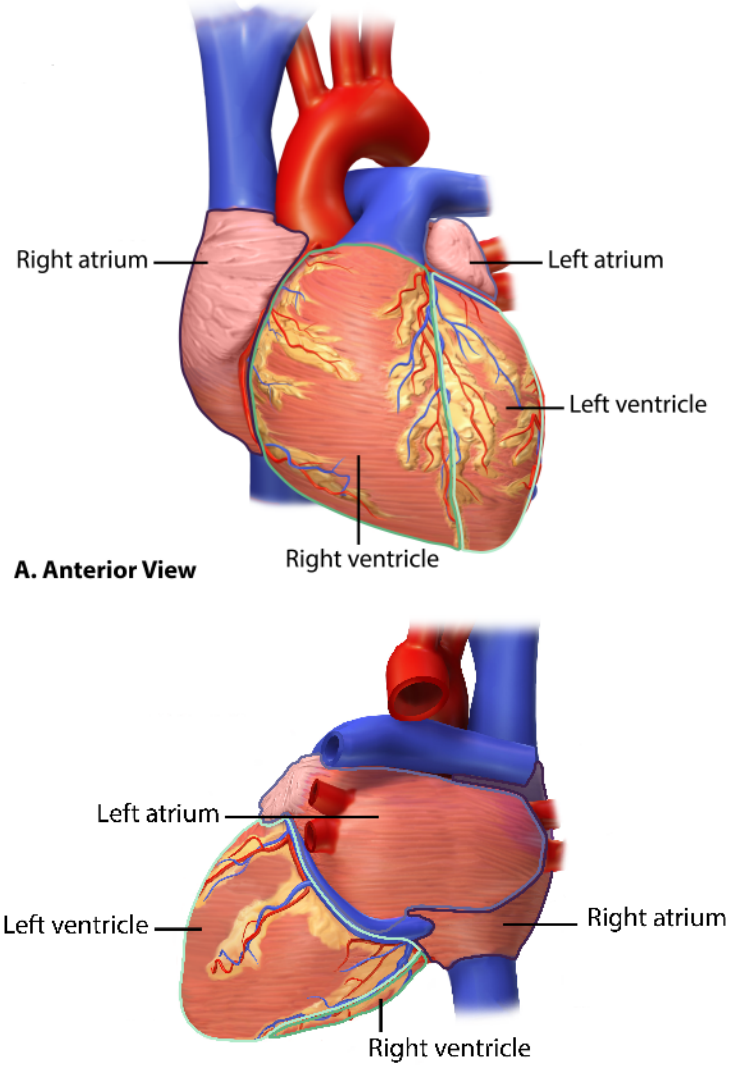


Figure 14.1.7: Superficial Heart Anatomy. Inside the pericardium, the surface features of the heart are visible. (Caption from OpenStax) *(Image credits: "Heart Chambers Anterior View" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original "Blausen 0451 - Anterior view of the heart - English labels" by Blausen Medical Communications, Inc.; "Heart Chambers Posterior View" by Jennifer Lange is licensed under under CC BY-NC-SA 4.0, modification of original "Blausen 0456 Heart Posterior" by Blausen Medical Communications, Inc.)*

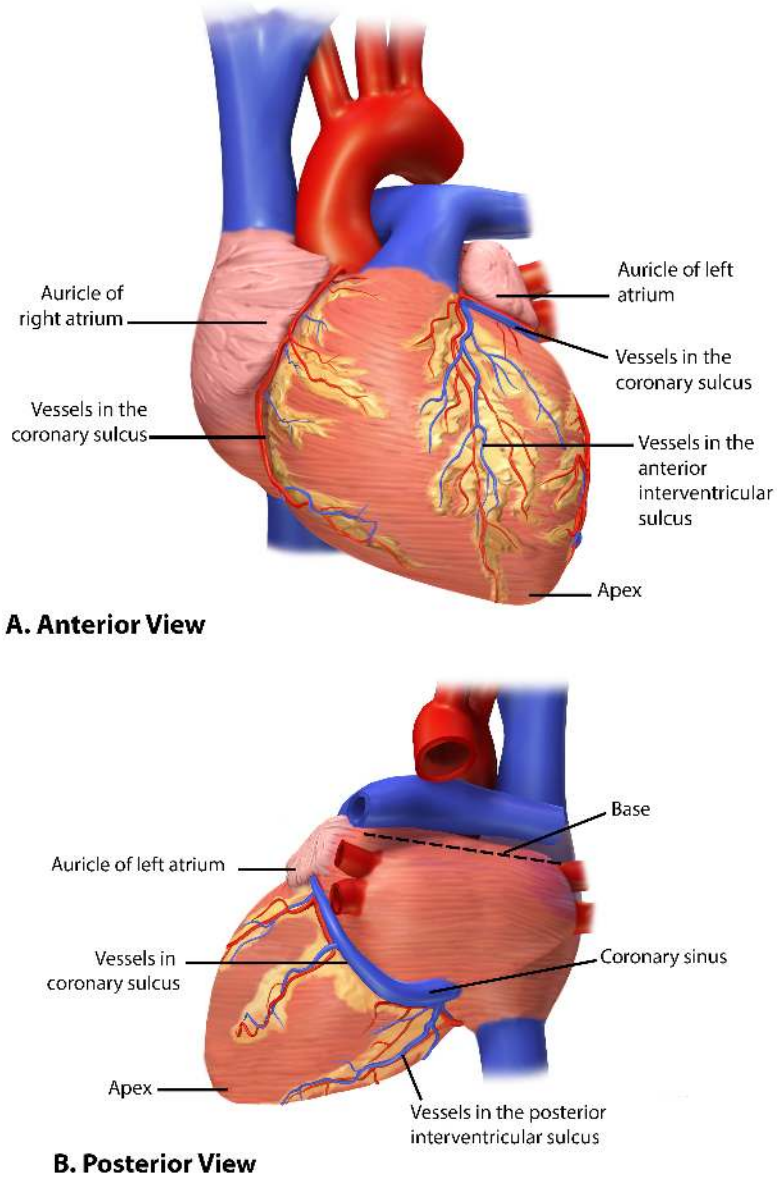


Figure 14.1.8: Superficial Heart Anatomy. Inside the pericardium, the surface features of the heart are visible. (Caption from OpenStax) *(Image credits: "Superficial Heart Anatomy Anterior View" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original "Blausen 0451 - Anterior view of the heart - English labels" by Blausen Medical Communications, Inc.; "Superficial Heart Anatomy - Posterior View" by Jennifer Lange is licensed under under CC BY-NC-SA 4.0, modification of original "Blausen 0456 Heart Posterior" by Blausen Medical Communications, Inc.)*

The Great Vessels

Blood enters and exits the heart through the largest arteries and veins, respectively, in the body. Termed the great vessels, these are the large arteries and veins directly connected with the heart, the: inferior vena cava, superior vena cava, pulmonary arteries, pulmonary veins, and the aorta (Figure 14.1.9).

The **pulmonary trunk** arises from the right ventricle and then splits into the **right** and **left pulmonary arteries**, each of which carries blood to the lung on their respective side. After circulating through the smaller blood vessels of the lungs the blood, which will have a relatively high oxygenation level and a relatively low carbon dioxide level, returns to the heart in the **right** and **left pulmonary veins** and enters the left atrium and then the left ventricle. The left side of the heart gives rise to the largest and thickest artery in the body, the **aorta**. The aorta directs blood along multiple systemic circuit routes to reach all of the body's organs. The systemic circuit returns blood to the right atrium through two of the great vessels. The **inferior vena cava** carries blood from regions inferior to the heart while the **superior vena cava** collects blood from the regions superior to the heart. The structure of these vessels will be discussed in Chapter 18.

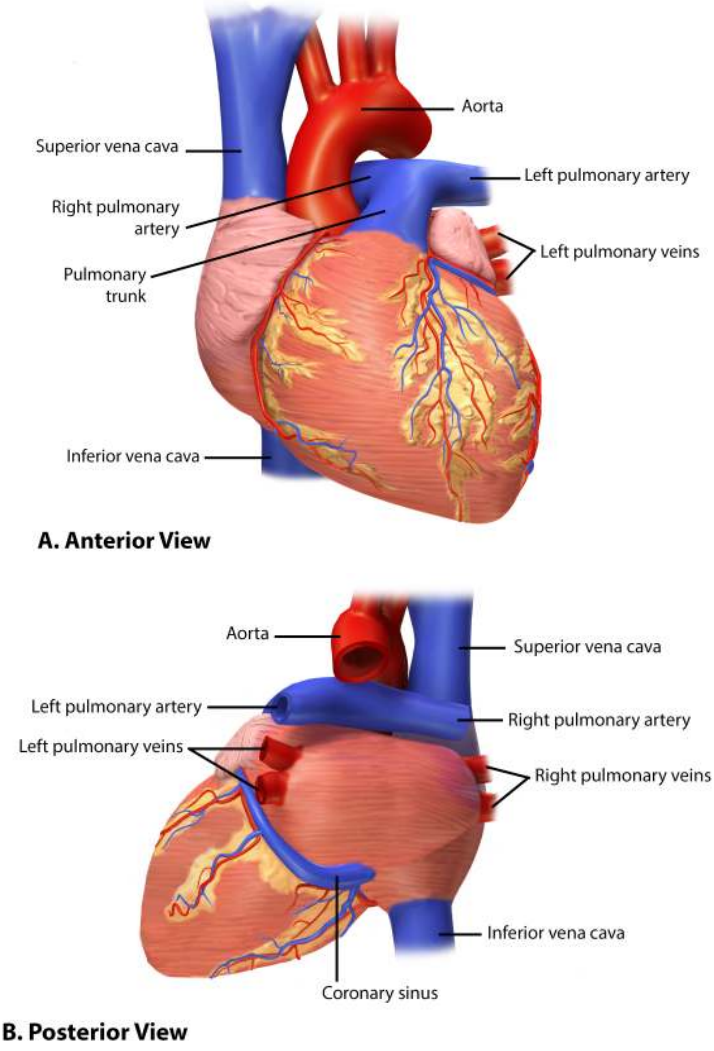


Figure 14.1.9: Great Vessels of the Heart. The base of the heart shows the location of the great vessels. Insert image caption. *(Image credits: "Great Vessels of the Heart, Anterior View" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original "Blausen 0451 - Anterior view of the heart - English labels" by Blausen Medical Communications, Inc.; "Great Vessels of the Heart, Posterior View" by Jennifer Lange is licensed under under CC BY-NC-SA 4.0, modification of original "Blausen 0456 Heart Posterior" by Blausen Medical Communications, Inc.)*

Internal Structures of the Heart

Figure 14.1.10 shows the internal anatomy of the heart and the relative positions and features of the four chambers. Muscular septa form the walls between adjacent chambers. The word septum is derived from the Latin for “something that encloses;” in this case, a **septum** (plural = septa) refers to a wall or partition that divides the heart into chambers. The septa are physical extensions of the myocardium lined with endocardium. Located between the two atria is the **interatrial septum**. Normally in an adult heart, the interatrial septum bears an oval-shaped depression known as the **fossa ovalis**, a remnant of an opening in the fetal heart known as the **foramen ovale**. The foramen ovale allowed blood in the fetal heart to pass directly from the right atrium to the left atrium, allowing some blood to bypass the pulmonary circuit. Within seconds after birth, a flap of tissue that previously acted as a valve closes the foramen ovale and establishes the typical cardiac circulation pattern. Between the two ventricles is a second septum known as the **interventricular septum**. Unlike the interatrial septum, the interventricular septum is normally intact after its formation during fetal development. It is substantially thicker than the interatrial septum, since the ventricles generate far greater pressure when they contract.

The septum between the atria and ventricles is known as the **atrioventricular septum**. It is marked by the presence of four openings that allow blood to move from the atria into the ventricles and from the ventricles into the pulmonary trunk and aorta. Located in each of these openings between the atria and ventricles is a **valve**, a specialized structure that ensures one-way flow of

blood. The valves between the atria and ventricles are known generically as **atrioventricular valves**. Each flap of an atrioventricular valve is attached to strong strands of connective tissue, the **chordae tendineae**, literally “tendinous cords,” or sometimes more poetically referred to as “heart strings” (Figure 14.1.11). There are several chordae tendineae associated with each of the valve flaps that are composed of approximately 80 percent collagenous fibers with the remainder consisting of elastic fibers and endothelium. They connect each of the flaps to a **papillary muscle**. The valves at the openings that lead to the pulmonary trunk and aorta are known generically as **semilunar valves**. The semilunar valves are both comprised of three small flaps of endothelium reinforced with dense connective tissue.

Right Atrium

The **right atrium** serves as the receiving chamber for blood returning to the heart from the systemic circulation. The two major systemic veins, the superior and inferior venae cavae, and the large coronary vein called the **coronary sinus** empty into the right atrium. The superior vena cava drains blood from regions superior to the diaphragm: the head, neck, upper limbs, and the thoracic region. It empties into the superior and posterior portions of the right atrium. The inferior vena cava drains blood from areas inferior to the diaphragm: the lower limbs and abdominopelvic region of the body. It, too, empties into the posterior portion of the atria, but inferior to the opening of the superior vena cava. Immediately superior and slightly medial to the opening of the inferior vena cava on the posterior surface of the atrium is the opening of the coronary sinus. This thin-walled vessel drains most of the coronary veins that return systemic blood from the heart into the right atrium. The majority of the internal heart structures discussed in this and subsequent sections are illustrated in Figure 14.1.10.

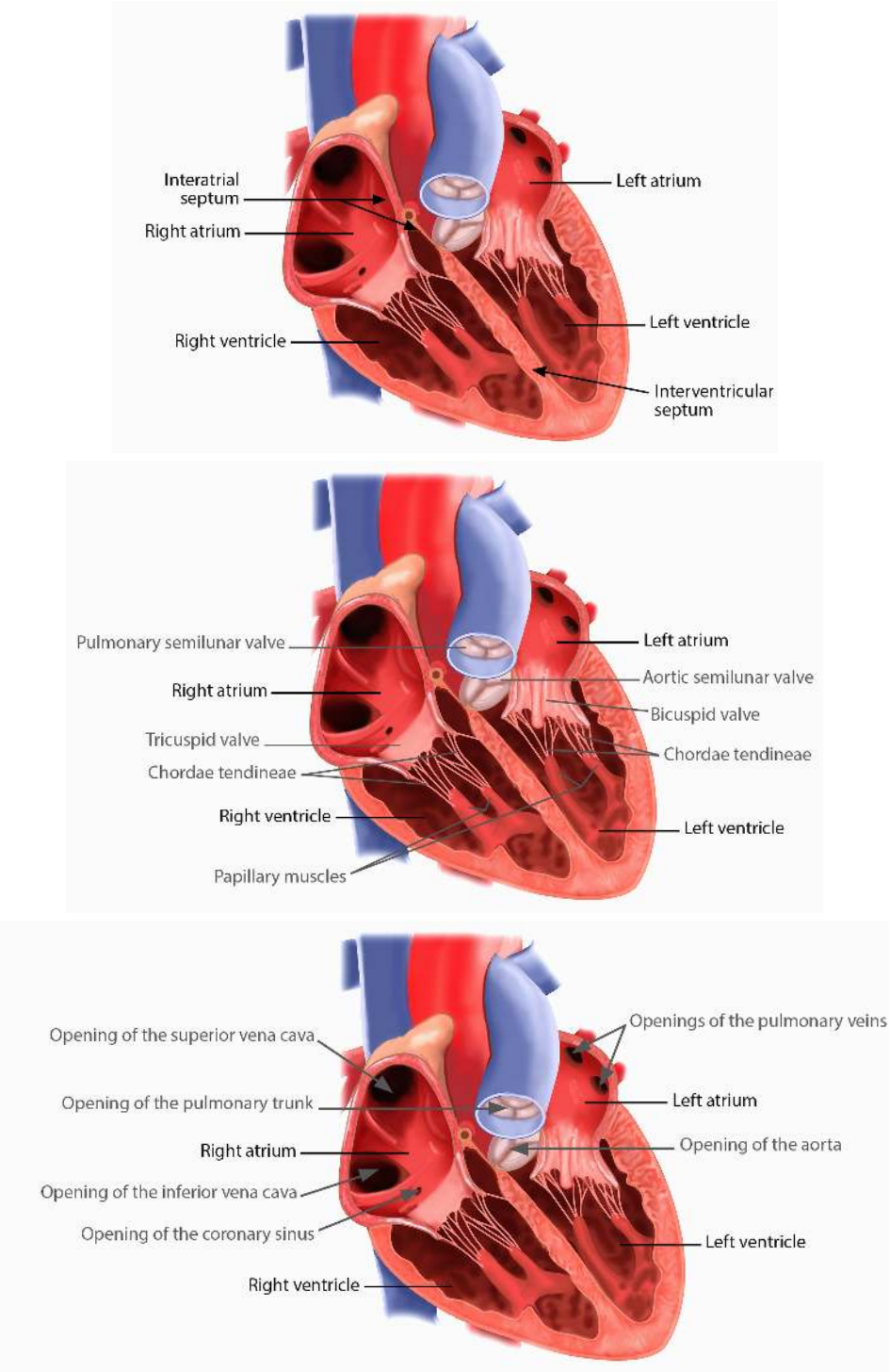


Figure 14.1.10: Interior Structures of the Heart. This anterior view of the heart shows the four chambers, the major vessels and their early branches, as well as the valves. The presence of the pulmonary trunk and aorta covers the interatrial septum, and the atrioventricular septum is cut away to show the atrioventricular valves. (Caption from OpenStax) *(Image credits: "Interior Structures of the Heart - illustration with multiple label sets" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original "Slagter - Drawing Anatomy of the heart and large vessels - no labels" by Ron Slagter, license: CC BY-NC-SA.)*

While the bulk of the internal surface of the right atrium is smooth, the depression of the fossa ovalis is medial, and the anterior surface demonstrates prominent ridges of muscle called the **pectinate muscles** (see Figure 14.1.11), which are thought to help spread the electrical signals to contract and strengthen the contraction of the atria. The right auricle also has pectinate muscles. The left atrium does not have pectinate muscles except in the auricle.

The atria receive venous blood on a nearly continuous basis, allowing the heart to continue to receive blood even while the ventricles are contracting. While most ventricular filling occurs while the atria are relaxed, they do demonstrate a contractile phase and actively pump blood into the ventricles just prior to ventricular contraction. The opening between the right atrium and right ventricle is guarded by the **tricuspid valve**.

Right Ventricle

The right ventricle receives blood from the right atrium through the tricuspid valve (also called the right atrioventricular valve). There are three papillary muscles in the right ventricle which correspond to the three flaps of the valve. (The third valve flap and papillary muscle would be on the anterior portion of the heart, which has been removed in this illustration.) When the myocardium of the ventricle contracts, pressure within the ventricular chamber rises. Blood, like any fluid, flows from higher pressure to lower pressure areas, in this case, toward the pulmonary trunk and the atrium. To prevent any potential backflow, the flaps of the tricuspid valve are pushed closed during ventricular contraction. The papillary muscles contract with the ventricular myocardium, generating tension on the chordae tendineae. This prevents the flaps of the valves from being forced into the atria and regurgitation of the blood back into the atria during ventricular contraction. Figure 14.1.11 shows papillary muscles and chordae tendineae attached to the bicuspid valve.

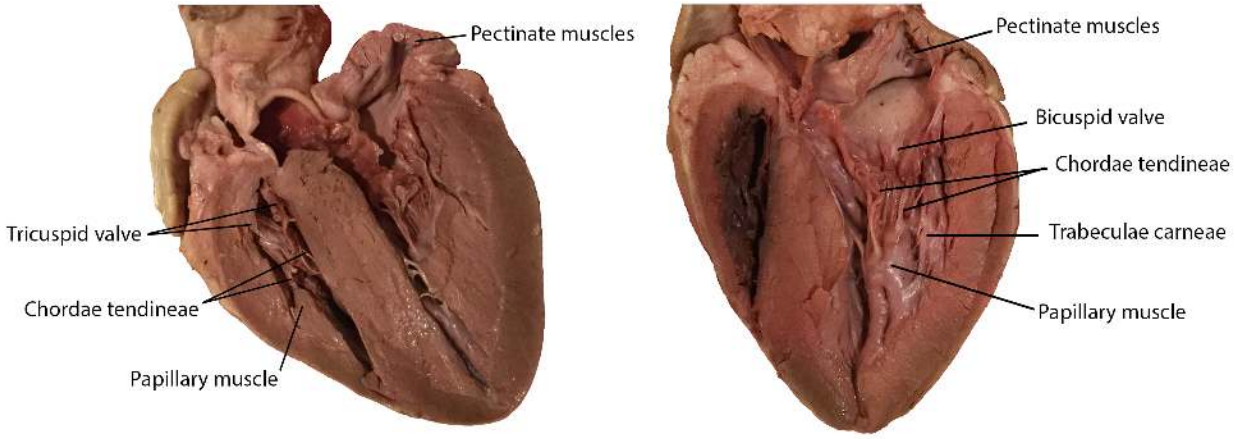


Figure 14.1.11: Interior of the Heart Chambers - Dissection. In these frontal sections, within in the ventricles you can see a papillary muscle attached to the atriventricular valve the via chordae tendineae as well as the trabeculae carneae ridges on the walls. Within the left atrium a few of the pectinate muscles are visible. *(Image credit: "Heart Dissection - Interior Features" by Jennifer Lange is licensed under CC BY-NC-SA 4.0.)*

The walls of the ventricle are lined with **trabeculae carneae**, ridges of cardiac muscle covered by endocardium (Figure 14.1.11) that increase the surface area of the ventricular wall.

When the right ventricle contracts, it ejects blood into the pulmonary trunk, which branches into the left and right pulmonary arteries that carry deoxygenated blood to each lung. The superior surface of the right ventricle begins to taper as it approaches the pulmonary trunk. At the base of the pulmonary trunk is the pulmonary semilunar valve that prevents backflow from the pulmonary trunk when the ventricle relaxes.

Left Atrium

After exchange of gases in the pulmonary capillaries, freshly oxygenated blood returns to the left atrium via one of the four pulmonary veins. The left atrium does not contain pectinate muscles so its walls are smoother than in the right atrium, but it does have an auricle that includes pectinate ridges. Blood flows nearly continuously from the pulmonary veins back into the atrium, which acts as the receiving chamber, and from here through an open bicuspid valve, also known as the mitral valve or the left atrioventricular valve, into the left ventricle. Most blood flows passively into the heart while both the atria and ventricles are relaxed, but toward the end of the ventricular relaxation period, the left atrium will contract, pumping blood into the ventricle. This atrial contraction accounts for approximately 20 percent of ventricular filling.

Left Ventricle

Recall that, although both sides of the heart will pump the same amount of blood, the muscular layer is much thicker in the left ventricle compared to the right (see Figure 14.1.7). The left ventricle is the major pumping chamber for the systemic circuit; it ejects blood into the aorta through the aortic semilunar valve. The primary driver of the myocardial thickness of the left ventricle is

the need to push blood into the head to ensure the brain has a constant supply - this requires more force because of the larger distance and the resistance of gravity.

The left ventricle also has trabeculae carneae, and they are more prominent here than in the right ventricle. The flaps of the bicuspid valve are connected to papillary muscles via chordae tendineae. There are two papillary muscles in the left ventricle—the anterior and posterior—as opposed to three in the right ventricle.

Heart Valve Function

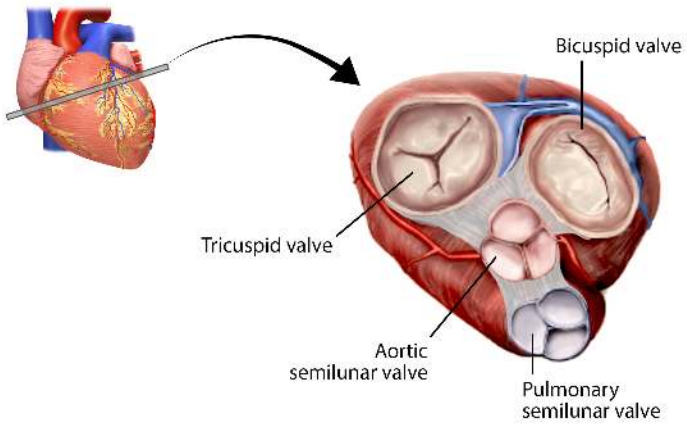
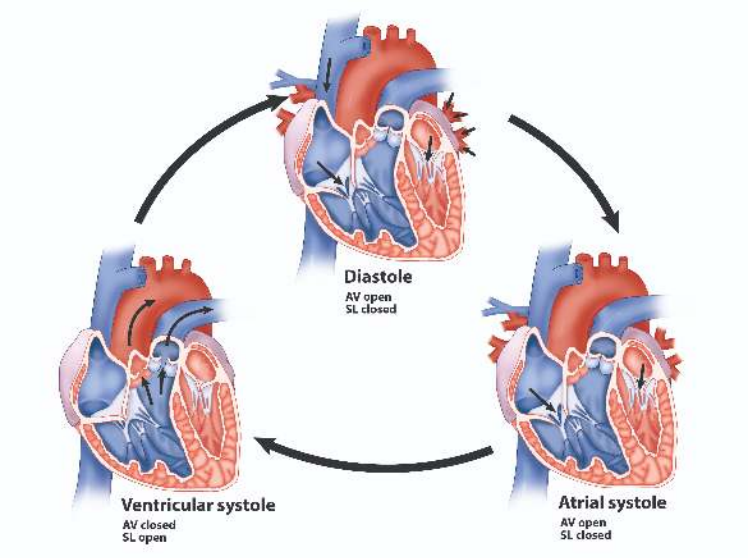


Figure 14.1.12: Valves and Cardiac Skeleton. With the atria and major vessels removed, all four valves are clearly visible. (Caption from OpenStax) *(Image credit: "Valves and the Cardiac Skeleton" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of originals "Blausen 0451 - Anterior view of the heart - English labels" by Blausen Medical Communications, Inc. and OLI - Drawing Valves of the heart from anterior and cross-section - English labels" by Open Learning Initiative.)*

A transverse section through the heart slightly above the level of the atrioventricular septum reveals all four heart valves along the same plane (Figure 14.1.12). The valves ensure unidirectional blood flow through the heart. Between the right atrium and the right ventricle is the **right atrioventricular valve**, or **tricuspid valve**. It typically consists of three flaps, or leaflets, made of endocardium reinforced with additional dense connective tissue. Each flap is connected by several chordae tendineae to a papillary muscle that protrudes from the ventricular wall.

Located at the opening between the left atrium and left ventricle is the **mitral valve**, also called the **bicuspid valve** or the **left atrioventricular valve**. In a clinical setting, the valve is referred to as the mitral valve, rather than the bicuspid valve, as the actual number of cusps has been found to vary greatly among individuals (Gunnal *et al*, 2012). The cusps of the mitral valve are attached by chordae tendineae to two papillary muscles that project from the trabeculae carneae of the wall of the ventricle.

When the ventricles begin to contract, pressure within the ventricles rises and blood flows toward the area of lowest pressure, which is initially in the atria. This movement of blood causes the cusps of the tricuspid and mitral valves to close. As the myocardium of the ventricle contracts, so do the papillary muscles. This creates tension on the chordae tendineae (see Figure 14.1.13 - ventricular systole), helping to hold the cusps of the atrioventricular valves in place and preventing them from everting into the atria. During the relaxation phase of the cardiac cycle, the papillary muscles are also relaxed and the tension on the chordae tendineae is slight.



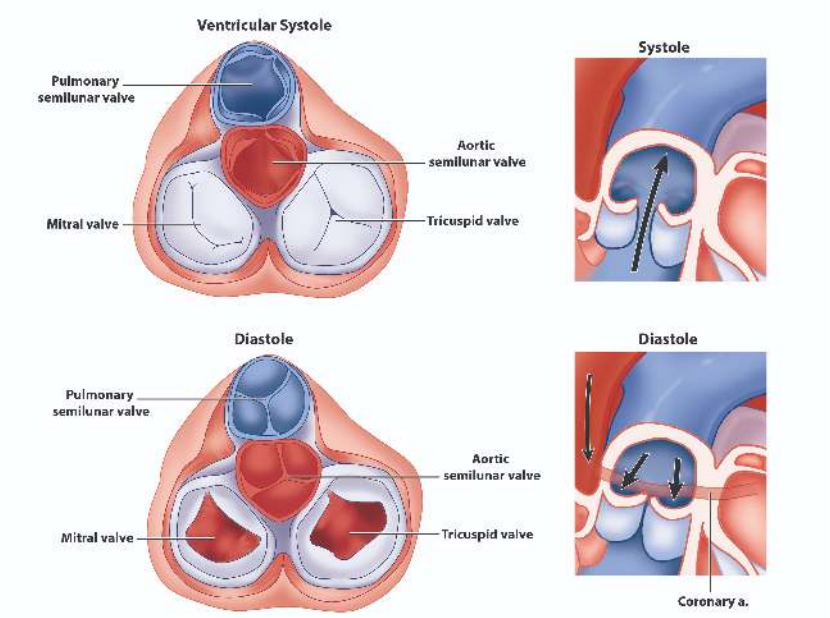


Figure 14.1.13: Bood Flow Through the Heart Valves and Chambers. During diastole, the blood will flow through the AV valves from the artia into the ventricles. During systole, the blood will flow through. the semilunar valves from the ventricles to the pulmonary and systemic circuit. *(Image credits: "Heart Cardiac Cycle" and "Heart Aortic Valve Action" by BlueLink are licensed under CC BY-NC 4.0 with notification of the original authors.)*

Emerging from the right ventricle at the base of the pulmonary trunk is the pulmonary semilunar valve, or the **pulmonary valve**; it is also known as the pulmonic valve. At the base of the aorta that emerges from the left ventricle is the aortic semilunar valve, or the **aortic valve**. The semilunar valves are both comprised of three small flaps of endothelium reinforced with dense connective tissue.

When the ventricle relaxes, the pressure differential causes blood to flow back towards the ventricle within the pulmonary trunk and aorta. This flow of blood fills the pocket-like flaps of each semilunar valve, causing the valve to close, disrupting the backflow of blood and producing an audible sound. Unlike the atrioventricular valves, there are no papillary muscles or chordae tendineae associated with the semilunar valves.

Since these openings and valves structurally weaken the atrioventricular septum, the remaining tissue is heavily reinforced with dense irregular connective tissue of the **cardiac skeleton**, or skeleton of the heart. It includes four rings that surround the openings between the atria and ventricles, and the openings to the pulmonary trunk and aorta, and serve as the point of attachment for the heart valves. The cardiac skeleton also provides the structural framework against which the cardiac muscle contracts and forms an important insulating boundary in the heart's electrical conducting system.

INTERACTIVE LINK

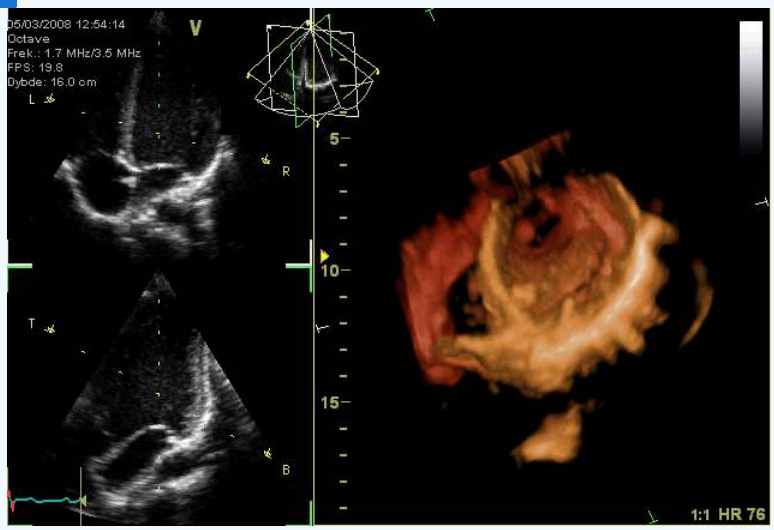


Figure 14.1.14: Echocardiogram of Heart Valves Opening and Closing. GIF-animation showing a moving echocardiogram; a 3D-loop of a heart viewed from the apex, with the apical part of the ventricles removed and the mitral valve clearly visible. Due to missing data the leaflet of the tricuspid and aortic valve is not clearly visible, but the openings are. To the left are two standard two-dimensional views taken from the 3D dataset. If not animated above, visit this site to observe an echocardiogram of actual heart valves opening and closing. (Image and caption credit: "Apikal4D" by Kjetil Lenes is licensed under CC BY-SA 3.0)

Valves and Heart Sounds

In a normal, healthy heart, there are primarily two audible **heart sounds**: S_1 and S_2. S_1 is the sound created by the closing of the atrioventricular valves during ventricular contraction and is normally described as a “lub,” or first heart sound. The second heart sound, S_2, is the sound of the closing of the semilunar valves during ventricular diastole and is described as a “dub”. In both cases, as the valves close, the openings within the atrioventricular septum guarded by the valves will become reduced, and blood flow through the opening will become more turbulent until the valves are fully closed. There is a third heart sound, S_3, but it is rarely heard in healthy individuals.

The term **murmur** is used to describe an unusual sound coming from the heart that is caused by the turbulent flow of blood. Murmurs are graded on a scale of 1 to 6, with 1 being the most common, the most difficult sound to detect, and the least serious. Placement of the stethoscope in four distinct locations enables optimal auscultation (listening with a stethoscope) of each valve: near transition of the ascending aorta to the aortic arch for the aortic valve, near the bifurcation of the pulmonary trunk for the pulmonary valve, near the superior portion of the right ventricle for the tricuspid valve, and near the apex of the heart for the bicuspid valve. Figure 14.1.15 indicates proper placement of the bell of the stethoscope to facilitate auscultation.

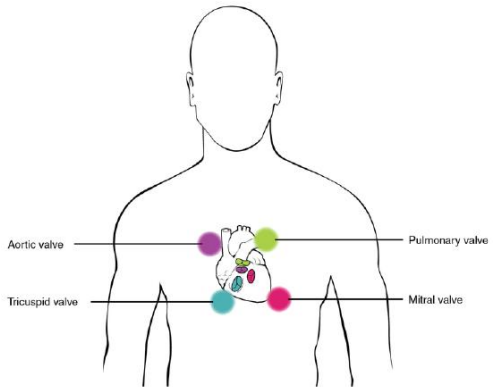


Figure 14.1.15: Stethoscope Placement for Auscultation. Proper placement of the bell of the stethoscope facilitates auscultation. At each of the four locations on the chest, a different valve can be heard. (Image credit: "Stethoscope Placement" by OpenStax is licensed under CC BY 3.0)

DISORDERS OF THE...

Heart Valves

When heart valves do not function properly, they are often described as incompetent and result in valvular heart disease, which can range from benign to lethal. Some of these conditions are congenital, that is, the individual was born with the defect, whereas others may be attributed to disease processes or trauma. Some malfunctions are treated with medications, others require surgery, and still others may be mild enough that the condition is merely monitored since treatment might trigger more serious consequences.

Valvular disorders are often caused by carditis, or inflammation of the heart. One common trigger for this inflammation is rheumatic fever, or scarlet fever, an autoimmune response to the presence of a bacterium, Streptococcus pyogenes, normally a disease of childhood.

While any of the heart valves may be involved in valve disorders, bicuspid regurgitation is the most common, detected in approximately 2 percent of the population, and the pulmonary semilunar valve is the least frequently involved. When a valve malfunctions, the flow of blood to a region will often be disrupted. The resulting inadequate flow of blood to this region will be described in general terms as an insufficiency. The specific type of insufficiency is named for the valve involved: aortic insufficiency, mitral insufficiency, tricuspid insufficiency, or pulmonary insufficiency.

If one of the cusps of the valve is forced backward by the force of the blood, the condition is referred to as a prolapsed valve. Prolapse may occur if the chordae tendineae are damaged or broken, causing the closure mechanism to fail. The failure of the valve to close properly disrupts the normal one-way flow of blood and results in regurgitation, when the blood flows backward from its normal path. Using a stethoscope, the disruption to the normal flow of blood produces a heart murmur.

Stenosis is a condition in which the heart valves become rigid and may calcify over time. The loss of flexibility of the valve interferes with normal function and may cause the heart to work harder to propel blood through the valve, which eventually weakens the heart. Aortic stenosis affects approximately 2 percent of the population over 65 years of age, and the percentage increases to approximately 4 percent in individuals over 85 years. Occasionally, one or more of the chordae tendineae will tear or the papillary muscle itself may die as a component of a myocardial infarction (heart attack). In this case, the patient's condition will deteriorate dramatically and rapidly, and immediate surgical intervention may be required.

Auscultation, or listening to a patient's heart sounds, is one of the most useful diagnostic tools, since it is proven, safe, and inexpensive. The term auscultation is derived from the Latin for "to listen," and the technique has been used for diagnostic purposes as far back as the ancient Egyptians. Valve and septal disorders will trigger abnormal heart sounds. If a valvular disorder is detected or suspected, a test called an echocardiogram, or simply an "echo," may be ordered. Echocardiograms are sonograms of the heart and can help in the diagnosis of valve disorders as well as a wide variety of heart pathologies.

Circulation Through the Heart

The right ventricle pumps **deoxygenated blood** into the **pulmonary trunk**, which ascends across the anterior surfaces of the ascending aorta and left atrium toward a bifurcation into the left and right **pulmonary arteries**. The right pulmonary artery passes under the aortic arch and delivers blood to the right lung. The left pulmonary artery delivers blood to the left lung. These arteries in turn branch many times in each lung before reaching the **pulmonary capillaries**, where gas exchange occurs: carbon dioxide exits the blood and oxygen enters. The pulmonary trunk, arteries, and their branches are the only arteries in the post-natal body that carry relatively deoxygenated blood. Highly oxygenated blood returning from the pulmonary capillaries in the lungs passes through a series of vessels that join together to form the **pulmonary veins**—the only post-natal veins in the body that carry highly oxygenated blood. The pulmonary veins conduct blood into the right and left sides of the left atrium posteriorly, which pumps the blood into the left ventricle, which in turn pumps oxygenated blood into the aorta, which ascends out of the left ventricle posterior to the pulmonary trunk, arches over the top of the heart and descends posterior to the heart. The aorta branches to deliver oxygenated blood throughout the body via the systemic circuit. Eventually, blood reaches systemic capillaries, where exchange with the tissue fluid and cells of the body occurs. In this case, oxygen and nutrients exit the systemic capillaries to be used by the cells in their metabolic processes, and carbon dioxide and waste products will enter the blood.

The blood exiting the systemic capillaries is lower in oxygen concentration than when it entered. The capillaries will ultimately unite to form venules, joining to form ever-larger veins, eventually flowing into the two major systemic veins, the **superior vena**

cava and the **inferior vena cava**, which return blood into the right atrium. The blood in the superior and inferior venae cavae flows into the right atrium, which pumps blood into the right ventricle (Figure 14.1.4).

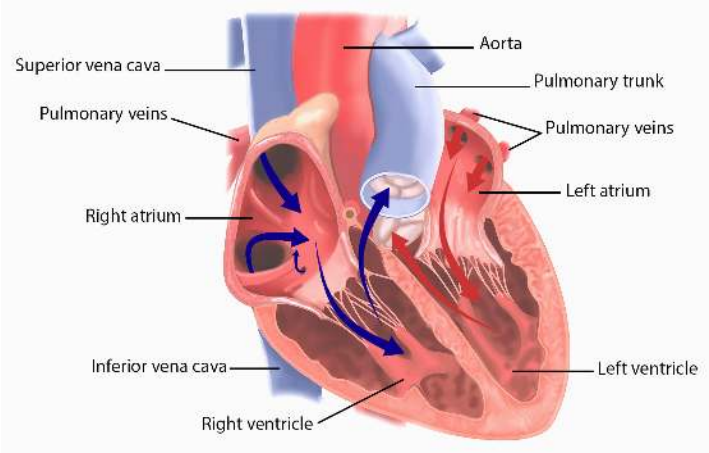


Figure 14.1.16: Circulation Through the Heart. Blood flows from the atria (right and left) to the ventricles (right and left), where it is pumped into the pulmonary circuit (from right ventricle) and systemic circuit (from left ventricle. *(Image credits: "Circulation Through the Heart" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original "Slagter - Drawing Anatomy of the heart and large vessels - no labels" by Ron Slagter, license: CC BY-NC-SA.)*

CAREER CONNECTION

Cardiovascular Technologist/Technician

Cardiovascular technologists/technicians are trained professionals who perform a variety of imaging techniques, such as sonograms or echocardiograms, used by physicians to diagnose and treat diseases of the heart. Nearly all of these positions require an associate degree, and these technicians earn a median salary of $68,750 as of 2019. Growth within the field is fast, projected at 12 percent from 2019 - 2029, according to the U.S. Bureau of Labor Statistics.

Visit this site for more information on cardiovascular technologists/technicians [statistics retrieved 10 Dec 2020].

There is a considerable overlap and complementary skills between cardiac technicians and vascular technicians, and so the term cardiovascular technician is often used. Special certifications within the field require documenting appropriate experience and completing additional and often expensive certification examinations. These subspecialties include Certified Rhythm Analysis Technician (CRAT), Certified Cardiographic Technician (CCT), Registered Congenital Cardiac Sonographer (RCCS), Registered Cardiac Electrophysiology Specialist (RCES), Registered Cardiovascular Invasive Specialist (RCIS), Registered Cardiac Sonographer (RCS), Registered Vascular Specialist (RVS), and Registered Phlebology Sonographer (RPhS).Concept Review

The heart resides within the pericardial sac and is located in the mediastinal space within the thoracic cavity. The pericardial sac consists of two fused layers: an outer fibrous layer and an inner parietal pericardial serous membrane. Between the pericardial sac and the heart is the pericardial cavity, which is filled with lubricating serous fluid. The walls of the heart are composed of an outer epicardium, a thick myocardium, and an inner lining layer of endocardium. The human heart consists of a pair of atria, which receive blood and pump it into a pair of ventricles, which pump blood into the vessels. The right atrium receives systemic blood relatively low in oxygen and pumps it into the right ventricle, which pumps it into the pulmonary circuit. Exchange of oxygen and carbon dioxide occurs in the lungs, and blood high in oxygen returns to the left atrium, which pumps blood into the left ventricle, which in turn pumps blood into the aorta and the remainder of the systemic circuit. The septa are the partitions that separate the chambers of the heart. They include the interatrial septum, the interventricular septum, and the atrioventricular septum. Two of these openings are guarded by the atrioventricular valves, the right tricuspid valve and the left mitral valve, which prevent the backflow of blood. Each is attached to chordae tendineae that extend to the papillary muscles, which are extensions of the myocardium, to prevent the valves from being blown back into the atria. The pulmonary semilunar valve is located at the base of the pulmonary trunk, and the aortic semilunar valve is located at the base of the aorta.

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14.2: Cardiac Muscle and Electrical Activity

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

- Describe the structure of cardiac muscle tissue and cells
- Identify and describe the components of the conducting system that distributes electrical impulses through the heart

Recall that cardiac muscle shares a few characteristics with both skeletal muscle and smooth muscle, but it has some unique properties of its own. Not the least of these exceptional properties is its ability to initiate an electrical potential at a fixed rate that spreads rapidly from cell to cell to trigger the contractile mechanism. This property is known as **autorhythmicity**. Skeletal muscle can not do this. Even though cardiac muscle has autorhythmicity, heart rate is modulated by the endocrine and nervous systems.

Structure of Cardiac Muscle Tissue and Cells

Compared to the giant cylinders of skeletal muscle, cardiac muscle cells, or cardiomyocytes, are considerably shorter with much smaller diameters. Cardiac muscle also demonstrates striations, the alternating pattern of dark A bands and light I bands attributed to the precise arrangement of the myofilaments and fibrils that are organized in sarcomeres along the length of the cell (Figure 14.2.1.a). These contractile elements are virtually identical to skeletal muscle. T (transverse) tubules penetrate from the surface plasma membrane, the sarcolemma, to the interior of the cell, allowing the electrical impulse to reach the interior. The T tubules are only found at the Z discs, whereas in skeletal muscle, they are found at the junction of the A and I bands. Therefore, there are one-half as many T tubules in cardiac muscle as in skeletal muscle. In addition, the sarcoplasmic reticulum of cardiomyocytes stores few calcium ions, so most of the calcium ions must come from outside the cells. The result is a slower onset of contraction. Mitochondria are plentiful, providing energy for the cross-bridge cycling responsible for contractions of the heart. Typically, cardiomyocytes have a single, central nucleus, but two or more nuclei may be found in some cells. Cardiac muscle undergoes aerobic respiration patterns, primarily metabolizing lipids and carbohydrates. Myoglobin, lipids, and glycogen are all stored within the cytoplasm.

Cardiac muscle cells branch freely. A junction between two adjoining cells is marked by a critical structure called an **intercalated disc**, which helps support the synchronized contraction of the muscle and structurally links the cells together (Figure 14.2.1). Intercalated discs are formed by regions of sarcolemma with specialized integral membrane proteins. These form desmosomes, fasciae adherens, and large numbers of gap junctions. Desmosomes and fasciae adherens anchor the cells together. Fasciae adherens also anchor actin filaments of the sarcomere directly to the sarcolemma. Gap junctions allow the passage of ions from cell-to-cell through their sarcoplasm, a feature essential to producing synchronized contractions (Figure 14.2.1). Intercellular connective tissue also helps to bind the cells together. The importance of strongly binding these cells together is necessitated by the forces exerted by contraction; unlike skeletal muscle in which cells are the length of the organ to pull collectively on a bone via collagenous connective tissue attachments, smaller cardiac muscle cells pull on each other and ultimately on the dense connective tissue of the cardiac skeleton when they contract.

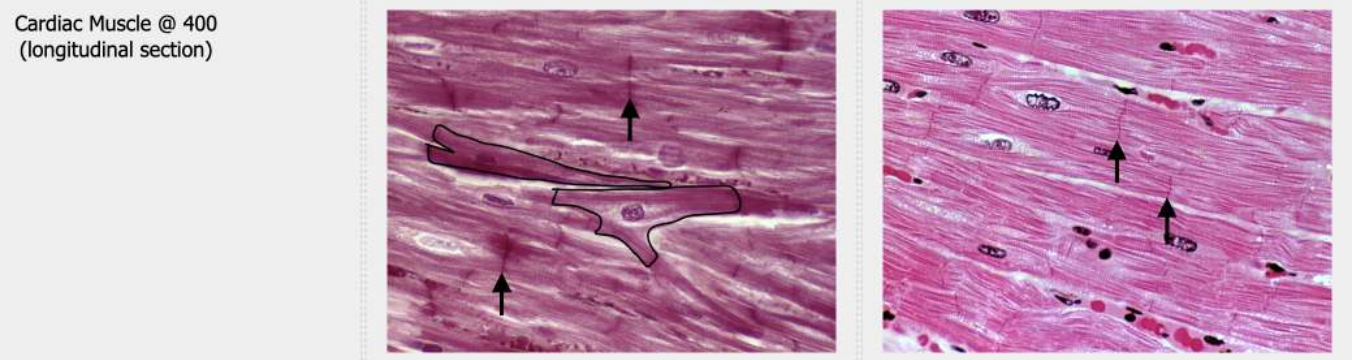


Figure 14.2.1:The cardiac muscle showing the intercalated discs (arrrows). *(Image credits: Types of Muscle Tissue by Jennifer Lange are licensed under CC-BY-SA-NC 4.0. Micrographs A1, A2, and C1 provided by the Regents of University of Michigan Medical School, micrographs B1, B2, and C2 provided by Virginia Commonwealth University.)*

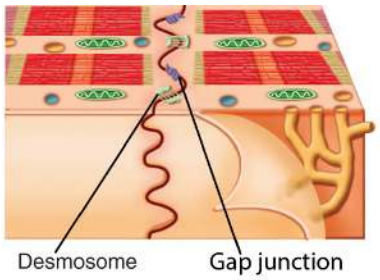


Figure 14.2.2: Intercalated discs are specialized cell junctions unique to cardiac muscle tissue that contain gap junctions and desmosomes. *(Image credit: "Intercalated Disc" by Jennifer Lange is licensed under CC-BY-SA-NC 4.0, modification of original work by Cenveo.)*

There are two major types of cardiac muscle cells: myocardial contractile cells and myocardial conducting cells. The **myocardial contractile cells** constitute the bulk (99 percent) of the cells in the myocardium of the atria and ventricles. Myocardial contractile cells are autorhythmic, but they are primarily responsible for the strong, synchronized contractions necessary to pump blood through the body. The **myocardial conducting cells** (1 percent of the cells) are generally much smaller than the contractile cells and have fewer myofibrils for contraction. Myocardial conducting cells are specialized to initiate and propagate the electrical activity that travels throughout the heart and triggers the contractions of the myocardial contractile cells that propel the blood.

EVERYDAY CONNECTION

Repair and Replacement of Cardiac Muscle

Damaged cardiac muscle cells have extremely limited abilities to repair themselves or to replace dead cells via mitosis. Recent evidence indicates that at least some stem cells remain within the heart that continue to divide and at least potentially replace these dead cells. However, newly formed or repaired cells are rarely as functional as the original cells, and cardiac function is reduced. In the event of a heart attack or myocardial infarction (MI), dead cells are often replaced by patches of scar tissue in a process called fibrosis. Autopsies performed on individuals who had successfully received heart transplants show some proliferation of original cells. If researchers can unlock the mechanism that generates new cells and restore full mitotic capabilities to heart muscle, the prognosis for heart attack survivors will be greatly enhanced. To date, myocardial cells produced within the patient (*in situ*) by cardiac stem cells seem to be nonfunctional, although those grown in Petri dishes (*in vitro*) do beat. Perhaps soon this mystery will be solved, and new advances in treatment will be commonplace.

Conducting System of the Heart

The myocardial conducting cells are concentrated in specific areas of the heart that make up the Conducting System. The components of the cardiac conducting system include the sinoatrial node, the atrioventricular node, the atrioventricular bundle, the atrioventricular bundle branches, and the Purkinje fibers (Figure 14.2.3).

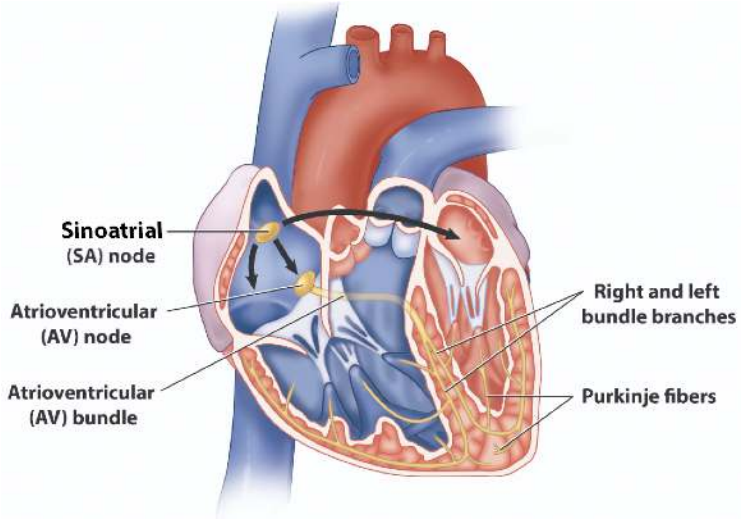


Figure 14.2.3: Conducting System of the Heart. Specialized conducting components of the heart include the sinoatrial node, the atrioventricular node, the atrioventricular bundle, the right and left bundle branches, and the Purkinje fibers. *(Image credit: "Conducting System of the Heart" by BlueLink is licensed under CC BY-NC 4.0 with notification of the original authors.)*

Normal cardiac rhythm is established by the **sinoatrial (SA) node**, a specialized clump of myocardial conducting cells located in the posterosuperior walls of the right atrium in close proximity to the orifice of the superior vena cava. The myocardial conducting cells of the SA node have the highest inherent rate of electrical signal initiation, so the SA node is known as the **pacemaker** of the heart. This impulse spreads from its initiation in the SA node throughout the atria and to the atrioventricular node. The **atrioventricular (AV) node** is a second clump of specialized myocardial conducting cells, located in the inferior portion of the right atrium within the atrioventricular septum.

Arising from the AV node, the **atrioventricular bundle**, or **bundle of His**, proceeds into the interventricular septum before dividing into two **atrioventricular bundle branches**, commonly called the left and right bundle branches. The left bundle branch supplies the left ventricle, and the right bundle branch the right ventricle. Both descend and reach the apex of the heart where they connect with the **Purkinje fibers** (see Figure 14.2.3), which then spread the impulse to the myocardial contractile cells in the ventricles. They extend throughout the myocardium from the apex of the heart toward the atrioventricular septum and the base of the heart at the top of the ventricles. Figure 14.2.4 show the spread of the electrical wave through these structures and the myocardial contractile cells.

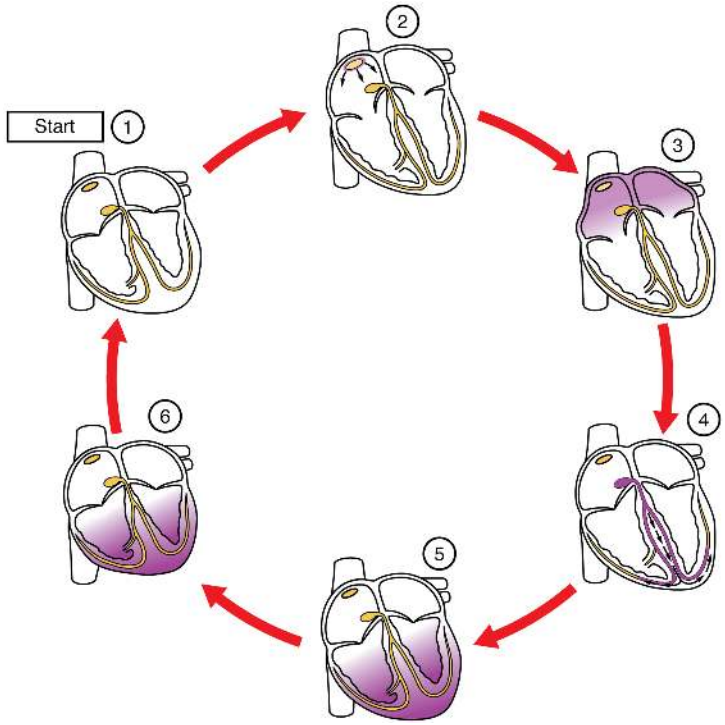


Figure 14.2.4: Cardiac Conduction. (1) The sinoatrial (SA) node and the remainder of the conducting system are at rest. (2) The SA node initiates the electrical wave, which sweeps across the atria. (3) After reaching the atrioventricular node the impulse is transmitted to the atrioventricular bundle. (4) The impulse travels through the atrioventricular bundle and bundle branches to the Purkinje fibers. (5) The impulse spreads to the contractile fibers of the ventricle. (6) Ventricular contraction begins. *(Image credit: "Cardiac Conduction" by OpenStax is licensed under CC BY 3.0.)*

DISORDERS OF THE...

Cardiovascular System: Conduction Block

A **heart block** refers to an interruption in the normal conduction pathway. The nomenclature for these is very straightforward:

- SA nodal blocks occur within the SA node.
- AV nodal blocks occur within the AV node.
- Infra-Hisian blocks involve the bundle of His.
- Bundle branch blocks occur within either the left or right atrioventricular bundle branches.

Clinically, the most common types are the AV nodal and infra-Hisian blocks.

When arrhythmias become a chronic problem, the heart maintains the rhythm of the AV node. In order to speed up the heart rate and restore full sinus rhythm, a cardiologist can implant an **artificial pacemaker**, which delivers electrical impulses to the heart muscle to ensure that the heart continues to contract and pump blood effectively.

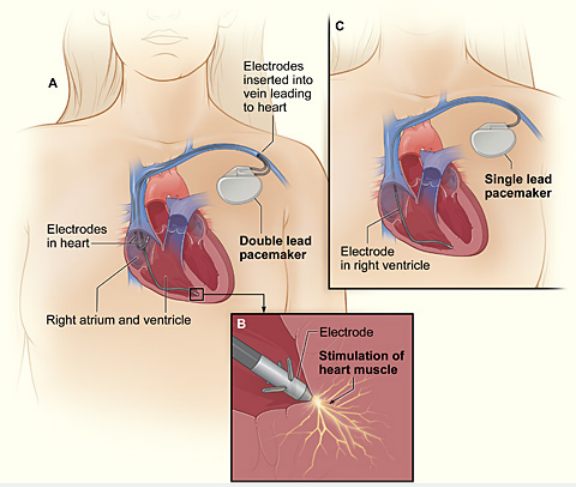


Figure 14.2.5: The image shows a cross-section of a chest and heart with a traditional pacemaker, which has wires (leads). Figure A shows a double-lead pacemaker (also called a double-chamber pacemaker) in the upper chest. Figure B shows an electrode using electrical signals to activate the heart muscle. Figure C shows a single lead pacemaker (also called a single-chamber pacemaker) in the upper chest. Wireless pacemakers (not pictured) are placed inside the right ventricle. *(Image credit: "Pacemaker NIH" by the National Heart Lung and Blood Institute (NIH) is in the Public domain, via Wikimedia Commons.)*

A traditional pacemaker generator is placed outside of the heart, either in the chest or abdomen. It connects via wires to electrodes inside one to three heart chambers: single- and double-lead pacemakers send pulses to the right side of the heart and biventricular pacemakers sends pulses to both ventricles and an atrium. Wireless, or leadless, pacemakers are smaller than traditional types because the pulse generator and electrodes are all in one device. This type of pacemaker is placed inside the heart from where it then sends pulses to the right ventricle.

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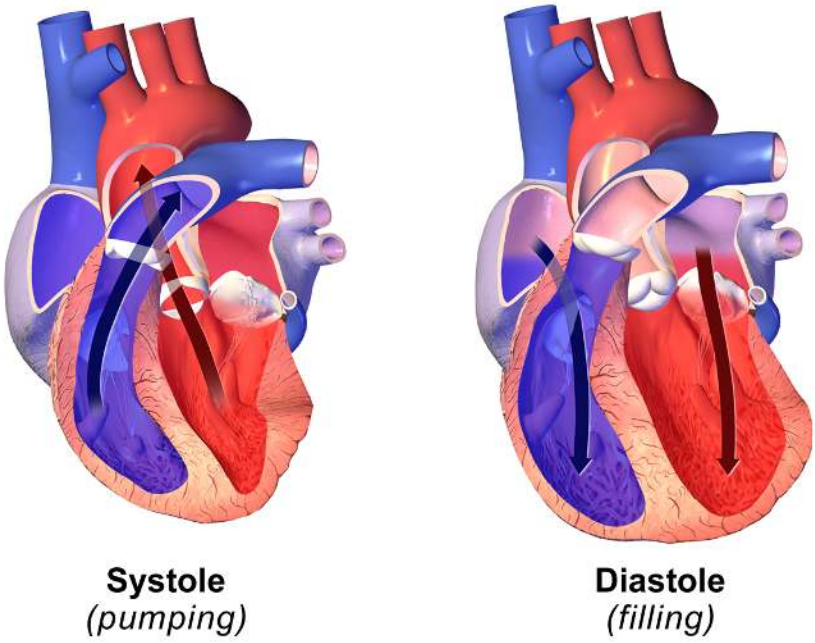
14.3: Cardiac Cycle

Learning Objectives

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

- Describe the relationship between blood pressure and blood flow
- Summarize the events of the cardiac cycle
- Compare atrial and ventricular systole and diastole
- Relate heart sounds detected by auscultation to action of heart's valves

The period of time that begins with contraction of the atria and ends with ventricular relaxation is known as the cardiac cycle (Figure 14.3.2). The period of contraction that the heart undergoes while it pumps blood into circulation is called **systole**. The period of relaxation that occurs as the chambers fill with blood is called **diastole**. Both the atria and ventricles undergo systole and diastole, and it is essential that these components be carefully regulated and coordinated to ensure blood is pumped efficiently to the body.



(Figure 14.3.1) Contraction and Relaxation of the Heart: The term systole is used to refer to contraction and the term diastole is used to refer to relaxation. When the ventricles are in systole, the pressure within the heart chamber increases, pushing blood into the arteries. When the ventricles are in diastole, they will fill with blood arriving from the atria. *(Image credit: "Systole vs Diastole" by BruceBlaus, licensed under CC BY-SA 4.0, via Wikimedia Commons)*

Pressures and Flow

Fluids, whether gases or liquids, are materials that flow according to **pressure gradients**—that is, they move from regions that are higher in pressure to regions that are lower in pressure. Accordingly, when the heart chambers are relaxed (**diastole**), blood will flow into the atria from the veins, which are higher in pressure. As blood flows into the atria, the pressure will rise, so the blood will initially move passively from the atria into the ventricles. When the action potential triggers the muscles in the atria to contract (**atrial systole**), the pressure within the atria rises further, pumping blood into the ventricles. During **ventricular systole**, pressure rises in the ventricles, pumping blood into the pulmonary trunk from the right ventricle and into the aorta from the left ventricle. Again, as you consider this flow and relate it to the conduction pathway, the elegance of the system should become apparent.

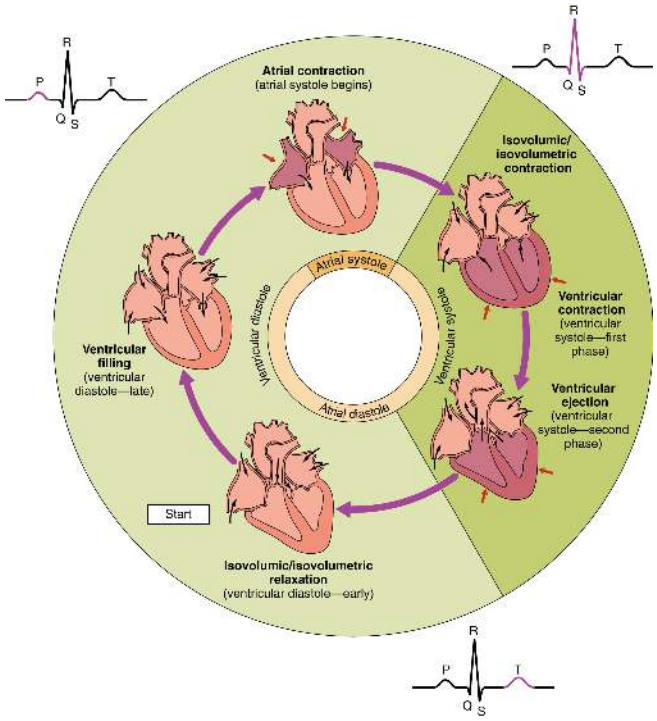


Figure 14.3.2: Overview of the Cardiac Cycle The cardiac cycle begins with atrial systole and progresses to ventricular systole, atrial diastole, and ventricular diastole, when the cycle begins again. Correlations to the ECG are highlighted.

Phases of the Cardiac Cycle

Ventricular Filling and Atrial Contraction

At the beginning of the cardiac cycle, both the atria and ventricles are relaxed (**diastole**). Blood is flowing into the right atrium from the superior and inferior venae cavae and the coronary sinus. Blood flows into the left atrium from the four pulmonary veins. The two atrioventricular valves, the tricuspid and mitral valves, are both open, so blood flows unimpeded from the atria and into the ventricles. Approximately 70–80 percent of ventricular filling occurs by this method. The two semilunar valves, the pulmonary and aortic valves, are closed, preventing backflow of blood into the right and left ventricles from the pulmonary trunk on the right and the aorta on the left. Contraction of the atria follows depolarization, represented by the P wave of the ECG. As the atrial muscles contract from the superior portion of the atria toward the atrioventricular septum, pressure rises within the atria and blood is pumped into the ventricles through the open atrioventricular (tricuspid, and mitral or bicuspid) valves. At the start of atrial systole, the ventricles are normally filled with approximately 70–80 percent of their capacity due to inflow during diastole. Atrial contraction, also referred to as the “atrial kick,” contributes the remaining 20–30 percent of filling (see Figure 14.3.2). Atrial systole lasts approximately 100 ms and ends prior to ventricular systole, as the atrial muscle returns to diastole and blood flow into the atria resumes.

Isovolumetric Contraction Phase

At the end of atrial systole and just prior to ventricular contraction, the ventricles contain approximately 130 mL blood in a resting adult in a standing position. This volume is known as the **end diastolic volume (EDV)** or preload.

Initially, as the muscles in the ventricle contract, the pressure of the blood within the chamber rises, but it is not yet high enough to open the semilunar (pulmonary and aortic) valves and be ejected from the heart. However, blood pressure quickly rises above that of the atria that are now relaxed and in diastole. This increase in pressure causes blood to flow back toward the atria, closing the tricuspid and mitral valves. Since blood is not being ejected from the ventricles at this early stage, the volume of blood within the

chamber remains constant. Consequently, this initial phase of ventricular systole is known as isovolumic contraction, also called **isovolumetric contraction** (see Figure 14.3.2).

Ventricular Ejection Phase

In the second phase of ventricular systole, the ventricular ejection phase, the contraction of the ventricular muscle has raised the pressure within the ventricle to the point that it is greater than the pressures in the pulmonary trunk and the aorta. Blood is pumped from the heart, pushing open the pulmonary and aortic semilunar valves. Pressure generated by the left ventricle will be appreciably greater than the pressure generated by the right ventricle, since the existing pressure in the aorta will be so much higher. Nevertheless, both ventricles pump the same amount of blood. This quantity is referred to as stroke volume. Stroke volume will normally be in the range of 70–80 mL. Since ventricular systole began with an EDV of approximately 130 mL of blood, this means that there is still 50–60 mL of blood remaining in the ventricle following contraction. This volume of blood is known as the **end systolic volume (ESV)**.

Isovolumetric Relaxation Phase

Ventricular relaxation, or diastole, follows repolarization of the ventricles and is represented by the T wave of the ECG. It too is divided into two distinct phases and lasts approximately 430 ms.

During the early phase of ventricular diastole, as the ventricular muscle relaxes, pressure on the remaining blood within the ventricle begins to fall. When pressure within the ventricles drops below pressure in both the pulmonary trunk and aorta, blood flows back toward the heart, producing the dicrotic notch (small dip) seen in blood pressure tracings. The semilunar valves close to prevent backflow into the heart. Since the atrioventricular valves remain closed at this point, there is no change in the volume of blood in the ventricle, so the early phase of ventricular diastole is called the isovolumic ventricular relaxation phase, also called isovolumetric ventricular relaxation phase (see Figure 14.3.2).

In the second phase of ventricular diastole, called late ventricular diastole, as the ventricular muscle relaxes, pressure on the blood within the ventricles drops even further. Eventually, it drops below the pressure in the atria. When this occurs, blood flows from the atria into the ventricles, pushing open the tricuspid and mitral valves. As pressure drops within the ventricles, blood flows from the major veins into the relaxed atria and from there into the ventricles. Both chambers are in diastole, the atrioventricular valves are open, and the semilunar valves remain closed (see Figure 14.3.2). The cardiac cycle is complete.

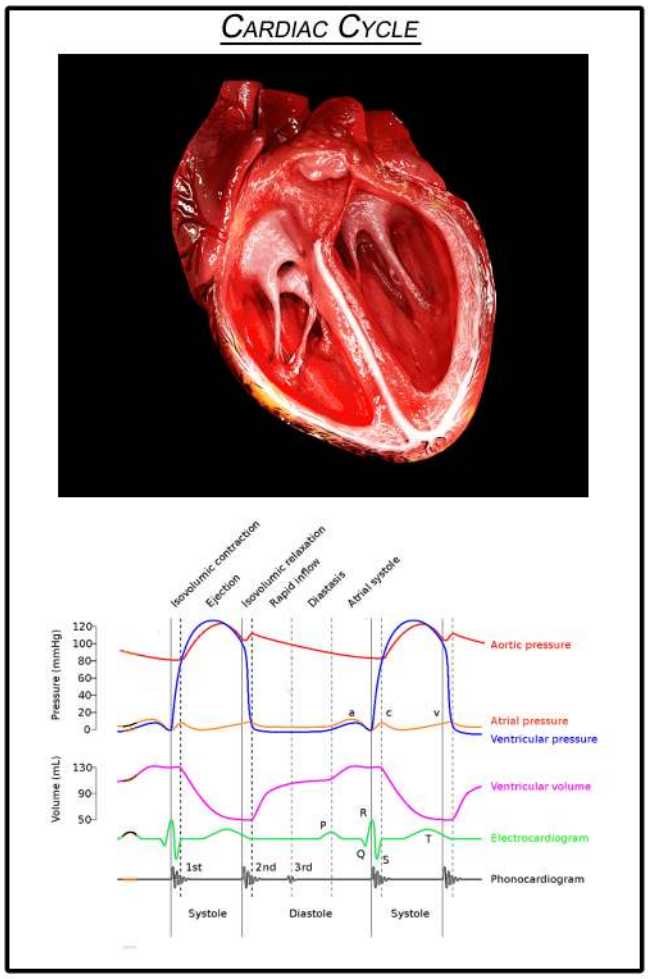


Figure 14.3.3 The Cardiac Cycle: The systole and diastole of the heart can be seen in the animation above. Seen are the rises and falls in pressure of the various chambers as blood is pumped through the heart. It can be seen that ventricular pressure is highest during ventricular ejection and lowest during ventricular filling. The term diastasis on the figure refers to the diastole of the ventricles as they fill with blood. The changes in volume of the ventricles as they fill with and eject blood can also be seen. *(Image credit: "Cardiac-Cycle-Animated" by DrJanaOfficial, licensed under CC BY-SA 4.0, via Wikimedia Commons)*

Figure 14.3.3 illustrates the relationship between the cardiac cycle and the ECG.

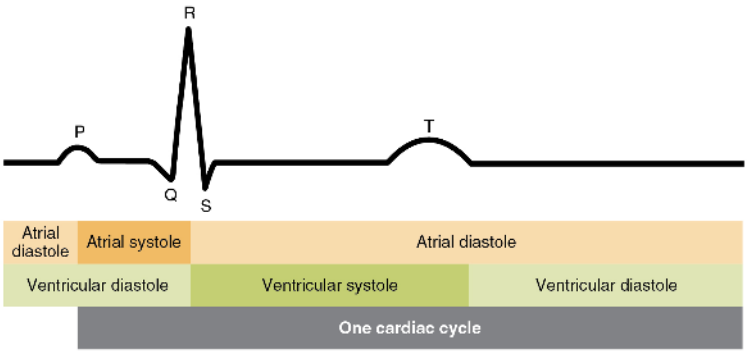


Figure 14.3.3: Relationship between the Cardiac Cycle and ECG Initially, both the atria and ventricles are relaxed (diastole). The P wave represents depolarization of the atria and is followed by atrial contraction (systole). Atrial systole extends until the QRS complex, at which point, the atria relax. The QRS complex represents depolarization of the ventricles and is followed by ventricular contraction. The T wave represents the repolarization of the ventricles and marks the beginning of ventricular relaxation.

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14.4: Structure and Function of Blood Vessels

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

- Compare and contrast the three tunics that make up the walls of most blood vessels
- Distinguish between elastic arteries, muscular arteries, and arterioles on the basis of structure, location, and function
- Compare and contrast the three types of capillaries on the basis of structure, location, and function
- Describe the basic structure of a capillary bed, from the supplying metarteriole to the venule into which it drains
- Compare and contrast veins and venules on the basis of structure, location, and function
- Discuss factors affecting blood flow in the venous system

Blood is carried through the body via blood vessels. An artery is a blood vessel that carries blood away from the heart, where it branches into ever-smaller vessels. Eventually, the smallest arteries, vessels called arterioles, further branch into tiny capillaries, where nutrients and wastes are exchanged, and then combine with other vessels that exit capillaries to form venules, small blood vessels that carry blood to a vein, a larger blood vessel that returns blood to the heart.

Blood flow is the movement of blood through a vessel, tissue, or organ. The slowing or blocking of blood flow is called resistance. **Blood pressure** is the force that blood exerts upon the walls of the blood vessels or chambers of the heart. The components of blood pressure include systolic pressure, which results from ventricular contraction, and diastolic pressure, which results from ventricular relaxation. Pulse, the expansion and recoiling of an artery, reflects the heartbeat. In the arterial system, vasodilation and vasoconstriction of the arterioles is a significant factor in systemic blood pressure: slight vasodilation greatly decreases resistance and increases flow, whereas slight vasoconstriction greatly increases resistance and decreases flow. In the arterial system, as resistance increases, blood pressure increases and flow decreases. In the venous system, constriction increases blood pressure as it does in arteries; the increasing pressure helps to return blood to the heart. In addition, constriction causes the vessel lumen to become more rounded, decreasing resistance and increasing blood flow.

Arteries and veins transport blood in two distinct circuits: the systemic circuit and the pulmonary circuit (Figure 14.4.1). The systemic circuit begins in the left atrium of the heart and ends in the venae cavae and coronary sinus that drain into the right atrium. Systemic arteries provide blood rich in oxygen to the body's tissues; this blood is often referred to as oxygenated blood. The blood returned to the heart through systemic veins has less oxygen, since much of the oxygen carried by the arteries has been delivered to the cells; this blood is often referred to as deoxygenated blood. In contrast, the pulmonary circuit begins in the right atrium and ends in the pulmonary veins that drain into the left atrium. Pulmonary arteries carry blood low in oxygen exclusively to the lungs for gas exchange. Pulmonary veins then return freshly oxygenated blood from the lungs to the heart to be pumped back out into systemic circulation. Although arteries and veins differ structurally and functionally, they share certain features.

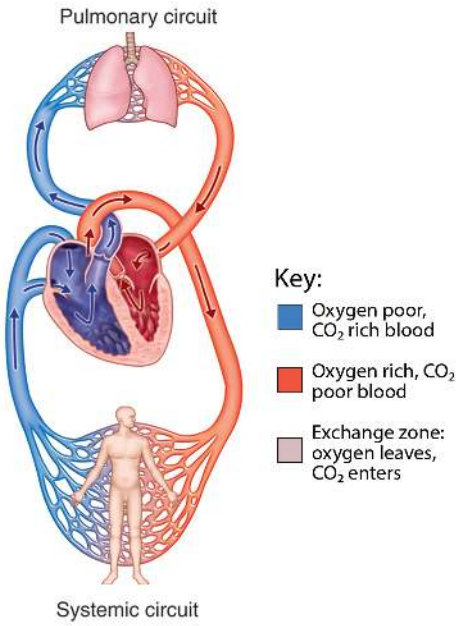


Figure 14.4.1: Cardiovascular Circulation in Pulmonary and Systemic Circuits. The pulmonary circuit moves blood from the heart to the lungs and back to the heart. The systemic circuit moves blood from the heart to the body and returns it to the heart. Within the lungs and the body regions are capillary beds where oxygen and carbon dioxide are exchanged. *(Image Credit: "Systemic and Pulmonary Circuits" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original by Open Learning Initiative.)*

Structural Characteristics of Blood Vessels

Blood Vessel Tunics

Different types of blood vessels vary slightly in their structures, but they share the same general features. Arteries and arterioles have thicker walls than veins and venules because they are closer to the heart and receive blood that is surging at a far greater pressure (Figure 14.4.2). Each type of vessel has a **lumen**—a hollow passageway through which blood flows. Arteries have smaller lumens than veins, a characteristic that helps to maintain the pressure of blood moving through the system. Together, their thicker walls and smaller diameters give arterial lumens a more rounded appearance in cross section than the lumens of veins.

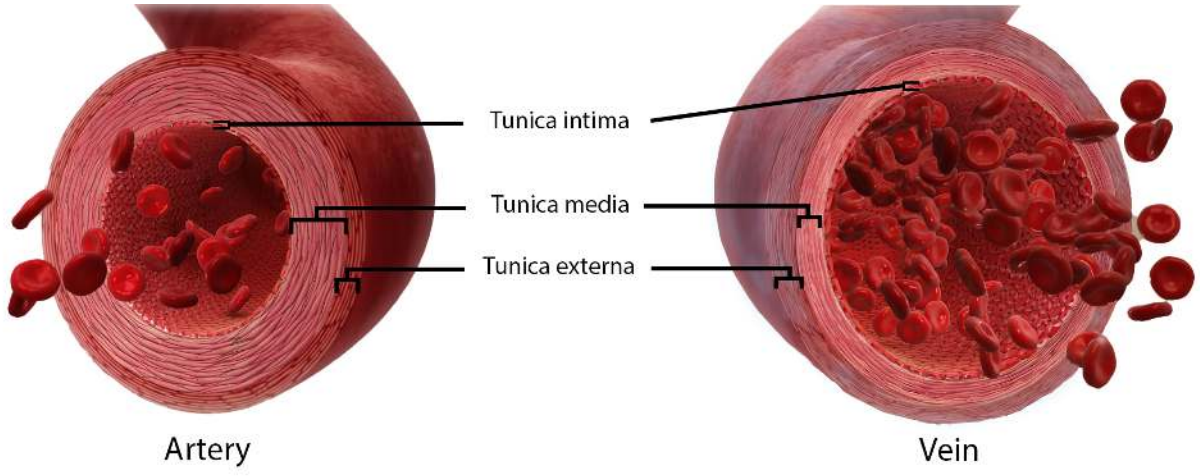


Figure 14.4.2: Structure of Blood Vessels. The walls of arteries and veins share the same general features, but the muscular layer of arteries is much thicker because of the higher pressure of the blood that flows through them. *(Image Credit: "Tunics of Arteries and Veins" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original by Scientific Animations.)*

By the time blood has passed through capillaries and entered venules, the pressure initially exerted upon it by heart contractions has diminished. In other words, in comparison to arteries, venules and veins withstand a much lower pressure from the blood that flows through them. Their walls are considerably thinner and their lumens are correspondingly larger in diameter, allowing more blood to flow with less vessel resistance. In addition, many veins of the body, particularly those of the limbs, contain valves that assist the unidirectional flow of blood toward the heart. This is critical because blood flow becomes sluggish in the extremities, as a result of the lower pressure and the effects of gravity.

Both arteries and veins have the same three distinct tissue layers, called tunics (from the Latin term tunica, for the garments first worn by ancient Romans). From the most interior layer to the outer, these tunics are the **tunica intima**, the **tunica media**, and the **tunica externa** (see Figure 14.4.2. Table 14.4.1 compares and contrasts the tunics of the arteries and veins.

Table 14.4.1: Comparison of Tunics in Arteries and Veins

Tunic (Layer)	Arteries	Veins
General Appearance	• Thick walls with small lumens • Generally appear rounded	• Thin walls with large lumens • Generally appear flattened
Tunica Intima	• Endothelium usually appears wavy due to constriction of smooth muscle • Internal elastic membrane present in larger vessels	• Endothelium appears smooth • Internal elastic membrane absent
Tunica Media	• Normally the thickest layer in arteries • Smooth muscle cells and elastic fibers predominate (the proportions of these vary with distance from the heart) • Nervi vasorum and vasa vasorum present • External elastic membrane present in larger vessels	• Normally thinner than the tunica externa • Smooth muscle cells with elastic and collagen fibers • Nervi vasorum and vasa vasorum present • External elastic membrane absent
Tunica Externa	• Normally thinner than the tunica media in all but the largest arteries • Collagen and elastic fibers • Nervi vasorum and vasa vasorum present	• Normally the thickest layer in veins • Collagen and smooth fibers predominate • Some smooth muscle fibers • Nervi vasorum and vasa vasorum present

Arterial Structure

An **artery** is a blood vessel that conducts blood away from the heart. All arteries have relatively thick walls that can withstand the high pressure of blood ejected from the heart. However, those close to the heart have the thickest walls, containing a high percentage of elastic fibers in all three of their tunics. This type of artery is known as an **elastic artery** (Figure 14.4.3). Vessels larger than 10 mm in diameter are typically elastic. Their abundant elastic fibers allow them to expand, as blood pumped from the ventricles passes through them, and then to recoil after the surge has passed. If artery walls were rigid and unable to expand and recoil, their resistance to blood flow would greatly increase and blood pressure would rise to even higher levels, which would in turn require the heart to pump harder to increase the volume of blood expelled by each pump and maintain adequate pressure and flow. Artery walls would have to become even thicker in response to this increased pressure. The elastic recoil of the vascular wall helps to maintain the pressure gradient that drives the blood through the arterial system. An elastic artery is also known as a conducting artery, because the large diameter of the lumen gives it a low resistance and enables it to accept a large volume of blood from the heart which is conducted to smaller branches within regions of the body.

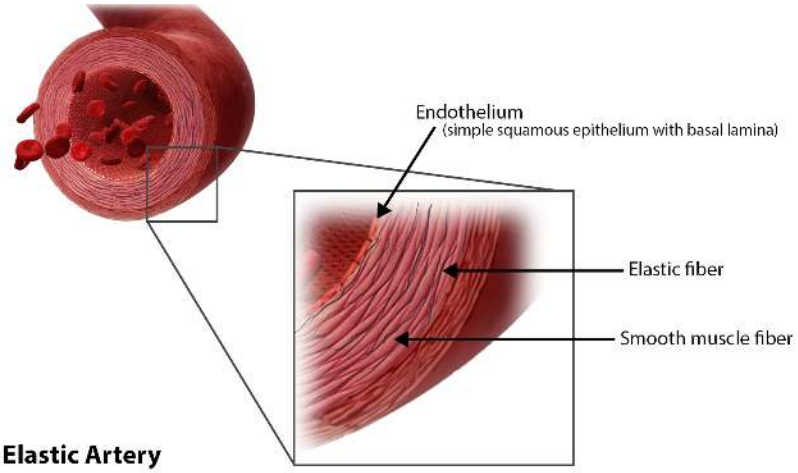


Figure 14.4.3: Elastic Artery. Elastic arteries have elastic fibers throughout their tunica media. *(Image Credit: "Elastic Artery" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original by Scientific Animations.)*

Farther from the heart, where the surge of blood has dampened, the percentage of elastic fibers in an artery's tunica media decreases and becomes restricted to two thin bands, one on each side of the tunic. The layer between the tunica intima and tunica media is the **internal elastic lamina** while the layer between the tunica media and tunica externa is the **external elastic lamina**. The artery at this point is described as a **muscular artery** (Figure 14.4.4). The diameter of muscular arteries typically ranges from 0.1 mm to 10 mm. Their thick tunica media allows muscular arteries to play a leading role in vasoconstriction which controls blood flow to individual organs. In contrast, their decreased quantity of elastic fibers limits their ability to expand. Fortunately, because the blood pressure has eased by the time it reaches these more distant vessels, elasticity has become less important.

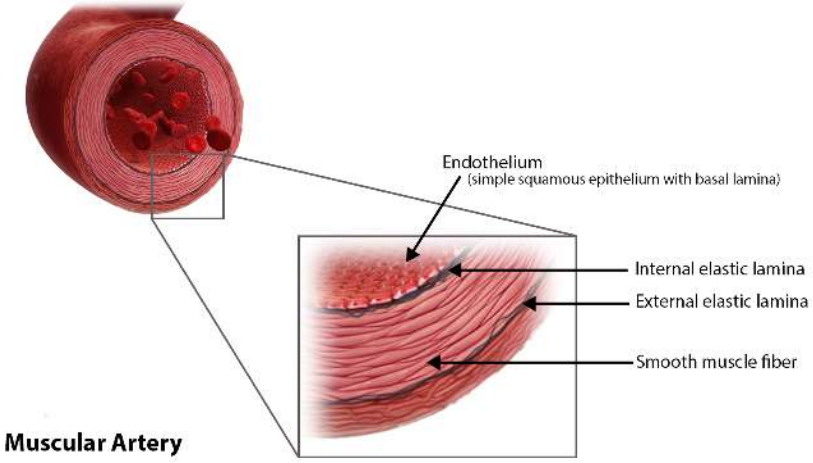


Figure 14.4.4: Muscular Artery. Muscular arteries have elastic fibers in two elastic laminae, one on each side of the tunica media. *(Image Credit: "Muscular Artery" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original by Scientific Animations.)*

Notice that although the distinctions between elastic and muscular arteries are important, there is no "line of demarcation" where an elastic artery suddenly becomes muscular. Rather, there is a gradual transition as the vascular tree repeatedly branches. In turn, muscular arteries branch to distribute blood to the vast network of arterioles that deliver blood to capillaries within specific organs and tissues. For this reason, a muscular artery is also known as a distributing artery.

Arteriole Structure

An **arteriole** is a very small artery that leads to a capillary. Arterioles have the same three tunics as the larger vessels, but the thickness of each is greatly diminished. The critical endothelial lining of the tunica intima is intact. The tunica media is restricted to one or two smooth muscle cell layers in thickness. The tunica externa remains but is very thin as arterioles are supported and held in place by their positioning within organs and tissues (see Figure 14.4.5). At the distal end of arterioles the tunica externa may be absent.

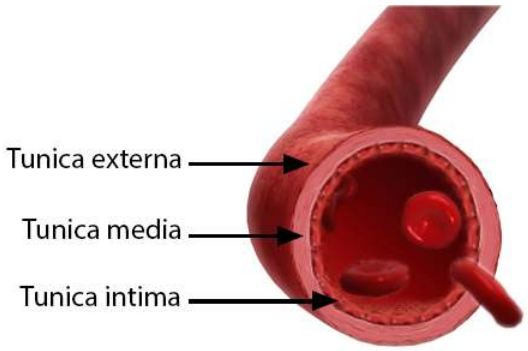


Figure 14.4.5: Arteriole. Arterioles have a much thinner wall and almost no tunica externa. *(Image Credit: "Arteriole" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original by Scientific Animations.)*

With a lumen averaging 30 micrometers or less in diameter, arterioles are critical in slowing down—or resisting—blood flow and, thus, causing a substantial drop in blood pressure. Because of this, you may see them referred to as resistance vessels. The muscle fibers in arterioles are normally slightly contracted, causing arterioles to maintain a consistent muscle tone—in this case referred to as vascular tone—in a similar manner to the muscular tone of skeletal muscle. In reality, all blood vessels exhibit vascular tone due to the partial contraction of smooth muscle. The importance of the arterioles is that they will be the primary site of both resistance and regulation of blood pressure. The precise diameter of the lumen of an arteriole at any given moment is determined by neural and chemical controls, and vasoconstriction and vasodilation in the arterioles are the primary mechanisms for distribution of blood flow to capillary beds as well as regulation of systemic blood pressure.

DISORDERS OF THE...

Cardiovascular System: Arteriosclerosis

Compliance allows an artery to expand when blood is pumped through it from the heart, and then to recoil after the surge has passed. This helps promote blood flow. In arteriosclerosis, compliance is reduced, and pressure and resistance within the vessel increase. This is a leading cause of hypertension and coronary heart disease, as it causes the heart to work harder to generate a pressure great enough to overcome the resistance.

Arteriosclerosis begins with injury to the endothelium of an artery, which may be caused by irritation from high blood glucose, infection, tobacco use, excessive blood lipids, and other factors. Artery walls that are constantly stressed by blood flowing at high pressure are also more likely to be injured—which means that hypertension can promote arteriosclerosis, as well as result from it.

Recall that tissue injury causes inflammation. As inflammation spreads into the artery wall, it weakens and scars it, leaving it stiff (sclerotic). As a result, compliance is reduced. Moreover, circulating triglycerides and cholesterol can seep between the damaged lining cells and become trapped within the artery wall, where they are frequently joined by leukocytes, calcium, and cellular debris. Eventually, this buildup, called plaque, can narrow arteries enough to impair blood flow. The term for this condition, atherosclerosis (athero- = “porridge”) describes the mealy deposits (Figure 14.4.6).

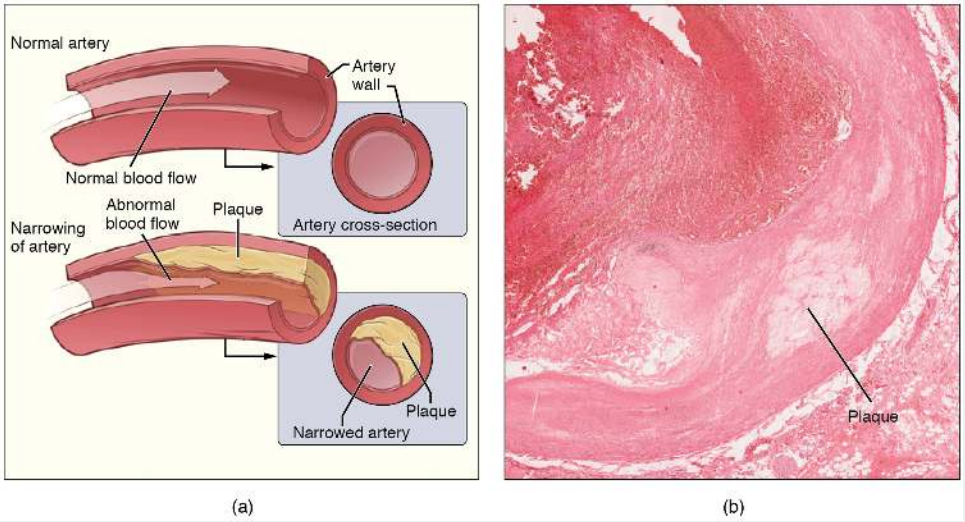


Figure 14.4.6: Atherosclerosis. (a) Atherosclerosis can result from plaques formed by the buildup of fatty, calcified deposits in an artery. (b) Plaques can also take other forms, as shown in this micrograph of a coronary artery that has a buildup of connective tissue within the artery wall. LM × 40. (Image credit: "Atherosclerosis" by OpenStax is licensed under CC BY 3.0; Micrograph provided by the Regents of University of Michigan Medical School © 2012)

Sometimes a plaque can rupture, causing microscopic tears in the artery wall that allow blood to leak into the tissue on the other side. When this happens, platelets rush to the site to clot the blood. This clot can further obstruct the artery and—if it occurs in a coronary or cerebral artery—cause a sudden heart attack or stroke. Alternatively, plaque can break off and travel through the bloodstream as an embolus until it blocks a more distant, smaller artery.

Even without total blockage, vessel narrowing leads to ischemia—reduced blood flow—to the tissue region "downstream" of the narrowed vessel. Ischemia in turn leads to hypoxia—decreased supply of oxygen to the tissues. Hypoxia involving cardiac muscle or brain tissue can lead to cell death and severe impairment of brain or heart function.

A major risk factor for both arteriosclerosis and atherosclerosis is advanced age, as the conditions tend to progress over time. Arteriosclerosis is normally defined as the more generalized loss of compliance, "hardening of the arteries," whereas atherosclerosis is a more specific term for the build-up of plaque in the walls of the vessel and is a specific type of arteriosclerosis. There is also a distinct genetic component, and pre-existing hypertension and/or diabetes also greatly increase the risk. However, obesity, poor nutrition, lack of physical activity, and tobacco use all are major risk factors.

Treatment includes lifestyle changes, such as weight loss, smoking cessation, regular exercise, and adoption of a diet low in sodium and saturated fats. Medications to reduce cholesterol and blood pressure may be prescribed. For blocked coronary arteries, surgery is warranted. In angioplasty, a catheter is inserted into the vessel at the point of narrowing, and a second catheter with a balloon-like tip is inflated to widen the opening. To prevent subsequent collapse of the vessel, a small mesh tube called a stent is often inserted. In an endarterectomy, plaque is surgically removed from the walls of a vessel. This operation is typically performed on the carotid arteries of the neck, which are a prime source of oxygenated blood for the brain. In a coronary bypass procedure, a non-vital superficial vessel from another part of the body (often the great saphenous vein) or a synthetic vessel is inserted to create a path around the blocked area of a coronary artery.

Capillary Structure

A **capillary** is a microscopic channel that supplies blood to the tissues, through a process called **perfusion**. Exchange of gases and other substances occurs in the capillaries between the blood and the surrounding cells and their tissue fluid (interstitial fluid). The diameter of a capillary lumen ranges from 5–10 micrometers; the smallest are just barely wide enough for an erythrocyte to squeeze through. Flow through capillaries is often described as **microcirculation**.

The wall of a capillary consists of the endothelial layer surrounded by a basement membrane with occasional smooth muscle fibers. Some variation in wall structure is seen depending on the size of the capillary. In a large capillary, several endothelial cells bordering each other may line the lumen, while in a small capillary, there may be only a single cell layer that wraps around to contact itself.

For capillaries to function, their walls must be leaky, or **permeable**, allowing some substances to pass through. There are three major types of capillaries, which differ according to their degree of permeability: continuous, fenestrated, and sinusoid capillaries.

Venous System

The venous system is the system of veins in the systemic and pulmonary circulations that return blood from the tissues to the heart. In the systemic circuit the venous return is of deoxygenated blood from the organs and tissues of the body. All of the systemic veins are tributaries of the two largest veins, the superior and inferior vena cavae, that empty the oxygen-depleted blood into the right atrium of the heart. In the pulmonary circuit the pulmonary veins return oxygenated blood from the lungs to the heart.

The whole of the venous system is a large volume, low pressure system. The thin walls of the veins and their larger cross-sectional area (total luminal diameter) allow them to hold a large volume of blood, giving them the term of capacitance vessels. Veins do not have a consistent pressure generator equivalent to the heart that propels the blood in a single direction. While the blood in some veins can rely on gravity to cause movement, most work against gravity and their structure is specialized to prevent backflow and to allow for fluctuations in blood volume.

Veins vary in size from the smallest post-capillary venules, to larger venules, small veins, medium veins, and large veins. The thickness of the walls of the veins varies according to their location – in the legs the vein walls are much thicker than those in the arms - as does the number of valves present.

Venules

A **venule** is an extremely small vein, generally 8–100 micrometers in diameter. Postcapillary venules drain multiple capillaries exiting from a capillary bed. Multiple venules join to form veins. The walls of venules consist of endothelium, a thin or non-existent middle layer with a few smooth muscle cells and elastic fibers, plus an outer layer of connective tissue fibers that constitute a thin tunica externa (Figure 14.4.7). Venules as well as capillaries are the primary sites of emigration or diapedesis, in which the white blood cells adhere to the endothelial lining of the vessels and then squeeze between adjacent cells to enter the tissue fluid.

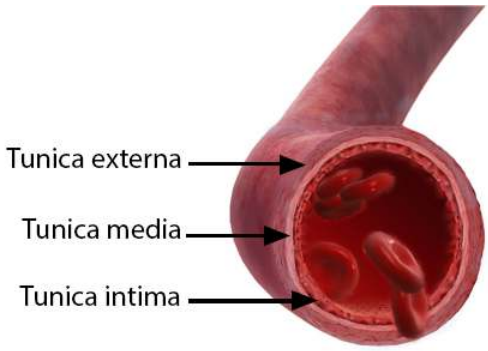


Figure 14.4.7: Venule. The wall of venules is also thin, with the tunica externa being thicker than the tunica media. *(Image Credit: "Venule" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original by Scientific Animations.)*

Veins

A **vein** is a larger blood vessel that conducts blood toward the heart. Compared to arteries, veins are thin-walled vessels with large and irregular lumens (see Figure 14.4.8). Because they are low-pressure vessels, larger veins are commonly equipped with valves that promote the unidirectional flow of blood toward the heart and prevent backflow toward the capillaries caused by the inherent low blood pressure in veins as well as the pull of gravity (Figure 14.4.8).

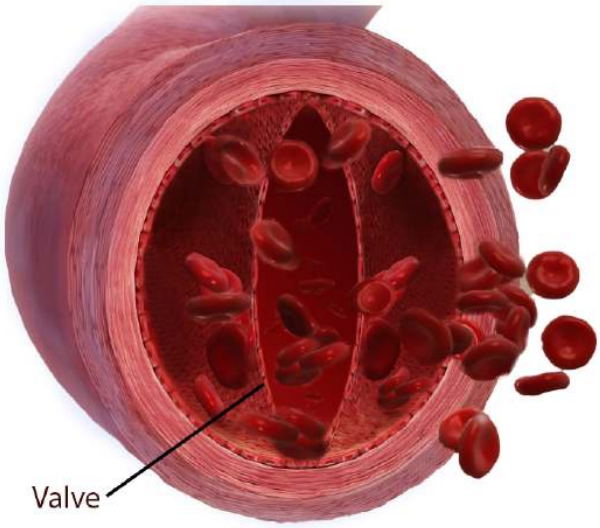


Figure 14.4.8: Vein with Valve. When pressure distal to the valve is higher than the pressure proximal to the valve the valve cusps will open and allow blood to flow toward the heart. When blood begins to flow in reverse, it will build up in the cusp pockets and cause the valve to close. This prevents further backflow. *(Image Credit: "Vein with Valve" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original by Scientific Animations.)*

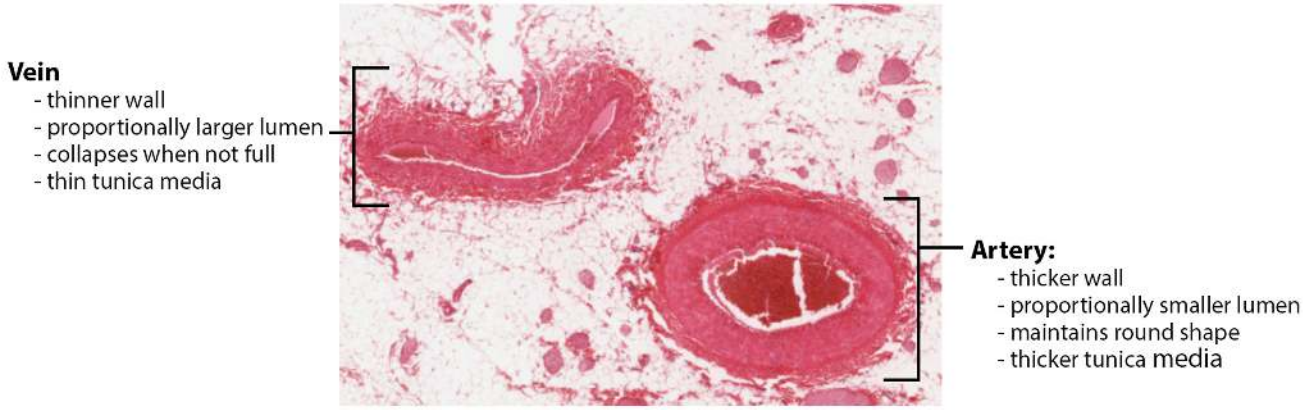


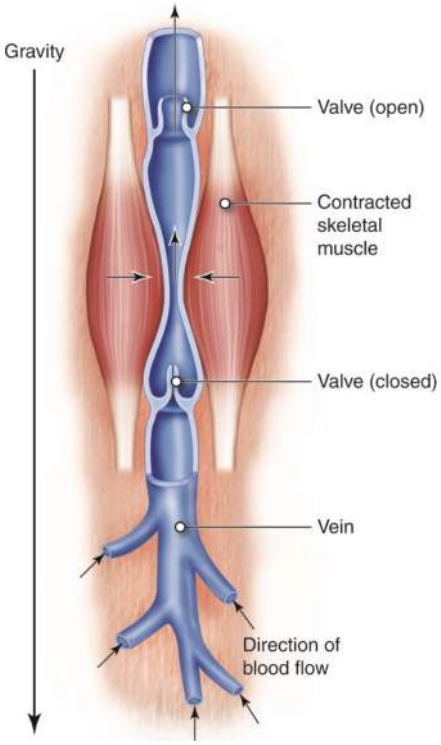
Figure 14.4.9: Small Artery and Vein. Small arteries and veins clearly demonstrate the histological differences between the two vessel types. Small veins have a thicker tunica externa and a very thin tunic media whereas small arteries have a thick tunica media and a relatively thinner tunica externa. *(Image credit: "Artery and Vein Histological Comparison" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, slide provided by the Regents of the University of Michigan Medical School © 2022.)*

Skeletal Muscle Pump

The pumping action of the heart propels the blood into the arteries, from an area of higher pressure toward an area of lower pressure. If blood is to flow from the veins back into the heart, the pressure in the veins must be greater than the pressure in the atria of the heart. Two factors help maintain this pressure gradient between the veins and the heart. First, the pressure in the atria during diastole is very low, often approaching zero when the atria are relaxed (atrial diastole). Second, two physiologic "pumps" increase pressure in the venous system. The use of the term "pump" implies a physical device that speeds flow. These physiological pumps are less obvious.

In many body regions, the pressure within the veins can be increased by the contraction of the surrounding skeletal muscle. This mechanism, known as the **skeletal muscle pump** (Figure 14.4.10), helps the lower-pressure veins counteract the force of gravity, increasing pressure to move blood back to the heart. As leg muscles contract, for example during walking or running, they exert pressure on nearby veins with their numerous one-way valves. This increased pressure causes blood to flow upward, opening valves superior to the contracting muscles so blood flows through. Simultaneously, valves inferior to the contracting muscles close;

thus, blood should not seep back downward toward the feet. Military recruits are trained to flex their legs slightly while standing at attention for prolonged periods. Failure to do so may allow blood to pool in the lower limbs rather than returning to the heart. Consequently, the brain will not receive enough oxygenated blood, and the individual may lose consciousness.



(Figure 14.4.10): *Venous blood flow due to muscle contraction. Some veins are located in between muscles (e.g. in the lower extremity). When the muscles contract the pressure increases. Therefore valves will open so that blood will flow towards the heart.* (Image Credit: "KnowledgeWorks - Drawing Venous blood flow due to muscle contraction - English labels" by KnowledgeWorks Global Ltd., license: CC BY)

DISORDERS OF THE...

Cardiovascular System: Edema and Varicose Veins

Despite the presence of valves and the contributions of other anatomical and physiological adaptations we will cover shortly, over the course of a day, some blood will inevitably pool, especially in the lower limbs, due to the pull of gravity. Any blood that accumulates in a vein will increase the pressure within it, which can then be reflected back into the smaller veins, venules, and eventually even the capillaries. Increased pressure will promote the flow of fluids out of the capillaries and into the interstitial fluid. The presence of excess tissue fluid around the cells leads to a condition called edema.

Most people experience a daily accumulation of tissue fluid, especially if they spend much of their work life on their feet (like most health professionals). However, clinical edema goes beyond normal swelling and requires medical treatment. Edema has many potential causes, including hypertension and heart failure, severe protein deficiency, renal failure, and many others. In order to treat edema, which is a sign rather than a discrete disorder, the underlying cause must be diagnosed and alleviated.



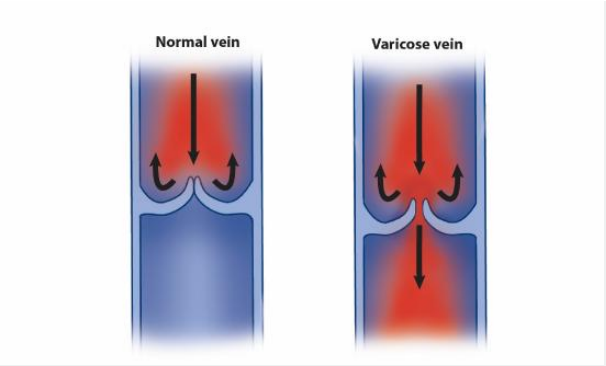


Figure 14.4.11: Varicose Veins. Varicose veins are commonly found in the superficial veins of the lower limbs. Defective valves cause localized pooling of blood in the veins that can lead to distention and deformity of the vessel appearing as lumps under the surface of the skin. *(Image credits: "Left Calf and Varicose Veins" by Thomas Kriese is licensed under CC BY 2.0; "Varicose Veins and Valves" by BlueLink is licensed under CC BY-NC 4.0 with notification of the original authors.)*

Edema may be accompanied by varicose veins, especially in the superficial veins of the legs (Figure 14.4.11). This disorder arises when defective valves allow blood to accumulate within the veins, causing them to distend, twist, and become visible on the surface of the integument. Varicose veins may occur in both sexes, but are more common in women and are often related to pregnancy. More than simple cosmetic blemishes, varicose veins are often painful and sometimes itchy or throbbing. Without treatment, they tend to grow worse over time. The use of support hose, as well as elevating the feet and legs whenever possible, may be helpful in alleviating this condition. Laser surgery and interventional radiologic procedures can reduce the size and severity of varicose veins. Severe cases may require conventional surgery to remove the damaged vessels. As there are typically redundant circulation patterns, that is, anastomoses, for the smaller and more superficial veins, removal does not typically impair the circulation. There is evidence that patients with varicose veins suffer a greater risk of developing a thrombus or clot.

Table 14.4.2: Comparison of General Features of Arteries and Veins

	Arteries	Veins
Direction of blood flow	Conducts blood away from the heart	Conducts blood toward the heart
General appearance	Rounded	Irregular, often collapsed
Pressure	High	Low
Wall thickness	Thick	Thin
Relative oxygen concentration	Higher in systemic arteries Lower in pulmonary arteries	Lower in systemic veins Higher in pulmonary veins
Valves	Not present	Present most commonly in limbs and in veins inferior to the heart

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14.5: Blood Flow, Blood Pressure, and Resistance

Learning Objectives

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

- Distinguish between systolic pressure and diastolic pressure
- Describe the clinical measurement of pulse and blood pressure
- Identify and discuss five variables affecting arterial blood flow and blood pressure
- Discuss several factors affecting blood flow in the venous system

Blood flow refers to the movement of blood through a vessel, tissue, or organ, and is usually expressed in terms of volume of blood per unit of time. It is initiated by the contraction of the ventricles of the heart. Ventricular contraction ejects blood into the major arteries, resulting in flow from regions of higher pressure to regions of lower pressure, as blood encounters smaller arteries and arterioles, then capillaries, then the venules and veins of the venous system. This section discusses a number of critical variables that contribute to blood flow throughout the body. It also discusses the factors that impede or slow blood flow, a phenomenon known as resistance.

As noted earlier, hydrostatic pressure is the force exerted by a fluid due to gravitational pull, usually against the wall of the container in which it is located. One form of hydrostatic pressure is **blood pressure**, the force exerted by blood upon the walls of the blood vessels or the chambers of the heart. Blood pressure may be measured in capillaries and veins, as well as the vessels of the pulmonary circulation; however, the term blood pressure without any specific descriptors typically refers to **systemic arterial blood pressure**—that is, the pressure of blood flowing in the arteries of the systemic circulation. In clinical practice, this pressure is measured in mm Hg and is usually obtained using the brachial artery of the arm.

Components of Arterial Blood Pressure

Arterial blood pressure in the larger vessels consists of several distinct components (Figure 14.5.1): systolic and diastolic pressures, pulse pressure, and mean arterial pressure.

Systolic and Diastolic Pressures

When systemic arterial blood pressure is measured, it is recorded as a ratio of two numbers (e.g., 120/80 is a normal adult blood pressure), expressed as **systolic pressure** over **diastolic pressure**. The systolic pressure is the higher value (typically around 120 mm Hg) and reflects the arterial pressure resulting from the ejection of blood during ventricular contraction, or systole. The diastolic pressure is the lower value (usually about 80 mm Hg) and represents the arterial pressure of blood during ventricular relaxation, or diastole.

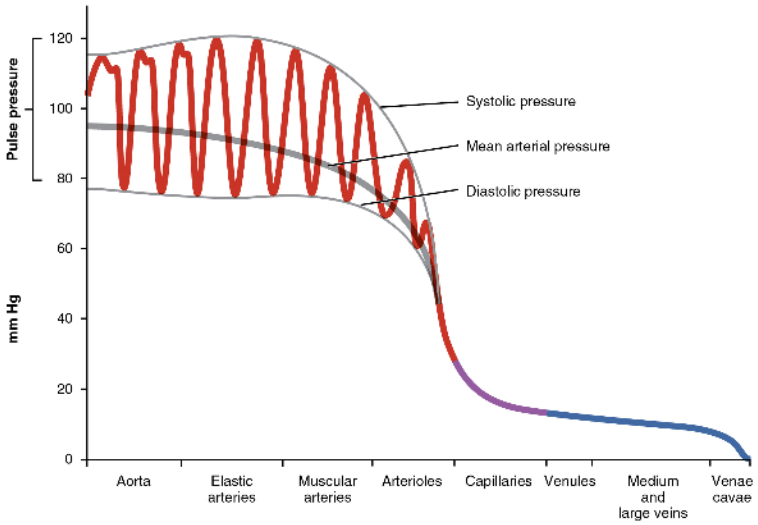


Figure 14.5.1: Systemic Blood Pressure The graph shows the components of blood pressure throughout the blood vessels, including systolic, diastolic, mean arterial, and pulse pressures.

Pulse

After blood is ejected from the heart, elastic fibers in the arteries help maintain a high-pressure gradient as they expand to accommodate the blood, then recoil. This expansion and recoiling effect, known as the **pulse**, can be palpated manually or measured electronically. Although the effect diminishes over distance from the heart, elements of the systolic and diastolic components of the pulse are still evident down to the level of the arterioles.

Because pulse indicates heart rate, it is measured clinically to provide clues to a patient's state of health. It is recorded as beats per minute. Both the rate and the strength of the pulse are important clinically. A high or irregular pulse rate can be caused by physical activity or other temporary factors, but it may also indicate a heart condition. The pulse strength indicates the strength of ventricular contraction and cardiac output. If the pulse is strong, then systolic pressure is high. If it is weak, systolic pressure has fallen, and medical intervention may be warranted.

Pulse can be palpated manually by placing the tips of the fingers across an artery that runs close to the body surface and pressing lightly. While this procedure is normally performed using the radial artery in the wrist or the common carotid artery in the neck, any superficial artery that can be palpated may be used (Figure 14.5.2). Common sites to find a pulse include temporal and facial arteries in the head, brachial arteries in the upper arm, femoral arteries in the thigh, popliteal arteries behind the knees, posterior tibial arteries near the medial tarsal regions, and dorsalis pedis arteries in the feet. A variety of commercial electronic devices are also available to measure pulse.

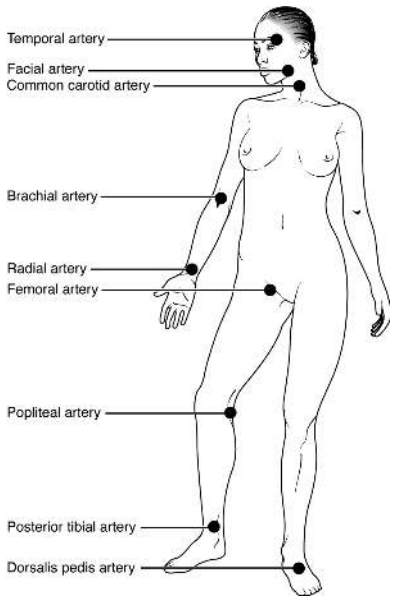


Figure 14.5.2: Pulse Sites The pulse is most readily measured at the radial artery, but can be measured at any of the pulse points shown.

Measurement of Blood Pressure

Blood pressure is one of the critical parameters measured on virtually every patient in every healthcare setting. The technique used today was developed more than 100 years ago by a pioneering Russian physician, Dr. Nikolai Korotkoff. Turbulent blood flow through the vessels can be heard as a soft ticking while measuring blood pressure; these sounds are known as **Korotkoff sounds**. The technique of measuring blood pressure requires the use of a sphygmomanometer (a blood pressure cuff attached to a measuring device) and a stethoscope. The technique is as follows:

- The clinician wraps an inflatable cuff tightly around the patient's arm at about the level of the heart.
- The clinician squeezes a rubber pump to inject air into the cuff, raising pressure around the artery and temporarily cutting off blood flow into the patient's arm.
- The clinician places the stethoscope on the patient's antecubital region and, while gradually allowing air within the cuff to escape, listens for the Korotkoff sounds.

Although there are five recognized Korotkoff sounds, only two are normally recorded. Initially, no sounds are heard since there is no blood flow through the vessels, but as air pressure drops, the cuff relaxes, and blood flow returns to the arm. As shown in Figure

14.5.3, the first sound heard through the stethoscope—the first Korotkoff sound—indicates systolic pressure. As more air is released from the cuff, blood is able to flow freely through the brachial artery and all sounds disappear. The point at which the last sound is heard is recorded as the patient's diastolic pressure.

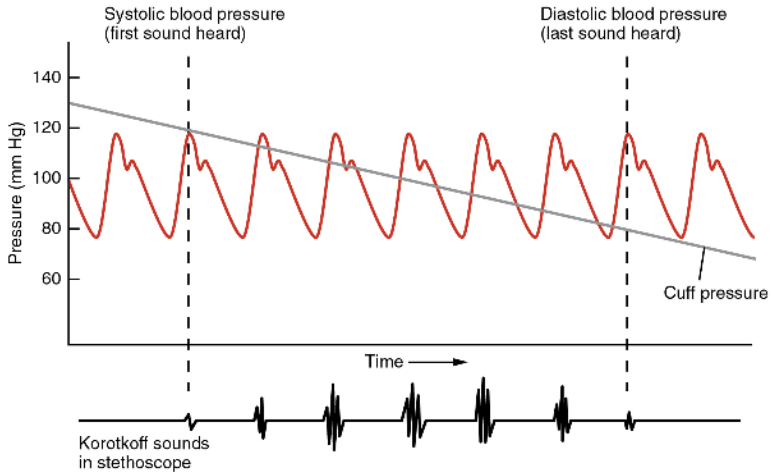


Figure 14.5.3: Blood Pressure Measurement When pressure in a sphygmomanometer cuff is released, a clinician can hear the Korotkoff sounds. In this graph, a blood pressure tracing is aligned to a measurement of systolic and diastolic pressures.

Factors Affecting Blood Flow and Blood Pressure

The three factors that affect blood pressure are:

- **Peripheral resistance**, which includes:
  - Vessel length
  - Vessel diameter
  - Blood viscosity
  - Obstructions in vessels
- **Cardiac output**, which depends on:
  - Heart rate
  - Stroke volume (the amount of blood ejected by each ventricle per heart beat)
- **Blood volume**, which depends on:
  - Water loss
  - Water gain

Recall that blood moves from higher pressure to lower pressure. It is pumped from the heart into the arteries at high pressure. If you increase pressure in the arteries (called afterload), and cardiac function does not compensate, blood flow will actually decrease. In the venous system, the opposite relationship is true. Increased pressure in the veins does not decrease flow as it does in arteries, but actually increases flow. Since pressure in the veins is normally relatively low, for blood to flow back into the heart, the pressure in the atria during atrial diastole must be even lower. It normally approaches zero, except when the atria contract (see Figure 14.5.1).

Peripheral Resistance

Peripheral resistance is defined as any factor that hinders blood flow through the vessels. Any factor that hinders blood flow through a vessel will increase the resistance of the circuit the blood is flowing through. The greater the peripheral resistance, the higher blood pressure must be to overcome that resistance.

Peripheral resistance is affected by vessel length. The length of a vessel is directly proportional to its resistance: the longer the vessel, the greater the resistance and the lower the flow. As with blood volume, this makes intuitive sense, since the increased surface area of the vessel will impede the flow of blood. Likewise, if the vessel is shortened, the resistance will decrease and flow will increase.

Peripheral resistance will also be affected by vessel diameter. Given the same volume of blood, an increased diameter means there is less blood contacting the vessel wall, thus lower friction and lower resistance, subsequently increasing flow. A decreased diameter means more of the blood contacts the vessel wall, and resistance increases, subsequently decreasing flow. Vessel diameter can be changed through vasodilation (dilation of the blood vessels) and vasoconstriction (constriction of the blood vessels). Vasodilation and vasoconstriction occur at various moments throughout the day depending on sympathetic and parasympathetic stimulation, exercise, and other factors.

Cardiac Output

Cardiac output is the measurement of blood flow from the heart through the ventricles, and is usually measured in liters per minute. Another way to think of cardiac output is to think of it as the volume of blood ejected by each ventricle per minute. Any factor that causes cardiac output to increase, by elevating **heart rate** or **stroke volume** or both, will elevate blood pressure and promote blood flow. These factors include sympathetic stimulation, the catecholamines epinephrine and norepinephrine, thyroid hormones, and increased calcium ion levels. Conversely, any factor that decreases cardiac output, by decreasing heart rate or stroke volume or both, will decrease arterial pressure and blood flow. These factors include parasympathetic stimulation, elevated or decreased potassium ion levels, decreased calcium levels, anoxia (severe lack of oxygen), and acidosis.

Obstructions in Vessels

Obstructions in the blood vessels can affect vascular compliance. Compliance is the ability of any compartment to expand to accommodate increased content. A metal pipe, for example, is not compliant, whereas a balloon is. The greater the compliance of an artery, the more effectively it is able to expand to accommodate surges in blood flow without increased resistance or blood pressure. Veins are more compliant than arteries and can expand to hold more blood. When vascular disease causes stiffening of arteries, compliance is reduced and resistance to blood flow is increased. The result is more turbulence, higher pressure within the vessel, and reduced blood flow. This increases the work of the heart. The presence of plaques within the blood vessels also obstructs blood flow, increasing the resistance in that circuit.



Figure 14.5.4 Plaque within the vessels can block or restrict blood flow, increasing resistance and affecting blood pressure. *(Image credit: "Arteriole" by Scientific Animations is licensed under CC BY-SA 4.0)*

Blood Volume

Blood volume depends on water gain and water loss. Gaining water can cause blood volume to increase, while losing water can cause blood volume to decrease. As blood volume decreases, pressure and flow decrease. As blood volume increases, pressure and flow increase.

Under normal circumstances, blood volume varies little. Low blood volume, called hypovolemia, may be caused by bleeding, dehydration, vomiting, severe burns, or some medications used to treat hypertension. It is important to recognize that other regulatory mechanisms in the body are so effective at maintaining blood pressure that an individual may be asymptomatic until 10–20 percent of the blood volume has been lost. Treatment typically includes intravenous fluid replacement.

Hypervolemia, excessive fluid volume, may be caused by retention of water and sodium, as seen in patients with heart failure, liver cirrhosis, some forms of kidney disease, hyperaldosteronism, and some glucocorticoid steroid treatments. Restoring homeostasis in these patients depends upon reversing the condition that triggered the hypervolemia.

Blood Viscosity

Viscosity is the thickness of fluids that affects their ability to flow. Clean water, for example, is less viscous than mud. The viscosity of blood is directly proportional to resistance and inversely proportional to flow; therefore, any condition that causes viscosity to increase will also increase resistance and decrease flow. For example, imagine sipping milk, then a milkshake, through the same size straw. You experience more resistance and therefore less flow from the milkshake. Conversely, any condition that causes viscosity to decrease (such as when the milkshake melts) will decrease resistance and increase flow.

Normally the viscosity of blood does not change over short periods of time. The two primary determinants of blood viscosity are the formed elements and plasma proteins. Since the vast majority of formed elements are erythrocytes, any condition affecting erythropoiesis, such as polycythemia or anemia, can alter viscosity. Since most plasma proteins are produced by the liver, any condition affecting liver function can also change the viscosity slightly and therefore alter blood flow. Liver abnormalities such as hepatitis, cirrhosis, alcohol damage, and drug toxicities result in decreased levels of plasma proteins, which decrease blood viscosity. While leukocytes and platelets are normally a small component of the formed elements, there are some rare conditions in which severe overproduction can impact viscosity as well.

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14.6: Review Questions

2.

Which of the following is not important in preventing backflow of blood?

1. chordae tendineae
2. papillary muscles
3. AV valves
4. endocardium

3.

Which valve separates the left atrium from the left ventricle?

1. mitral
2. tricuspid
3. pulmonary
4. aortic

4.

Which of the following lists the valves in the order through which the blood flows from the vena cava through the heart?

1. tricuspid, pulmonary semilunar, bicuspid, aortic semilunar
2. mitral, pulmonary semilunar, bicuspid, aortic semilunar
3. aortic semilunar, pulmonary semilunar, tricuspid, bicuspid
4. bicuspid, aortic semilunar, tricuspid, pulmonary semilunar

5.

Which chamber initially receives blood from the systemic circuit?

1. left atrium
2. left ventricle
3. right atrium
4. right ventricle

6.

The _____ layer secretes chemicals that help to regulate ionic environments and strength of contraction and serve as powerful vasoconstrictors.

1. pericardial sac
2. endocardium
3. myocardium
4. epicardium

7.

The myocardium would be the thickest in the _____.

1. left atrium
2. left ventricle
3. right atrium
4. right ventricle

8.

In which septum is it normal to find openings in the adult?

1. interatrial septum
2. interventricular septum
3. atrioventricular septum
4. all of the above

9.

Which of the following is unique to cardiac muscle cells?

1. Only cardiac muscle contains a sarcoplasmic reticulum.
2. Only cardiac muscle has gap junctions.
3. Only cardiac muscle is capable of autorhythmicity
4. Only cardiac muscle has a high concentration of mitochondria.

10.

The influx of which ion accounts for the plateau phase?

1. sodium
2. potassium
3. chloride
4. calcium

11.

Which portion of the ECG corresponds to repolarization of the atria?

1. P wave
2. QRS complex
3. T wave
4. none of the above: atrial repolarization is masked by ventricular depolarization

12.

Which component of the heart conduction system would have the slowest rate of firing?

1. atrioventricular node
2. atrioventricular bundle
3. bundle branches
4. Purkinje fibers

13.

The cardiac cycle consists of a distinct relaxation and contraction phase. Which term is typically used to refer ventricular contraction while no blood is being ejected?

1. systole
2. diastole
3. quiescent
4. isovolumic contraction

14.

Most blood enters the ventricle during _____.

1. atrial systole
2. atrial diastole
3. ventricular systole
4. isovolumic contraction

15.

The first heart sound represents which portion of the cardiac cycle?

1. atrial systole
2. ventricular systole
3. closing of the atrioventricular valves
4. closing of the semilunar valves

16.

Ventricular relaxation immediately follows _____.

1. atrial depolarization

2. ventricular repolarization
3. ventricular depolarization
4. atrial repolarization

17.

The force the heart must overcome to pump blood is known as _____.

1. preload
2. afterload
3. cardiac output
4. stroke volume

18.

The cardiovascular centers are located in which area of the brain?

1. medulla oblongata
2. pons
3. mesencephalon (midbrain)
4. cerebrum

19.

In a healthy young adult, what happens to cardiac output when heart rate increases above 160 bpm?

1. It increases.
2. It decreases.
3. It remains constant.
4. There is no way to predict.

20.

What happens to preload when there is venous constriction in the veins?

1. It increases.
2. It decreases.
3. It remains constant.
4. There is no way to predict.

21.

Which of the following is a positive inotrope?

1. Na^+
2. K^+
3. Ca^{2+}
4. both Na^+ and K^+

22.

The earliest organ to form and begin function within the developing human is the _____.

1. brain
2. stomach
3. lungs
4. heart

23.

Of the three germ layers that give rise to all adult tissues and organs, which gives rise to the heart?

1. ectoderm
2. endoderm
3. mesoderm
4. placenta

24.

The two tubes that eventually fuse to form the heart are referred to as the _____.

1. primitive heart tubes
2. endocardial tubes
3. cardiogenic region
4. cardiogenic tubes

25.

Which primitive area of the heart will give rise to the right ventricle?

1. bulbus cordis
2. primitive ventricle
3. sinus venosus
4. truncus arteriosus

26.

The pulmonary trunk and aorta are derived from which primitive heart structure?

1. bulbus cordis
2. primitive ventricle
3. sinus venosus
4. truncus arteriosus

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CHAPTER OVERVIEW

15: The Respiratory System

15.1: Organs and Structures of the Respiratory System
15.2: The Lungs
15.3: The Process of Breathing
15.4: Gas Exchange
15.5: Review Questions

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15.1: Organs and Structures of the Respiratory System

Learning Objectives

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

- List the structures that make up the respiratory system
- Describe how the respiratory system processes oxygen and CO_2
- Compare and contrast the functions of upper respiratory tract with the lower respiratory tract

The major organs of the respiratory system function primarily to provide oxygen to body tissues for cellular respiration, remove the waste product carbon dioxide, and help to maintain acid-base balance. Portions of the respiratory system are also used for non-vital functions, such as sensing odors, speech production, and for straining, such as during childbirth or coughing (Figure 15.1.1).

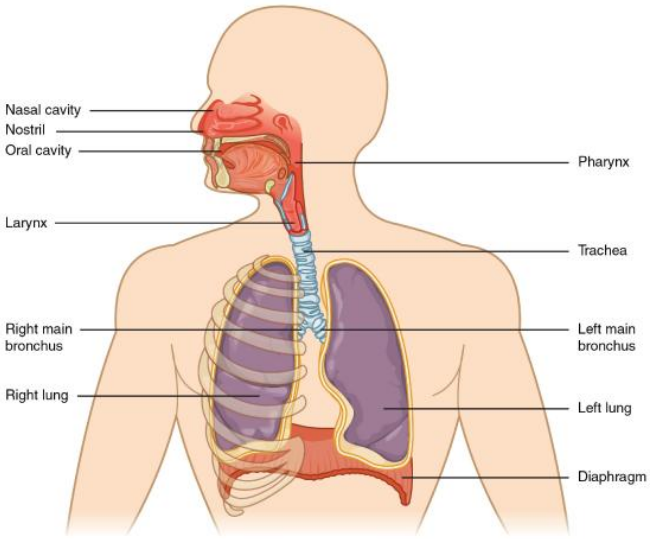


Figure 15.1.1: Major Respiratory Structures The major respiratory structures span the nasal cavity to the diaphragm.

Functionally, the respiratory system can be divided into a **conducting zone** and a **respiratory zone**. The **conducting zone** of the respiratory system includes the organs and structures not directly involved in gas exchange. The **respiratory zone** includes structures involved in **gas exchange**. Gas exchange is the process in which oxygen diffuses from our lungs into blood through inhalation, and carbon dioxide diffuses from our blood into our lungs to be exhaled.

The structures of the conducting zone broadly include:

- The nostrils and nasal cavity
- The pharynx and its subdivisions
- The larynx
- Trachea
- Bronchial tree
- Bronchi
- Bronchioles, until reaching the terminal bronchioles

The structures of the respiratory zone include:

- Respiratory bronchioles
- Alveolar ducts
- Alveolar sacs
- Alveoli

Conducting Zone

The major functions of the conducting zone are to provide a route for incoming and outgoing air, remove debris and pathogens from the incoming air, and warm and humidify the incoming air. The conducting zone "conducts" air. Several structures within the conducting zone perform other functions as well. The epithelium of the nasal passages, for example, is essential to sensing odors, and the bronchial epithelium that lines the lungs can metabolize some airborne carcinogens.

The Nose and its Adjacent Structures

The major entrance and exit for the respiratory system is through the nose. When discussing the nose, it is helpful to divide it into two major sections: the external nose, and the nasal cavity or internal nose. We will briefly discuss the structures of the internal nose.

The nares (nostrils) open into the nasal cavity. Each lateral wall of the nasal cavity has three bony projections, called the superior, middle, and inferior nasal conchae. The inferior conchae are separate bones, whereas the superior and middle conchae are portions of the ethmoid bone. Conchae serve to increase the surface area of the nasal cavity and to disrupt the flow of air as it enters the nose, causing air to bounce along the epithelium, where it is cleaned and warmed. The conchae also conserve water and prevent dehydration of the nasal epithelium by trapping water during exhalation. Air exits the nasal cavities via the internal nares and moves into the pharynx.

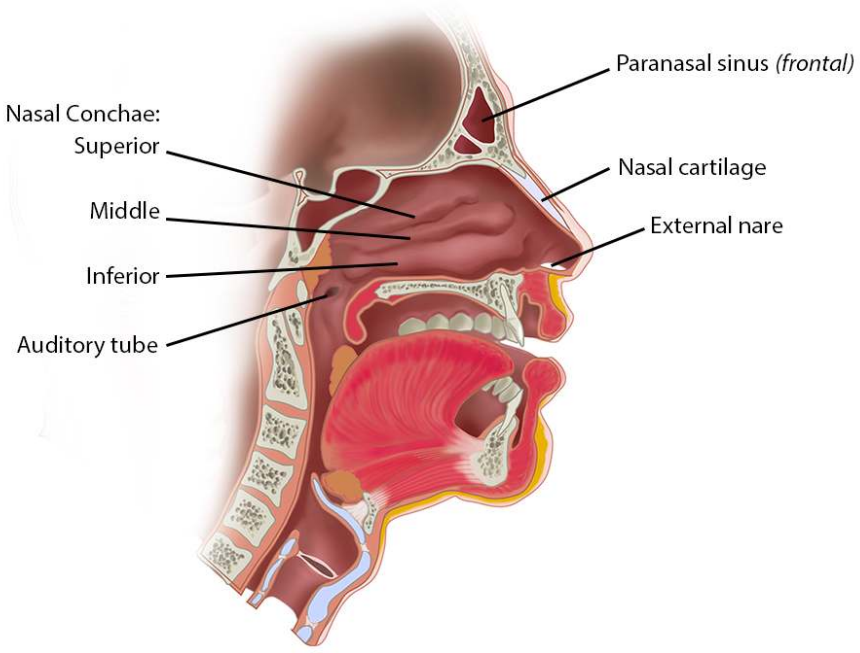


Figure 15.1.3 Nasal Passages - Sagittal Section: Air passes through the external naris and enters the nasal cavity, which has raised nasal conchae protruding into the space. *(Image and caption credit: "Nasal Cavities" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of "Slagter - Drawing Head and neck: sagittal section - no labels" by Ron Slagter.)*

The nares and anterior portion of the nasal cavities are lined with mucous membranes, containing sebaceous glands and hair follicles that serve to prevent the passage of large debris, such as dirt, through the nasal cavity. An olfactory epithelium used to detect odors is found deeper in the nasal cavity.

The conchae are lined by respiratory epithelium composed of pseudostratified ciliated columnar epithelium (Figure 15.1.4). The epithelium contains goblet cells, one of the specialized, columnar epithelial cells that produce mucus to trap debris. The cilia of the respiratory epithelium help remove the mucus and debris from the nasal cavity with a constant beating motion, sweeping materials towards the throat to be swallowed. Interestingly, cold air slows the movement of the cilia, resulting in accumulation of mucus that may in turn lead to a runny nose during cold weather. This moist epithelium functions to warm and humidify incoming air. Capillaries located just beneath the nasal epithelium warm the air by convection. Serous and mucus-producing cells also secrete the lysozyme enzyme and proteins called defensins, which have antibacterial properties. Immune cells that patrol the connective tissue deep to the respiratory epithelium provide additional protection.

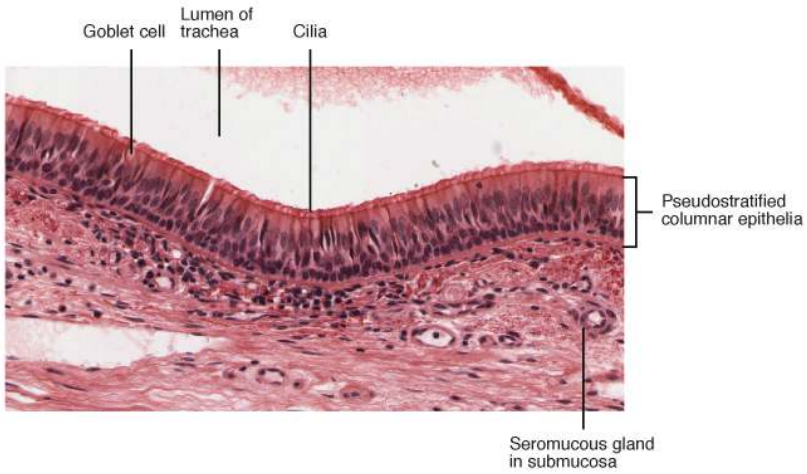


Figure 15.1.4: Pseudostratified Ciliated Columnar Epithelium Respiratory epithelium is pseudostratified ciliated columnar epithelium. Seromucous glands provide lubricating mucus. LM × 680. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

Interactive Link

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

Pharynx

The pharynx is a tube formed by skeletal muscle and lined by mucous membrane that is continuous with that of the nasal cavities. The pharynx is divided into three major regions: the nasopharynx, the oropharynx, and the laryngopharynx (Figure 15.1.5).

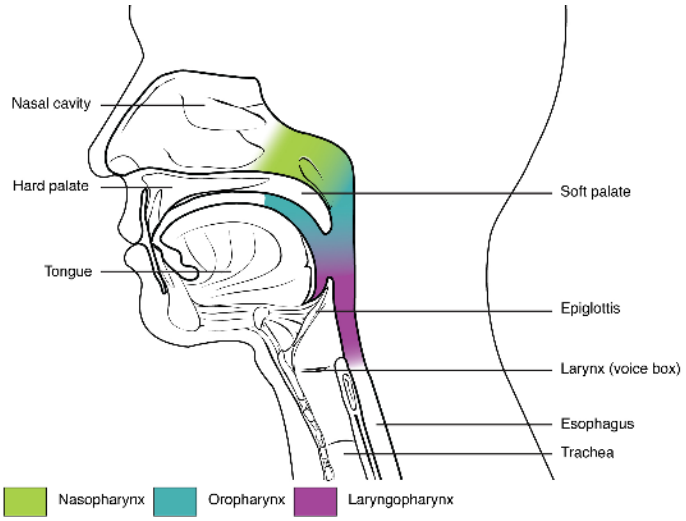


Figure 15.1.5: Divisions of the Pharynx The pharynx is divided into three regions: the nasopharynx, the oropharynx, and the laryngopharynx.

The nasopharynx is flanked by the conchae of the nasal cavity, and it serves only as an airway. In addition, auditory (Eustachian) tubes that connect to each middle ear cavity open into the nasopharynx. This connection is why colds often lead to ear infections.

The oropharynx is a passageway for both air and food. The oropharynx is bordered superiorly by the nasopharynx and anteriorly by the oral cavity. As the nasopharynx becomes the oropharynx, the epithelium changes from pseudostratified ciliated columnar epithelium to stratified squamous epithelium.

The laryngopharynx is inferior to the oropharynx and posterior to the larynx. It continues the route for ingested material and air until its inferior end, where the digestive and respiratory systems diverge. The stratified squamous epithelium of the oropharynx is

continuous with the laryngopharynx. Anteriorly, the laryngopharynx opens into the larynx, which continues into the trachea, whereas posteriorly, it enters the esophagus, which continues into the stomach.

Larynx

The larynx is a cartilaginous structure inferior to the laryngopharynx that connects the pharynx to the trachea and helps regulate the volume of air that enters and leaves the lungs (Figure 15.1.6). The structure of the larynx is formed by several pieces of cartilage. Three large cartilage pieces—the thyroid cartilage (anterior), epiglottis (superior), and cricoid cartilage (inferior)—form the major structure of the larynx. The thyroid cartilage is the largest piece of cartilage that makes up the larynx. The thyroid cartilage consists of the laryngeal prominence, or "Adam's apple," which tends to be more prominent in males. The thick cricoid cartilage forms a ring, with a wide posterior region and a thinner anterior region. Three smaller, paired cartilages—the arytenoids, corniculates, and cuneiforms—attach to the epiglottis and the vocal cords and muscle that help move the vocal cords to produce speech.

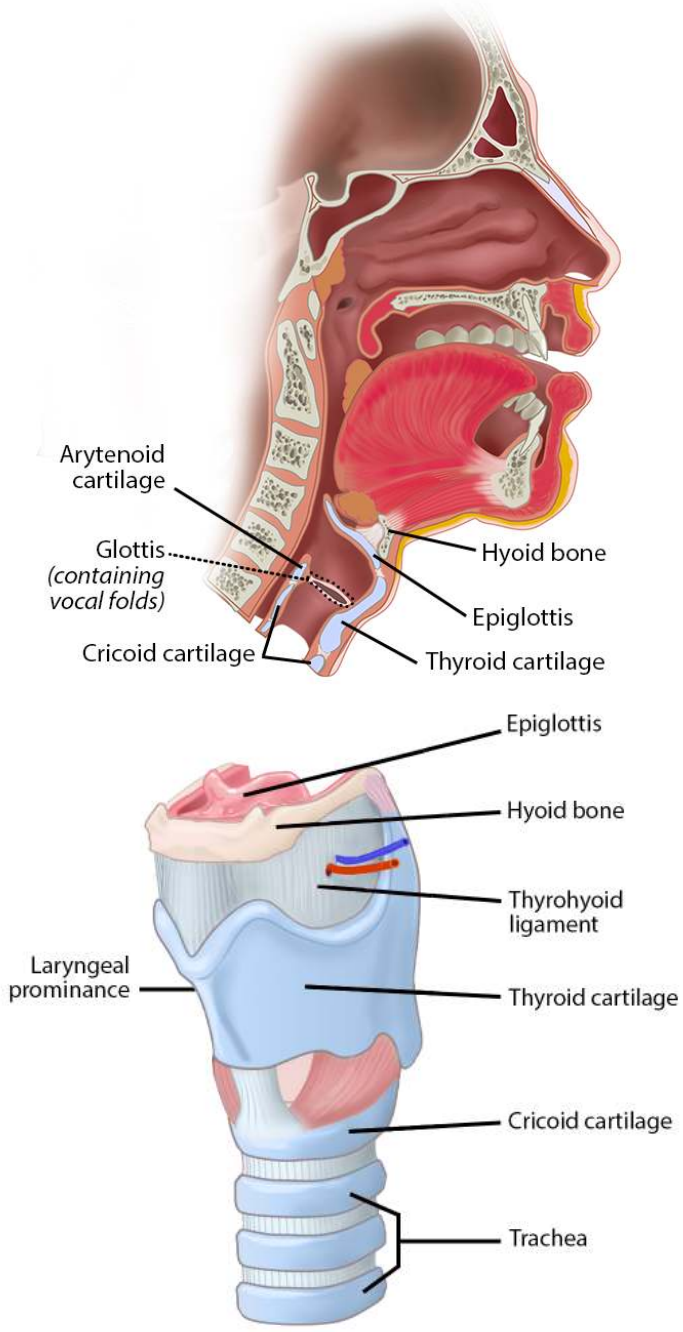


Figure 15.1.6: Larynx. The larynx is comprised of several cartilaginous structures connected by ligaments. Within the larynx the vocal folds attach anteriorly to the thyroid cartilage and posteriorly to the arytenoid cartilage. *(Image credit: "Larynx - Midsagittal View" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of "Slagter - Drawing Head and neck: sagittal section - no labels" by Ron Slagter. "Larynx - Anterolateral View" by Jennifer Lange and John Polos is licensed under CC BY-NC-SA 4.0, modification of "Slagter - Drawing Larynx anatomy: anterior lateral view - no labels" by Ron Slagter.)*

The **epiglottis**, attached to the thyroid cartilage, is a very flexible piece of elastic cartilage that covers the opening of the trachea (see Figure 15.1.6). When in the "closed" position, the unattached end of the epiglottis rests on the glottis. The **glottis** is composed of the vestibular folds, the true vocal cords, and the space between these folds through which air passes to and from the trachea. A **vestibular fold**, or false vocal cord, is one of a pair of folded sections of mucous membrane that sit superior to the vocal folds and may function to protect the vocal folds and amplify sound. A **true vocal cord (or vocal fold)** is one of the white, membranous folds attached by muscle to the thyroid and arytenoid cartilages of the larynx on their outer edges.

Continuous with the laryngopharynx, the superior portion of the larynx is lined with stratified squamous epithelium, transitioning into pseudostratified ciliated columnar epithelium that contains goblet cells. Similar to the nasal cavity and nasopharynx, this

specialized epithelium produces mucus to trap debris and pathogens as they enter the trachea. The cilia beat the mucus upward towards the laryngopharynx, where it can be swallowed down the esophagus.

Trachea

The **trachea** (windpipe) extends from the larynx toward the lungs (Figure 15.1.8). The mucosal layer of the wall of the trachea is lined with ciliated pseudostratified columnar epithelium featuring mucus-secreting goblet cells and covering a lamina propria of areolar connective tissue. The submucosa contains dense irregular connective tissue and houses seromucous glands that secrete a lubricating mucus that shares properties with serous fluid. The wall of the trachea contains 16 to 20 stacked, C-shaped pieces of hyaline cartilage that are positioned horizontally with the opening in the C at the back of the trachea. The incomplete rings of cartilage provide structural support that prevent the trachea from collapsing and protect it. The cartilages are connected to one another by dense connective tissue.

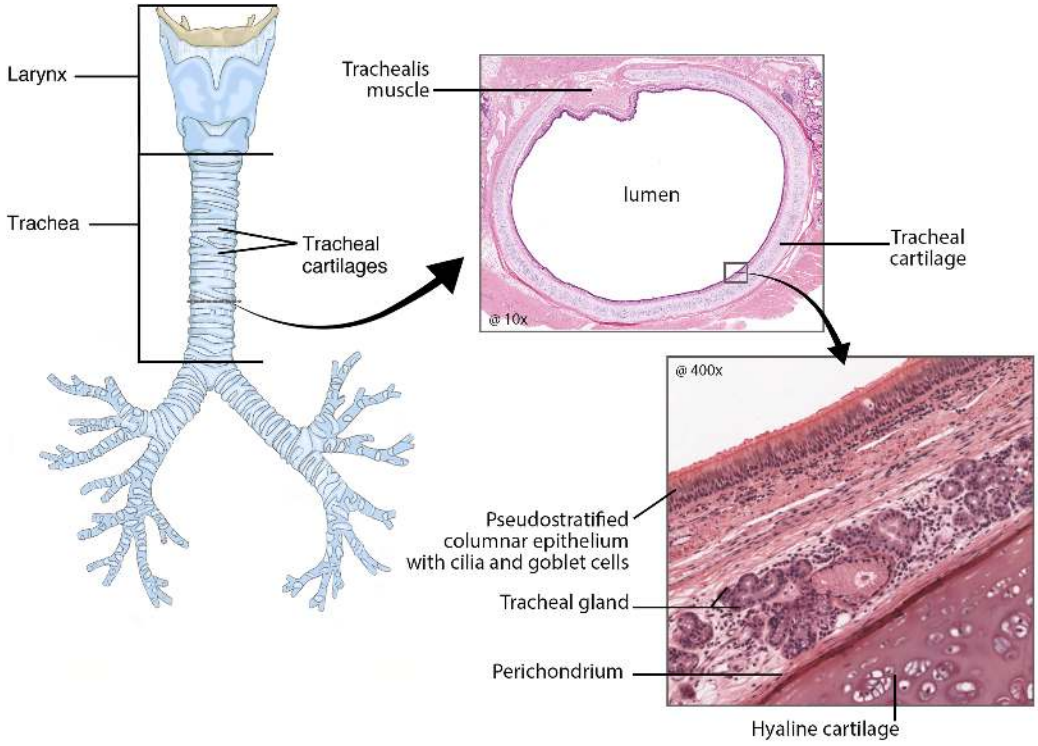


Figure 15.1.9: Trachea. The mucosa lining the hollow lumen of the trachea is comprised of ciliated pseudostratified columnar epithelium that contains goblet cells covering a lamina propria of connective tissue. The submucosa houses seromucous tracheal glands. The C-shaped rings of hyaline cartilage are positioned deep to the mucosa with the opening at the posterior, which is spanned by the trachealis muscle and connective tissue. The superficial layer of the trachea is adventitia. The esophagus is positioned posterior to the trachea. *(Image credit: "Trachea" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of illustration by Open Stax College, slide @ 10x provided by Virginia Commonwealth University and slide @ 400x provided by the Regents of the University of Michigan Medical School © 2022.)*

Bronchial Tree

The trachea branches into the right and left **primary (main) bronchi** (singular = bronchus) at the **carina**. The carina is a raised structure that contains specialized nervous tissue that induces violent coughing if a foreign body, such as food, is present. These bronchi are also lined by ciliated pseudostratified columnar epithelium containing mucus-producing goblet cells (Figure 15.1.10). Rings of cartilage, similar to those of the trachea, support the structure of the bronchi and prevent their collapse. The primary bronchi branch to the **secondary (lobar) bronchi** that deliver air to the individual lobes of each lung. The secondary bronchi branch to the **tertiary (segmental) bronchi** that deliver air to the bronchopulmonary segments that comprise each lobe.

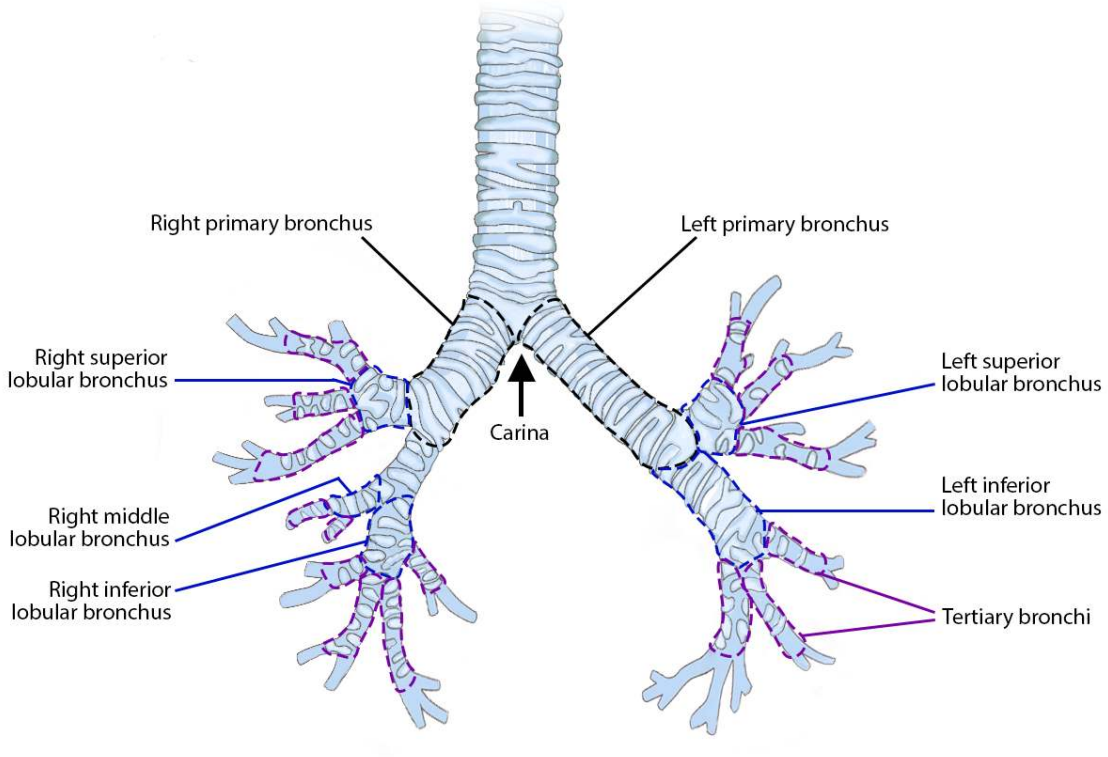


Figure 15.1.10: Bronchi. The trachea branches at the carina into the right and left primary bronchi that deliver air to each lung. The primary bronchi branch into the secondary bronchi that deliver air to the lobes of each lung. The secondary bronchi branch into the tertiary bronchi that deliver air into the bronchopulmonary segments of each lobe. *(Image credit: "Bronchi" by Jennifer Lange is licensed under CC BY-NC-SA 4.0; contains modification of original by OpenStax College.)*

The **bronchial tree** is the collective term used for these highly branching bronchi, since they resemble branches of an upside-down tree (Figure 15.1.10 and Figure 15.1.11). The main function of the bronchi, like other conducting zone structures, is to provide a passageway for air to move into and out of each lung. In addition, the mucous membrane traps debris and pathogens, cilia continue to work as a mucous escalator moving mucus up toward the laryngopharynx to be swallowed. Hyaline cartilage is featured within the wall of all the bronchi to reinforce the airways and help them stay open through pressure changes, but its quantity decreases with each branch point. The C-shaped rings of cartilage in the trachea become irregular plates of cartilage in the bronchi that are smaller and more sporadic in the tertiary bronchi than in the primary bronchi. A layer of smooth muscle is present in the bronchi that may **bronchoconstrict**, make the lumen diameter smaller by contracting the smooth muscle, or **bronchodilate**, make the lumen diameter larger by relaxing the smooth muscle, to adjust air flow in each passage. The quantity of smooth muscle in the wall relative to the lumen diameter increases with each branch point, meaning that the capability to adjust air flow is greater in the tertiary bronchi than in the primary bronchi.

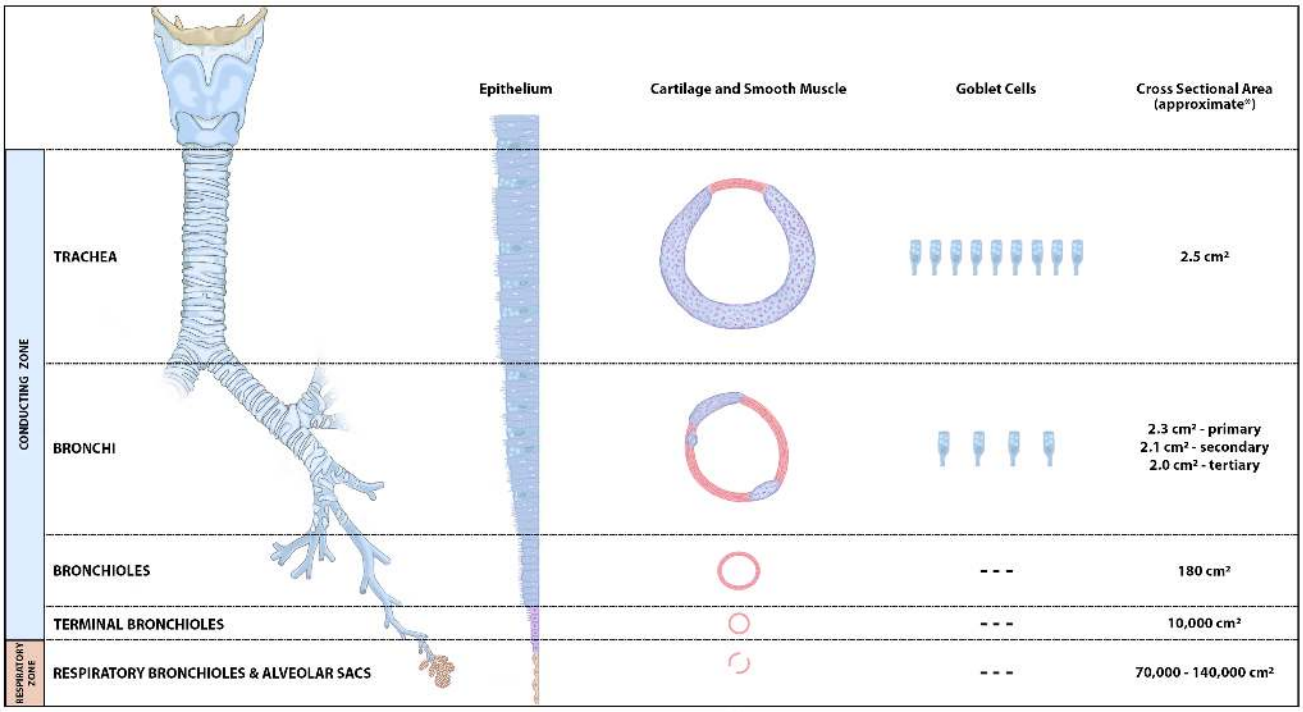


Figure 15.1.11: Tracheobronchial Tree. As the airways branch and spread out within the lungs the histological structure changes and the total cross sectional area increases logarithmically. *Values are intended to be illustrative because actual values differ based on the technique used for calculation (see Rao & Johncy, 2022). *(Image credit: "Tracheobronchial Tree" by Jennifer Lange is licensed under CC BY-NC-SA 4.0; contains modification of original by OpenStax College.)*

Bronchi continue to branch from the tertiary bronchi, getting smaller and smaller, until they become bronchioles. **Bronchioles**, which are 1 mm in diameter or less, further branch until they become the tiny terminal bronchioles, which lead to the structures of gas exchange. There are approximately 30,000 terminal bronchioles in each lung. As they branch, the epithelium of the bronchioles transitions from ciliated pseudostratified columnar epithelium to a thinner simple columnar epithelium to an even thinner simple cuboidal epithelium in the terminal bronchioles. Cilia and mucus-producing cells are sporadic in the largest bronchioles and then disappear as the bronchioles get smaller. The walls of the bronchioles do not contain cartilage like those of the bronchi, but they feature a significant layer of smooth muscle to change their diameter to adjust air flow.

DISORDERS OF THE...

Respiratory System: Asthma

Asthma is common condition that affects the lungs in both adults and children. Approximately 8.2 percent of adults (18.7 million) and 9.4 percent of children (7 million) in the United States suffer from asthma. In addition, asthma is the most frequent cause of hospitalization in children.

Asthma is a chronic disease characterized by inflammation and edema of the airway, and bronchospasms (that is, constriction of the bronchioles), which can inhibit air from entering the lungs. In addition, excessive mucus secretion can occur, which further contributes to airway occlusion (Figure 15.1.11). Cells of the immune system, such as eosinophils and macrophages, may also be involved in infiltrating the walls of the bronchi and bronchioles.

Bronchospasms occur periodically and lead to an “asthma attack.” An attack may be triggered by environmental factors such as dust, pollen, pet hair, or dander, changes in the weather, mold, tobacco smoke, and respiratory infections, or by exercise and stress.

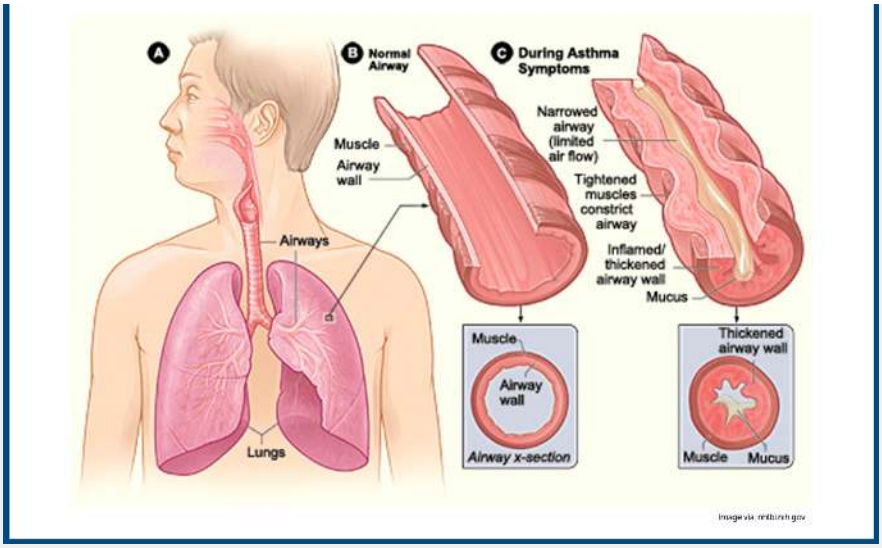


Figure 15.1.12: Normal and Asthmatic Bronchial Tissues. The picture shows a closeup of normal and asthmatic lung tissue. Normal lung tissue (B) does not have the characteristics of lung tissue during an asthma attack (C), which include thickened mucosa, increased mucus-producing goblet cells, increased numbers of macrophages and mast cells, and eosinophil infiltrates. (Image credit: "Asthma by NIH is licensed under CC BY 2.0)

Symptoms of an asthma attack involve coughing, shortness of breath, wheezing, and tightness of the chest. Symptoms of a severe asthma attack that requires immediate medical attention would include difficulty breathing that results in blue (cyanotic) lips or face, confusion, drowsiness, a rapid pulse, sweating, and severe anxiety. The severity of the condition, frequency of attacks, and identified triggers influence the type of medication that an individual may require. Longer-term treatments are used for those with more severe asthma. Short-term, fast-acting drugs that are used to treat an asthma attack are typically administered via an inhaler. For young children or individuals who have difficulty using an inhaler, asthma medications can be administered via a nebulizer.

In many cases, the underlying cause of the condition is unknown. However, recent research has demonstrated that certain viruses, such as human rhinovirus C (HRVC), and the bacteria *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* that are contracted in infancy or early childhood, may contribute to the development of many cases of asthma.

Respiratory Zone

In contrast to the conducting zone, the **respiratory zone** includes structures that are directly involved in gas exchange. The respiratory zone begins where the terminal bronchioles transition into a **respiratory bronchiole**, the smallest type of bronchiole (Figure 15.1.9), which then leads to an alveolar duct, opening into a cluster of alveoli. A respiratory bronchiole is distinguished from a terminal bronchiole by the presence of alveoli within the walls of a respiratory bronchiole.

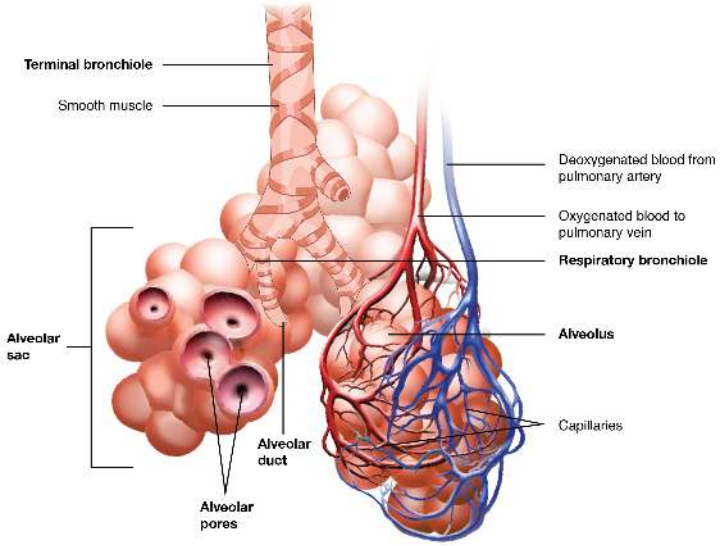


Figure 15.1.13: Respiratory Zone Bronchioles lead to alveolar sacs in the respiratory zone, where gas exchange occurs.

Alveoli

Respiratory bronchioles divide distally to form **alveolar ducts**. An **alveolar duct** does not have its own walls, but are channels created by the walls of the alveoli that line it. Each **alveolar duct** opens into a cluster of alveoli. An alveolar duct and all of the alveoli connected to it form a cluster called an **alveolar sac**. There are an average of 480 million **alveoli** in the lungs, yielding an incredibly large surface area for gas exchange.

Each **alveolar sac** is surrounded by a capillary bed with a network of capillaries that distribute several capillaries to route along the outside of each **alveolus** in the **alveolar sac** 15.1.14. Deoxygenated blood is delivered to the capillary bed via an arteriole branching from the pulmonary artery and oxygenated blood is collected by a venule that drains to the pulmonary vein. An alveolus is **approximately** 200 μm in diameter with elastic walls that allow the alveolus to stretch during air intake like a balloon inflating, which greatly increases the surface area available for gas exchange, and then return to a smaller size to assist with expiration.

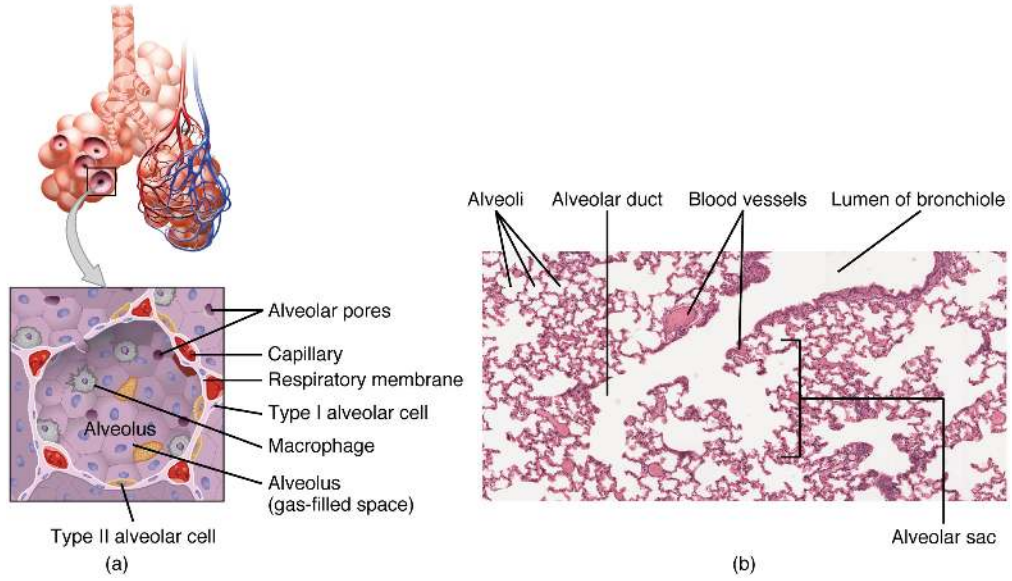


Figure 15.1.14: Structures of the Respiratory Zone (a) The alveolus is responsible for gas exchange. (b) A micrograph shows the alveolar structures within lung tissue. LM × 178. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

The alveolar wall consists of three major cell types: type I alveolar cells, type II alveolar cells, and alveolar macrophages. A type I alveolar cell is a squamous epithelial cell of the alveoli, which constitute up to 97 percent of the alveolar surface area. These cells are about 25 nm thick and are highly permeable to gases. A type II alveolar cell is interspersed among the type I cells and secretes pulmonary surfactant, a substance composed of phospholipids and proteins that reduces the surface tension of the alveoli. Roaming around the alveolar wall is the alveolar macrophage, a phagocytic cell of the immune system that removes debris and pathogens that have reached the alveoli.

The simple squamous epithelium formed by type I alveolar cells is attached to a thin, elastic basement membrane. This epithelium is extremely thin and borders the endothelial membrane of capillaries. Taken together, the alveoli and capillary membranes form a respiratory membrane that is approximately 0.5 µm (micrometers) thick. The respiratory membrane allows gases to cross by simple diffusion, allowing oxygen to be picked up by the blood for transport and CO_2 to be released into the air of the alveoli.

Diseases of the...

Respiratory System: Asthma

Asthma is common condition that affects the lungs in both adults and children. Approximately 8.2 percent of adults (18.7 million) and 9.4 percent of children (7 million) in the United States suffer from asthma. In addition, asthma is the most frequent cause of hospitalization in children.

Asthma is a chronic disease characterized by inflammation and edema of the airway, and bronchospasms (that is, constriction of the bronchioles), which can inhibit air from entering the lungs. In addition, excessive mucus secretion can occur, which further contributes to airway occlusion (Figure 15.1.11). Cells of the immune system, such as eosinophils and mononuclear cells, may also be involved in infiltrating the walls of the bronchi and bronchioles.

Bronchospasms occur periodically and lead to an “asthma attack.” An attack may be triggered by environmental factors such as dust, pollen, pet hair, or dander, changes in the weather, mold, tobacco smoke, and respiratory infections, or by exercise and

stress.

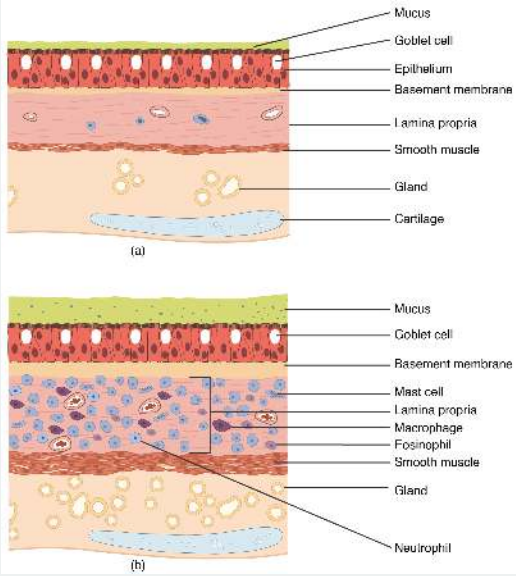
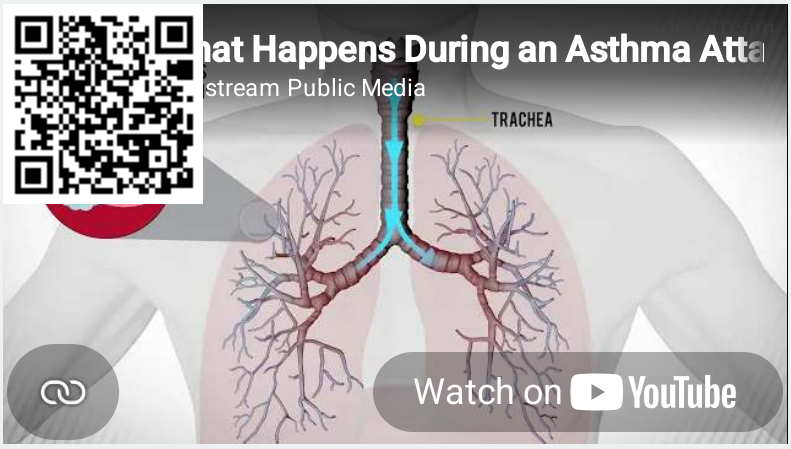


Figure 15.1.11 Normal and Bronchial Asthma Tissues (a) Normal lung tissue does not have the characteristics of lung tissue during (b) an asthma attack, which include thickened mucosa, increased mucus-producing goblet cells, and eosinophil infiltrates.

Symptoms of an asthma attack involve coughing, shortness of breath, wheezing, and tightness of the chest. Symptoms of a severe asthma attack that requires immediate medical attention would include difficulty breathing that results in blue (cyanotic) lips or face, confusion, drowsiness, a rapid pulse, sweating, and severe anxiety. The severity of the condition, frequency of attacks, and identified triggers influence the type of medication that an individual may require. Longer-term treatments are used for those with more severe asthma. Short-term, fast-acting drugs that are used to treat an asthma attack are typically administered via an inhaler. For young children or individuals who have difficulty using an inhaler, asthma medications can be administered via a nebulizer.

In many cases, the underlying cause of the condition is unknown. However, recent research has demonstrated that certain viruses, such as human rhinovirus C (HRVC), and the bacteria *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* that are contracted in infancy or early childhood, may contribute to the development of many cases of asthma.

Interactive Link



Visit this site to learn more about what happens during an asthma attack. What are the three changes that occur inside the airways during an asthma attack?

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15.2: The Lungs

Learning Objectives

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

- Describe the overall function of the lung
- Describe the pleura of the lungs and their function

A major organ of the respiratory system, each lung houses structures of both the conducting and respiratory zones. The main function of the lungs is to perform the exchange of oxygen and carbon dioxide with air from the atmosphere. To this end, the lungs exchange respiratory gases across a very large epithelial surface area—about 70 square meters—that is highly permeable to gases.

Gross Anatomy of the Lungs

The lungs are pyramid-shaped, paired organs that are connected to the trachea by the right and left bronchi; on the inferior surface, the lungs are bordered by the **diaphragm**. The diaphragm is a dome-shaped muscle located at the base of the lungs and thoracic cavity. The lungs are enclosed by the **pleurae**, which are attached to the mediastinum. The right lung is shorter and wider than the left lung, and the left lung occupies a smaller volume than the right. The cardiac notch is an indentation on the surface of the left lung, and it allows space for the heart (Figure 15.2.1). The apex of the lung is the superior region, whereas the base is the opposite region near the diaphragm. The costal surface of the lung borders the ribs. The mediastinal surface faces the midline.

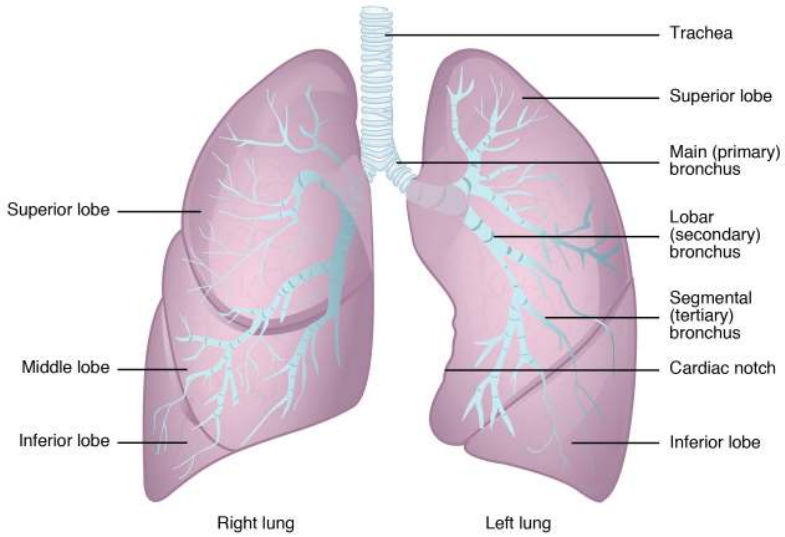


Figure 15.2.1: Gross Anatomy of the Lungs

Each lung is composed of smaller units called **lobes**. Fissures separate these lobes from each other. The right lung consists of three lobes: the superior, middle, and inferior lobes. The left lung consists of two lobes: the superior and inferior lobes. A bronchopulmonary segment is a division of a lobe, and each lobe houses multiple bronchopulmonary segments. Each segment receives air from its own tertiary bronchus and is supplied with blood by its own artery. Some diseases of the lungs typically affect one or more bronchopulmonary segments, and in some cases, the diseased segments can be surgically removed with little influence on neighboring segments. A pulmonary lobule is a subdivision formed as the bronchi branch into bronchioles. Each lobule receives its own large bronchiole that has multiple branches. An interlobular septum is a wall, composed of connective tissue, which separates lobules from one another.

Nervous Innervation

Dilation and constriction of the airway are achieved through nervous control by the parasympathetic and sympathetic nervous systems. The parasympathetic system causes bronchoconstriction, whereas the sympathetic nervous system stimulates bronchodilation. Reflexes such as coughing, and the ability of the lungs to regulate oxygen and carbon dioxide levels, also result from this autonomic nervous system control. Sensory nerve fibers arise from the vagus nerve, and from the second to fifth thoracic

ganglia. The pulmonary plexus is a region on the lung root formed by the entrance of the nerves at the hilum. The nerves then follow the bronchi in the lungs and branch to innervate muscle fibers, glands, and blood vessels.

Pleura of the Lungs

Each lung is enclosed within a cavity that is surrounded by the **pleura**. The pleura (plural = pleurae) is a serous membrane that surrounds the lung. The right and left pleurae, which enclose the right and left lungs, respectively, are separated by the mediastinum. The pleurae consist of two layers. The **visceral pleura** is the layer that is superficial to the lungs, and extends into and lines the lung fissures (Figure 15.2.2). In contrast, the **parietal pleura** is the outer layer that connects to the thoracic wall, the mediastinum, and the diaphragm. The visceral and parietal pleurae connect to each other at the hilum. The pleural cavity is the space between the visceral and parietal layers.

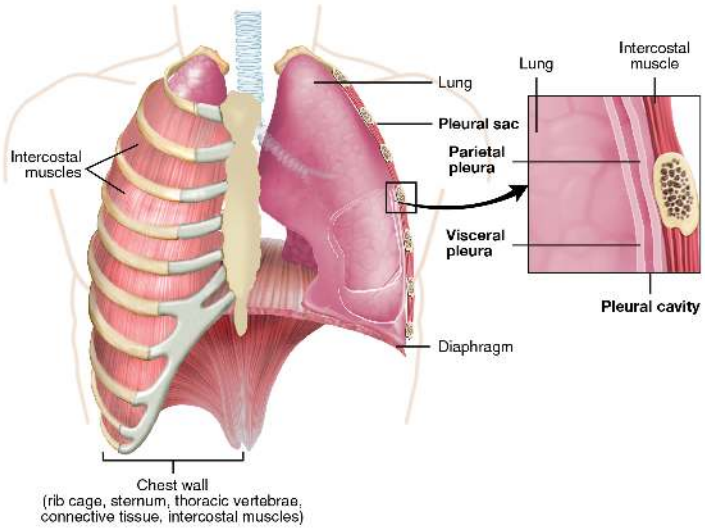


Figure 15.2.2: Parietal and Visceral Pleurae of the Lungs

The pleurae perform two major functions: They produce pleural fluid and create cavities that separate the major organs. Pleural fluid is secreted by mesothelial cells from both pleural layers and acts to lubricate their surfaces. This lubrication reduces friction between the two layers to prevent trauma during breathing, and creates surface tension that helps maintain the position of the lungs against the thoracic wall. This adhesive characteristic of the pleural fluid causes the lungs to enlarge when the thoracic wall expands during ventilation, allowing the lungs to fill with air. The pleurae also create a division between major organs that prevents interference due to the movement of the organs, while preventing the spread of infection.

Everyday Connection

The Effects of Second-Hand Tobacco Smoke

The burning of a tobacco cigarette creates multiple chemical compounds that are released through mainstream smoke, which is inhaled by the smoker, and through sidestream smoke, which is the smoke that is given off by the burning cigarette. Second-hand smoke, which is a combination of sidestream smoke and the mainstream smoke that is exhaled by the smoker, has been demonstrated by numerous scientific studies to cause disease. At least 40 chemicals in sidestream smoke have been identified that negatively impact human health, leading to the development of cancer or other conditions, such as immune system dysfunction, liver toxicity, cardiac arrhythmias, pulmonary edema, and neurological dysfunction. Furthermore, second-hand smoke has been found to harbor at least 250 compounds that are known to be toxic, carcinogenic, or both. Some major classes of carcinogens in second-hand smoke are polyaromatic hydrocarbons (PAHs), N-nitrosamines, aromatic amines, formaldehyde, and acetaldehyde.

Tobacco and second-hand smoke are considered to be carcinogenic. Exposure to second-hand smoke can cause lung cancer in individuals who are not tobacco users themselves. It is estimated that the risk of developing lung cancer is increased by up to 30 percent in nonsmokers who live with an individual who smokes in the house, as compared to nonsmokers who are not regularly exposed to second-hand smoke. Children are especially affected by second-hand smoke. Children who live with an individual who smokes inside the home have a larger number of lower respiratory infections, which are associated with

hospitalizations, and higher risk of sudden infant death syndrome (SIDS). Second-hand smoke in the home has also been linked to a greater number of ear infections in children, as well as worsening symptoms of asthma.

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15.3: The Process of Breathing

Learning Objectives

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

- Describe the mechanisms that drive breathing
- Discuss how pressure, volume, and resistance are related
- List the steps involved in pulmonary ventilation
- Discuss the physical factors related to breathing
- Discuss the meaning of respiratory volume and capacities
- Discuss factors that can influence the respiratory rate

Pulmonary ventilation is the act of breathing, which can be described as the movement of air into and out of the lungs. The major mechanisms that drive pulmonary ventilation are **atmospheric pressure** (P_{atm}); the air pressure within the alveoli, called intra-alveolar pressure (P_{alv}); and the pressure within the pleural cavity, called **intrapleural pressure** (P_{ip})**.** The intra-alveolar pressure is also referred to as the **intrapulmonary pressure**.

Mechanisms of Breathing

The intra-alveolar and intrapleural pressures are dependent on certain physical features of the lung. However, the ability to breathe —to have air enter the lungs during inspiration and air leave the lungs during expiration—is dependent on the air pressure of the atmosphere and the air pressure within the lungs.

Pressure Relationships

Inspiration (or inhalation) and expiration (or exhalation) are dependent on the differences in pressure between the atmosphere and the lungs. In a gas, pressure is a force created by the movement of gas molecules that are confined. For example, a certain number of gas molecules in a two-liter container has more room than the same number of gas molecules in a one-liter container (Figure 15.3.1). In this case, the force exerted by the movement of the gas molecules against the walls of the two-liter container is lower than the force exerted by the gas molecules in the one-liter container. Therefore, the pressure is lower in the two-liter container and higher in the one-liter container. At a constant temperature, changing the volume occupied by the gas changes the pressure, as does changing the number of gas molecules. **Boyle's law** describes the relationship between volume and pressure in a gas at a constant temperature. Boyle discovered that the pressure of a gas is inversely proportional to its volume: If volume increases, pressure decreases. Likewise, if volume decreases, pressure increases. Pressure and volume are inversely related.

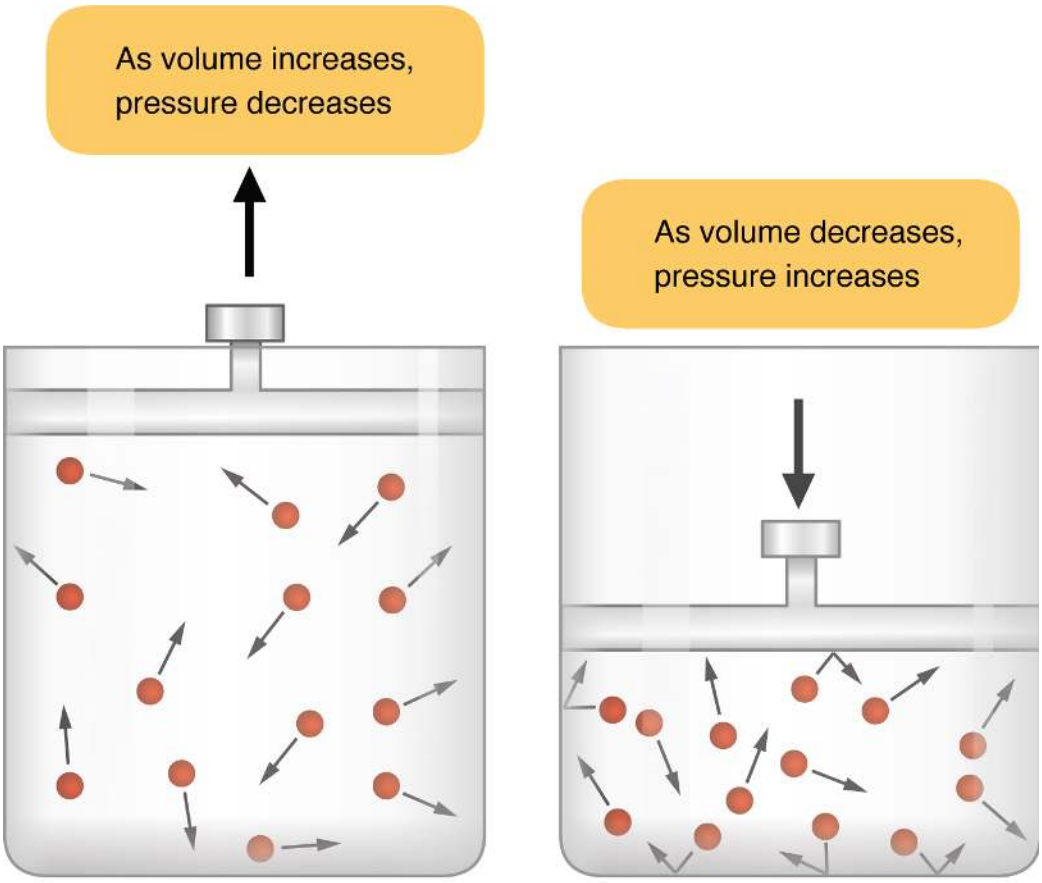


Figure 15.3.1: Boyle's Law In a gas, pressure increases as volume decreases. / Cropped from original

Figure 15.3.1: Boyle's Law In a gas, pressure increases as volume decreases.

Pulmonary ventilation is dependent on three types of pressure: atmospheric, intrapulmonary, and intrapleural. **Atmospheric pressure** is the amount of force that is exerted by gases in the air surrounding any given surface, such as the body. Atmospheric pressure can be expressed in terms of the unit atmosphere, abbreviated atm, or in millimeters of mercury (mm Hg). One atm is equal to 760 mm Hg, which is the atmospheric pressure at sea level. Typically, for respiration, other pressure values are discussed in relation to atmospheric pressure. Therefore, negative pressure is pressure lower than the atmospheric pressure, whereas positive pressure is pressure that it is greater than the atmospheric pressure. A pressure that is equal to the atmospheric pressure is expressed as zero.

Intra-alveolar pressure (intrapulmonary pressure) is the pressure of the air within the alveoli, which changes during the different phases of breathing (Figure 15.3.2). Because the alveoli are connected to the atmosphere via the tubing of the airways (similar to the two- and one-liter containers in the example above), the intrapulmonary pressure of the alveoli always equalizes with the atmospheric pressure.

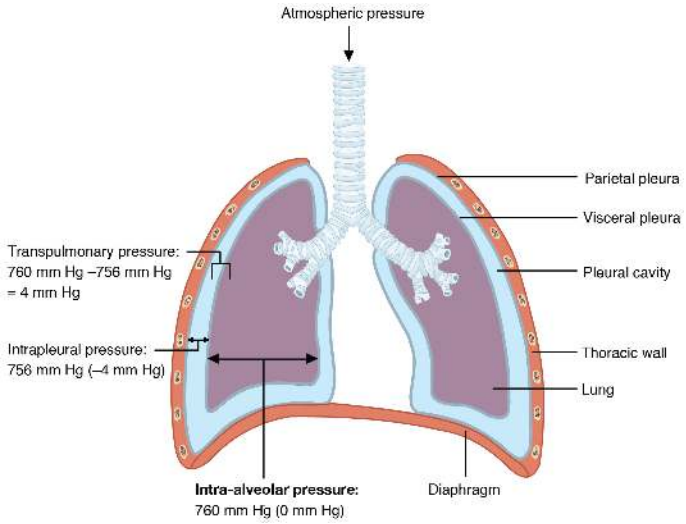


Figure 15.3.2: Intrapulmonary and Intrapleural. Pressure Intra-alveolar pressure changes during the different phases of the cycle. It equalizes at 760 mm Hg but does not remain at 760 mm Hg.

Intrapleural pressure is the pressure of the air within the pleural cavity, between the visceral and parietal pleurae. Similar to intra-alveolar pressure, intrapleural pressure also changes during the different phases of breathing. However, due to certain characteristics of the lungs, the intrapleural pressure is always lower than, or negative to, the intra-alveolar pressure (and therefore also to atmospheric pressure). Although it fluctuates during inspiration and expiration, intrapleural pressure remains approximately –4 mm Hg throughout the breathing cycle.

Pulmonary Ventilation

The difference in pressures drives pulmonary ventilation because air flows down a pressure gradient, that is, air flows from an area of higher pressure to an area of lower pressure.

Pulmonary ventilation comprises two major steps: inspiration and expiration. Inspiration is the process that causes air to enter the lungs, and expiration is the process that causes air to leave the lungs (Figure 15.3.3). A respiratory cycle is one sequence of inspiration and expiration. In general, two muscle groups are used during normal inspiration: the diaphragm and the external intercostal muscles. Additional muscles can be used if a bigger breath is required. When the diaphragm contracts, it moves inferiorly toward the abdominal cavity, creating a larger thoracic cavity and more space for the lungs. Contraction of the external intercostal muscles moves the ribs upward and outward, causing the rib cage to expand, which increases the volume of the thoracic cavity.

In inspiration, the intrapulmonary pressure drops as the lungs expand. Recall Boyle's law which states that pressure and volume are in an inverse relationship. Thus, when the lungs expand, the volume of the lungs increases, and the intrapulmonary pressure decreases. Intrapulmonary pressure becomes less than atmospheric pressure. Air will flow into the lungs down its pressure gradient, from an area of high atmospheric pressure outside the lungs to an area of low intrapulmonary pressure inside the lungs.

In expiration, the intrapulmonary pressure increases as the lungs shrink. As the lungs shrink, the volume of the lungs decreases, and the intrapulmonary pressure increases. Intrapulmonary pressure becomes greater than atmospheric pressure. This drives air out of the lungs from a high intrapulmonary pressure to an area of lower atmospheric pressure outside of the lungs.

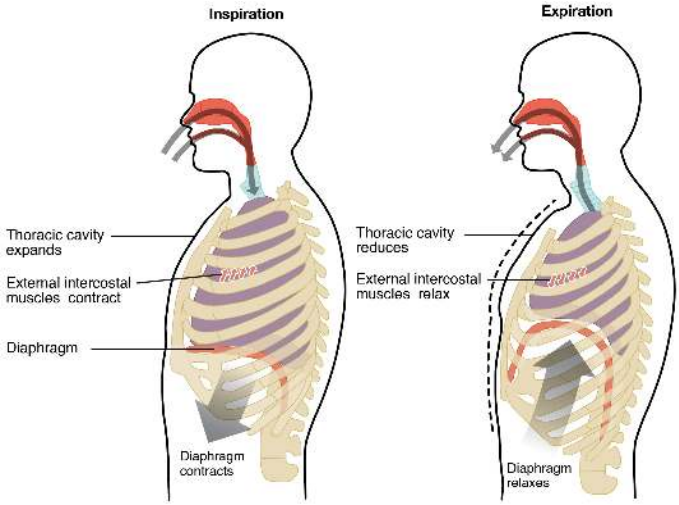


Figure 15.3.3: Inspiration and Expiration Inspiration and expiration occur due to the expansion and contraction of the thoracic cavity, respectively.

Respiratory Volumes and Capacities

Respiratory volume is the term used for various volumes of air moved by or associated with the lungs at a given point in the respiratory cycle. There are four major types of respiratory volumes: tidal, residual, inspiratory reserve, and expiratory reserve (Figure 15.3.4). Tidal volume (TV) is the amount of air that normally enters the lungs during quiet breathing, which is about 500 milliliters. Expiratory reserve volume (ERV) is the amount of air you can forcefully exhale past a normal tidal expiration, up to 1200 milliliters for males. Inspiratory reserve volume (IRV) is produced by a deep inhalation, past a tidal inspiration. This is the extra volume that can be brought into the lungs during a forced inspiration. Residual volume (RV) is the air left in the lungs if you exhale as much air as possible. The residual volume makes breathing easier by preventing the alveoli from collapsing. Respiratory volume is dependent on a variety of factors, and measuring the different types of respiratory volumes can provide important clues about a person's respiratory health (Figure 15.3.5).

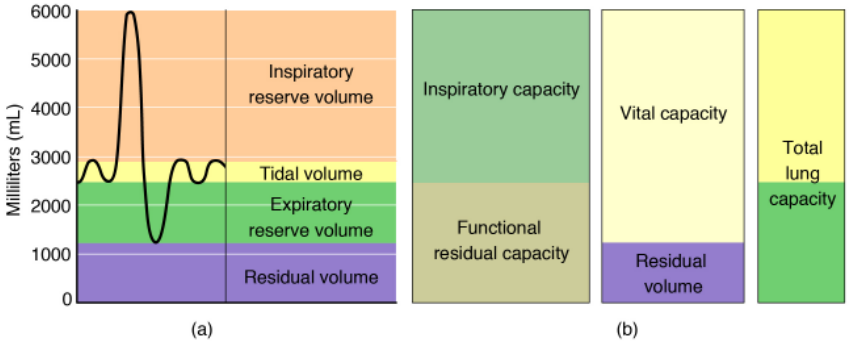


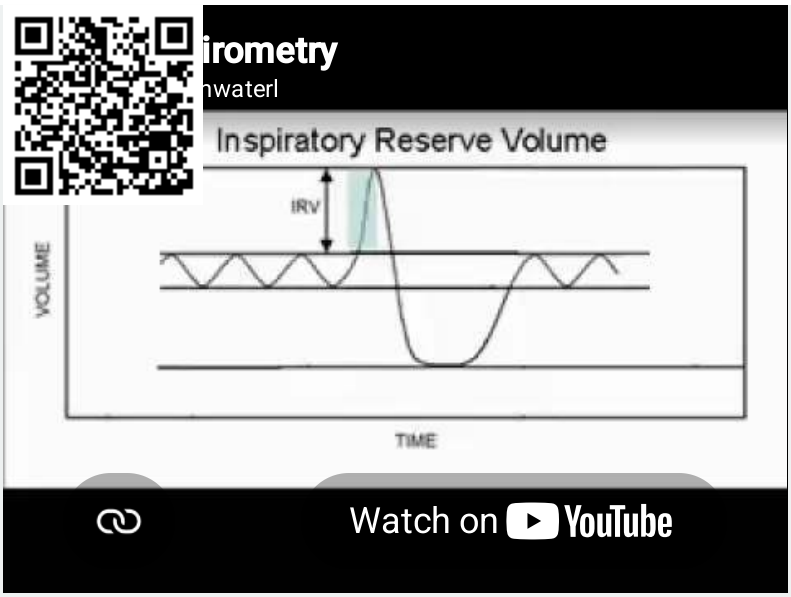
Figure 15.3.4: Respiratory Volumes and Capacities These two graphs show (a) respiratory volumes and (b) the combination of volumes that results in respiratory capacity.

Pulmonary function test	Instrument	Measures	Function
Spirometry	Spirometer	Forced vital capacity (FVC)	Volume of air that is exhaled after maximum inhalation
		Forced expiratory volume (FEV)	Volume of air exhaled during one forced breath
		Forced expiratory flow, 25–75 percent	Air flow in the middle of exhalation
		Peak expiratory flow (PEF)	Rate of exhalation
		Maximum voluntary ventilation (MVV)	Volume of air that can be inspired and expired in 1 minute
		Slow vital capacity (SVC)	Volume of air that can be slowly exhaled after inhaling past the tidal volume
		Total lung capacity (TLC)	Volume of air in the lungs after maximum inhalation
		Functional residual capacity (FRC)	Volume of air left in the lungs after normal expiration
		Residual volume (RV)	Volume of air in the lungs after maximum exhalation
		Total lung capacity (TLC)	Maximum volume of air that the lungs can hold
		Expiratory reserve volume (ERV)	The volume of air that can be exhaled beyond normal exhalation
Gas diffusion	Blood gas analyzer	Arterial blood gases	Concentration of oxygen and carbon dioxide in the blood

Figure 15.3.5: Pulmonary Function Testing

Respiratory capacity is the combination of two or more selected volumes, which further describes the amount of air in the lungs during a given time. For example, total lung capacity (TLC) is the sum of all of the lung volumes (TV, ERV, IRV, and RV), which represents the total amount of air a person can hold in the lungs after a forceful inhalation. TLC is about 6000 mL air for males, and about 4200 mL for females. Vital capacity (VC) is the amount of air a person can move into or out of their lungs, and is the sum of all of the volumes except residual volume (TV, ERV, and IRV), which is between 4000 and 5000 milliliters. Inspiratory capacity (IC) is the maximum amount of air that can be inhaled past a normal tidal expiration, is the sum of the tidal volume and inspiratory reserve volume. On the other hand, the functional residual capacity (FRC) is the amount of air that remains in the lung after a normal tidal expiration; it is the sum of expiratory reserve volume and residual volume (see Figure 22.18).

Interactive Link



Watch this video to learn more about lung volumes and spirometers. Explain how spirometry test results can be used to diagnose respiratory diseases or determine the effectiveness of disease treatment.

In addition to the air that creates respiratory volumes, the respiratory system also contains anatomical dead space, which is air that is present in the airway that never reaches the alveoli and therefore never participates in gas exchange. Alveolar dead space involves air found within alveoli that are unable to function, such as those affected by disease or abnormal blood flow. Total dead space is the anatomical dead space and alveolar dead space together, and represents all of the air in the respiratory system that is not being used in the gas exchange process.

Factors That Affect the Rate and Depth of Respiration

The respiratory rate and the depth of inspiration are regulated by the medulla oblongata and pons; however, these regions of the brain do so in response to systemic stimuli. It is a dose-response, negative-feedback relationship in which the greater the stimulus, the greater the response. Thus, increasing stimuli results in forced breathing. Multiple systemic factors are involved in stimulating the brain to produce pulmonary ventilation.

The major factor that stimulates the medulla oblongata and pons to produce respiration is surprisingly not oxygen concentration, but rather the concentration of carbon dioxide in the blood. As you recall, carbon dioxide is a waste product of cellular respiration and can be toxic. Concentrations of chemicals are sensed by chemoreceptors. Concentration changes in certain substances, such as carbon dioxide or hydrogen ions, stimulate these receptors, which in turn signal the respiration centers of the brain. In the case of carbon dioxide, as the concentration of CO_2 in the blood increases, it readily diffuses across the blood-brain barrier, where it collects in the extracellular fluid. Increased carbon dioxide levels lead to increased levels of hydrogen ions, decreasing pH. The increase in hydrogen ions in the brain triggers the chemoreceptors to stimulate the respiratory centers to initiate contraction of the diaphragm and intercostal muscles. As a result, the rate and depth of respiration increase, allowing more carbon dioxide to be expelled, which brings more air into and out of the lungs promoting a reduction in the blood levels of carbon dioxide, and therefore hydrogen ions, in the blood. In contrast, low levels of carbon dioxide in the blood cause low levels of hydrogen ions in the brain, leading to a decrease in the rate and depth of pulmonary ventilation, producing shallow, slow breathing.

Another factor involved in influencing the respiratory activity of the brain is systemic arterial concentrations of hydrogen ions. Increasing carbon dioxide levels can lead to increased H^+ levels, as mentioned above, as well as other metabolic activities, such as lactic acid accumulation after strenuous exercise. Chemoreceptors of the aortic arch and carotid arteries sense arterial levels of hydrogen ions. When chemoreceptors sense decreasing, or more acidic, pH levels, they stimulate an increase in ventilation to remove carbon dioxide from the blood at a quicker rate. Removal of carbon dioxide from the blood helps to reduce hydrogen ions, thus increasing systemic pH.

Blood levels of oxygen are also important in influencing respiratory rate. The chemoreceptors are responsible for sensing large changes in blood oxygen levels. If blood oxygen levels become quite low—about 60 mm Hg or less—then peripheral chemoreceptors stimulate an increase in respiratory activity. The chemoreceptors are only able to sense dissolved oxygen

molecules, not the oxygen that is bound to hemoglobin. As you recall, the majority of oxygen is bound by hemoglobin; when dissolved levels of oxygen drop, hemoglobin releases oxygen. Therefore, a large drop in oxygen levels is required to stimulate the chemoreceptors of the aortic arch and carotid arteries.

The hypothalamus and other brain regions associated with the limbic system also play roles in influencing the regulation of breathing by interacting with the respiratory centers. The hypothalamus and other regions associated with the limbic system are involved in regulating respiration in response to emotions, pain, and temperature. For example, an increase in body temperature causes an increase in respiratory rate. Feeling excited or the fight-or-flight response will also result in an increase in respiratory rate.

Disorders of the...

Respiratory System: Sleep Apnea

Sleep apnea is a chronic disorder that can occur in children or adults, and is characterized by the cessation of breathing during sleep. These episodes may last for several seconds or several minutes, and may differ in the frequency with which they are experienced. Sleep apnea leads to poor sleep, which is reflected in the symptoms of fatigue, evening napping, irritability, memory problems, and morning headaches. In addition, many individuals with sleep apnea experience a dry throat in the morning after waking from sleep, which may be due to excessive snoring.

There are two types of sleep apnea: obstructive sleep apnea and central sleep apnea. Obstructive sleep apnea is caused by an obstruction of the airway during sleep, which can occur at different points in the airway, depending on the underlying cause of the obstruction. For example, the tongue and throat muscles of some individuals with obstructive sleep apnea may relax excessively, causing the muscles to push into the airway. Another example is obesity, which is a known risk factor for sleep apnea, as excess adipose tissue in the neck region can push the soft tissues towards the lumen of the airway, causing the trachea to narrow.

In central sleep apnea, the respiratory centers of the brain do not respond properly to rising carbon dioxide levels and therefore do not stimulate the contraction of the diaphragm and intercostal muscles regularly. As a result, inspiration does not occur and breathing stops for a short period. In some cases, the cause of central sleep apnea is unknown. However, some medical conditions, such as stroke and congestive heart failure, may cause damage to the pons or medulla oblongata. In addition, some pharmacologic agents, such as morphine, can affect the respiratory centers, causing a decrease in the respiratory rate. The symptoms of central sleep apnea are similar to those of obstructive sleep apnea.

A diagnosis of sleep apnea is usually done during a sleep study, where the patient is monitored in a sleep laboratory for several nights. The patient's blood oxygen levels, heart rate, respiratory rate, and blood pressure are monitored, as are brain activity and the volume of air that is inhaled and exhaled. Treatment of sleep apnea commonly includes the use of a device called a continuous positive airway pressure (CPAP) machine during sleep. The CPAP machine has a mask that covers the nose, or the nose and mouth, and forces air into the airway at regular intervals. This pressurized air can help to gently force the airway to remain open, allowing more normal ventilation to occur. Other treatments include lifestyle changes to decrease weight, eliminate alcohol and other sleep apnea–promoting drugs, and changes in sleep position. In addition to these treatments, patients with central sleep apnea may need supplemental oxygen during sleep.

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15.4: Gas Exchange

Learning Objectives

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

- Compare the composition of atmospheric air and alveolar air
- Describe the mechanisms that drive pulmonary gas exchange and tissue gas exchange

The purpose of the respiratory system is to perform **gas exchange**. Pulmonary ventilation provides air to the alveoli for this gas exchange process. At the respiratory membrane, where the alveolar and capillary walls meet, gases move across the membranes, with oxygen entering the bloodstream and carbon dioxide exiting. It is through this mechanism that blood is oxygenated and carbon dioxide, the waste product of cellular respiration, is removed from the body. **Tissue gas exchange** refers to the process where oxygen that has entered the blood from the lungs is transported to the body's tissues. Oxygen in blood diffuses into the tissues and carbon dioxide diffuses out of the tissues into the blood. Carbon dioxide is then carried in the blood to the lungs to be removed, and the blood oxygen will diffuse back into the blood.

Gas Exchange

In order to understand the mechanisms of gas exchange in the lung, it is important to understand the underlying principles of gases and their behavior. In addition to Boyle's law, several other gas laws help to describe the behavior of gases.

Gas Laws and Air Composition

Gas molecules exert force on the surfaces with which they are in contact; this force is called pressure. In natural systems, gases are normally present as a mixture of different types of molecules. For example, the atmosphere consists of oxygen, nitrogen, carbon dioxide, and other gaseous molecules, and this gaseous mixture exerts a certain pressure referred to as atmospheric pressure (Table 15.4.1). **Partial pressure** (P_x) is the pressure of a single type of gas in a mixture of gases. For example, in the atmosphere, oxygen exerts a partial pressure, and nitrogen exerts another partial pressure, independent of the partial pressure of oxygen (Figure 15.4.1). Total pressure is the sum of all the partial pressures of a gaseous mixture. Dalton's law describes the behavior of nonreactive gases in a gaseous mixture and states that a specific gas type in a mixture exerts its own pressure; thus, the total pressure exerted by a mixture of gases is the sum of the partial pressures of the gases in the mixture.

Table 15.4.1: Partial Pressures of Atmospheric Gases

Gas	Percent of total composition	Partial pressure (mm Hg)
Nitrogen (N_2)	78.6	597.4
Oxygen (O_2)	20.9	158.8
Water (H_2O)	0.4	3.0
Carbon dioxide (CO_2)	0.04	0.3
Others	0.06	0.5
Total composition/total atmospheric pressure	100%	760.0

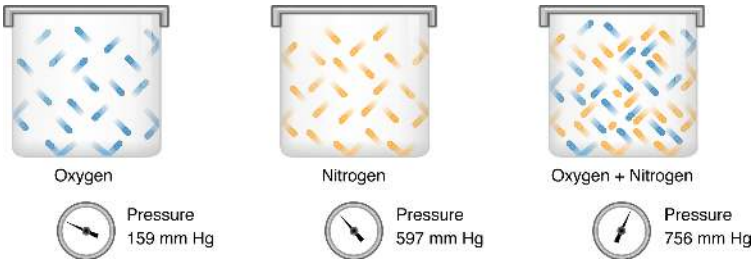


Figure 15.4.1: Partial and Total Pressures of a Gas Partial pressure is the force exerted by a gas. The sum of the partial pressures of all the gases in a mixture equals the total pressure.

Partial pressure is extremely important in predicting the movement of gases. Recall that gases tend to equalize their pressure in two regions that are connected. A gas will move from an area where its partial pressure is higher to an area where its partial pressure is lower. In addition, the greater the partial pressure difference between the two areas, the more rapid is the movement of gases.

The composition of air in the atmosphere and in the alveoli differs. In both cases, the relative concentration of gases is nitrogen > oxygen > water vapor > carbon dioxide. The amount of water vapor present in alveolar air is greater than that in atmospheric air (Table 15.4.2). Recall that the respiratory system works to humidify incoming air, thereby causing the air present in the alveoli to have a greater amount of water vapor than atmospheric air. In addition, alveolar air contains a greater amount of carbon dioxide and less oxygen than atmospheric air. This is no surprise, as gas exchange removes oxygen from and adds carbon dioxide to alveolar air. Both deep and forced breathing cause the alveolar air composition to be changed more rapidly than during quiet breathing. As a result, the partial pressures of oxygen and carbon dioxide change, affecting the diffusion process that moves these materials across the membrane. This will cause oxygen to enter and carbon dioxide to leave the blood more quickly.

Table 15.4.2: Composition and Partial Pressures of Alveolar Air

Gas	Percent of total composition	Partial pressure (mm Hg)
Nitrogen (N_2)	74.9	569
Oxygen (O_2)	13.7	104
Water (H_2O)	6.2	40
Carbon dioxide (CO_2)	5.2	47
Total composition/total alveolar pressure	100%	760.0

Gas Exchange

Gas exchange occurs at two sites in the body: in the lungs, where oxygen is picked up and carbon dioxide is released at the respiratory membrane, and at the tissues, where oxygen is released and carbon dioxide is picked up. **Pulmonary gas exchange** is the exchange of gases within the lungs, and occurs in the alveoli of the lungs. **Tissue gas exchange** is the exchange of gases with the tissues. The actual exchange of gases occurs due to simple diffusion. Energy is not required to move oxygen or carbon dioxide across membranes. Instead, these gases follow pressure gradients that allow them to diffuse. The anatomy of the lung maximizes the diffusion of gases: The respiratory membrane is highly permeable to gases; the respiratory and blood capillary membranes are very thin; and there is a large surface area throughout the lungs.

Pulmonary Gas Exchange

The pulmonary artery carries deoxygenated blood into the lungs from the heart, where it branches and eventually becomes the capillary network composed of pulmonary capillaries. These pulmonary capillaries create the respiratory membrane with the alveoli (Figure 15.4.2). As the blood is pumped through this capillary network and arrives at the lungs, gas exchange occurs. The partial pressure of oxygen within the alveoli is higher than the partial pressure of oxygen in the blood as it arrives at the lungs. This causes oxygen to move down its pressure gradient, from high (the lungs) to low (into the blood). Carbon dioxide travels in the opposite direction. The partial pressure of carbon dioxide is slightly higher in the blood at the lungs compared to the partial pressure of carbon dioxide in the alveoli. Carbon dioxide moves down its pressure gradient from higher in the blood to lower in the alveoli. Carbon dioxide is then exhaled.

Although a small amount of the oxygen is able to dissolve directly into plasma from the alveoli, most of the oxygen is picked up by erythrocytes (red blood cells) and binds to a protein called hemoglobin. Oxygenated hemoglobin is red, causing the overall appearance of bright red oxygenated blood, which returns to the heart through the pulmonary veins. Carbon dioxide is released in the opposite direction of oxygen, from the blood to the alveoli. Some of the carbon dioxide is returned on hemoglobin, but can also be dissolved in plasma or is present as a converted form.

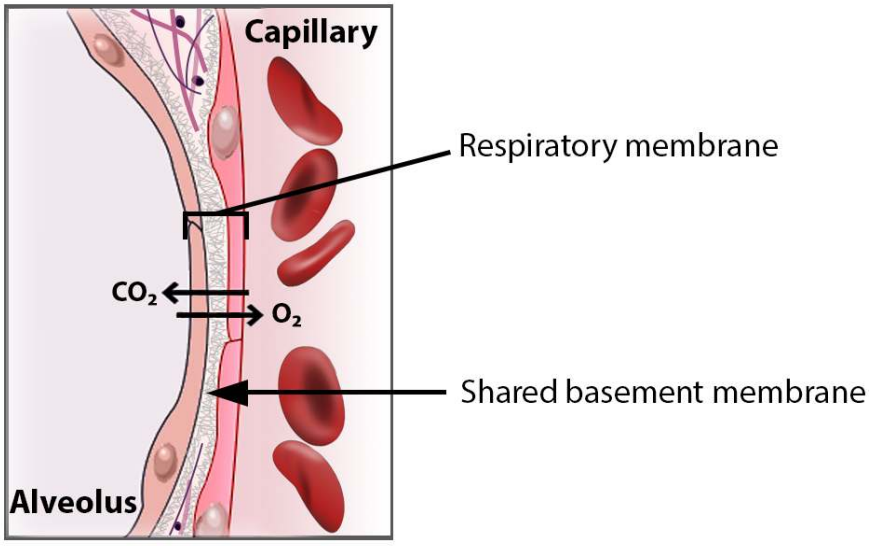


Figure 15.4.1 Pulmonary Gas Exchange: The alveolus is responsible for pulmonary gas exchange with the blood in capillaries. Their areas of closest contact are is called the respiratory membrane, which is made of two layers of simple squamous epithelium with a shared basement membrane. *(Image and caption credit: "Respiratory Membrane" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of The Respiratory Zone by OpenStax; includes Red blood cells by Jessica Polka.) / Cropped from original*

Tissue Gas Exchange

Similar to pulmonary gas exchange, tissue gas exchange also occurs as simple diffusion due to a partial pressure gradient. However, the partial pressure gradients are opposite of those present at the respiratory membrane. The partial pressure of oxygen in tissues is low, about 40 mm Hg, because oxygen is continuously used for cellular respiration. In contrast, the partial pressure of oxygen in the blood is about 100 mm Hg. This creates a pressure gradient that causes oxygen to dissociate from hemoglobin, diffuse out of the blood, cross the interstitial space, and enter the tissue. Hemoglobin that has little oxygen bound to it loses much of its brightness, so that blood returning to the heart is more burgundy in color.

Considering that cellular respiration (a metabolic process) continuously produces carbon dioxide, the partial pressure of carbon dioxide is lower in the blood than it is in the tissue, causing carbon dioxide to diffuse out of the tissue, cross the interstitial fluid, and enter the blood. It is then carried back to the lungs either bound to hemoglobin, dissolved in plasma, or in a converted form. By the time blood returns to the heart, the partial pressure of oxygen has returned to about 40 mm Hg, and the partial pressure of carbon dioxide has returned to about 45 mm Hg. The blood is then pumped back to the lungs to be oxygenated once again during external respiration.

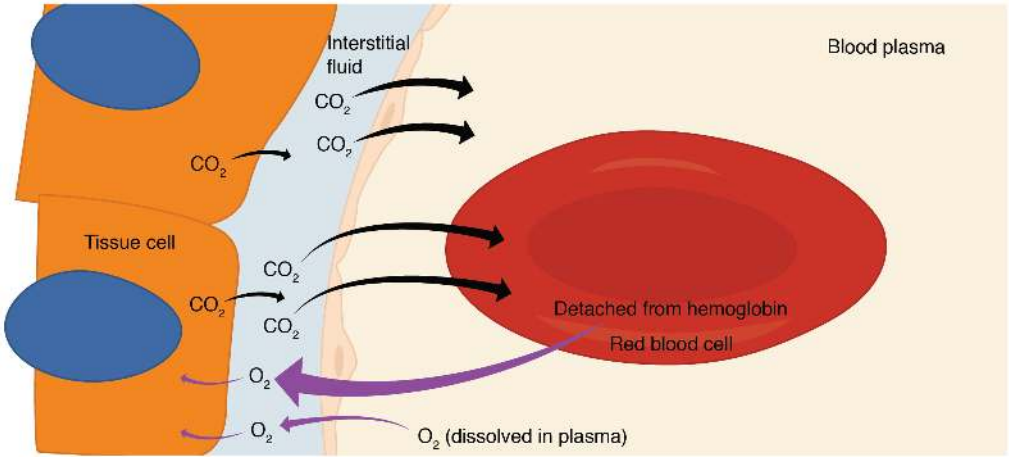


Figure 15.4.3: Internal Respiration Oxygen diffuses out of the capillary and into cells, whereas carbon dioxide diffuses out of cells and into the capillary.

Everyday Connection

Hyperbaric Chamber Treatment

A type of device used in some areas of medicine that exploits the behavior of gases is hyperbaric chamber treatment. A hyperbaric chamber is a unit that can be sealed and expose a patient to either 100 percent oxygen with increased pressure or a mixture of gases that includes a higher concentration of oxygen than normal atmospheric air, also at a higher partial pressure than the atmosphere. There are two major types of chambers: monoplace and multiplace. Monoplace chambers are typically for one patient, and the staff tending to the patient observes the patient from outside of the chamber (Figure 22.24). Some facilities have special monoplace hyperbaric chambers that allow multiple patients to be treated at once, usually in a sitting or reclining position, to help ease feelings of isolation or claustrophobia. Multiplace chambers are large enough for multiple patients to be treated at one time, and the staff attending these patients is present inside the chamber. In a multiplace chamber, patients are often treated with air via a mask or hood, and the chamber is pressurized.



Figure 22.24 Hyperbaric Chamber (credit: “komunews”/flickr.com)

Hyperbaric chamber treatment is based on the behavior of gases. As you recall, gases move from a region of higher partial pressure to a region of lower partial pressure. In a hyperbaric chamber, the atmospheric pressure is increased, causing a greater amount of oxygen than normal to diffuse into the bloodstream of the patient. Hyperbaric chamber therapy is used to treat a variety of medical problems, such as wound and graft healing, anaerobic bacterial infections, and carbon monoxide poisoning. Exposure to and poisoning by carbon monoxide is difficult to reverse, because hemoglobin's affinity for carbon monoxide is much stronger than its affinity for oxygen, causing carbon monoxide to replace oxygen in the blood. Hyperbaric chamber therapy can treat carbon monoxide poisoning, because the increased atmospheric pressure causes more oxygen to diffuse into the bloodstream. At this increased pressure and increased concentration of oxygen, carbon monoxide is displaced from hemoglobin. Another example is the treatment of anaerobic bacterial infections, which are created by bacteria that cannot or prefer not to live in the presence of oxygen. An increase in blood and tissue levels of oxygen helps to kill the anaerobic bacteria that are responsible for the infection, as oxygen is toxic to anaerobic bacteria. For wounds and grafts, the chamber stimulates the healing process by increasing energy production needed for repair. Increasing oxygen transport allows cells to ramp up cellular respiration and thus ATP production, the energy needed to build new structures.

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15.5: Review Questions

4.

Which of the following anatomical structures is *not* part of the conducting zone?

1. pharynx
2. nasal cavity
3. alveoli
4. bronchi

5.

What is the function of the conchae in the nasal cavity?

1. increase surface area
2. exchange gases
3. maintain surface tension
4. maintain air pressure

6.

The fauces connects which of the following structures to the oropharynx?

1. nasopharynx
2. laryngopharynx
3. nasal cavity
4. oral cavity

7.

Which of the following are structural features of the trachea?

1. C-shaped cartilage
2. smooth muscle fibers
3. cilia
4. all of the above

8.

Which of the following structures is *not* part of the bronchial tree?

1. alveoli
2. bronchi
3. terminal bronchioles
4. respiratory bronchioles

9.

What is the role of alveolar macrophages?

1. to secrete pulmonary surfactant
2. to secrete antimicrobial proteins
3. to remove pathogens and debris
4. to facilitate gas exchange

10.

Which of the following structures separates the lung into lobes?

1. mediastinum
2. fissure
3. root
4. pleura

11.

A section of the lung that receives its own tertiary bronchus is called the _____.

1. bronchopulmonary segment
2. pulmonary lobule
3. interpulmonary segment
4. respiratory segment

12.

The _____ circulation picks up oxygen for cellular use and drops off carbon dioxide for removal from the body.

1. pulmonary
2. interlobular
3. respiratory
4. bronchial

13.

The pleura that surrounds the lungs consists of two layers, the _____.

1. visceral and parietal pleurae.
2. mediastinum and parietal pleurae.
3. visceral and mediastinum pleurae.
4. none of the above

14.

Which of the following processes does atmospheric pressure play a role in?

1. pulmonary ventilation
2. production of pulmonary surfactant
3. resistance
4. surface tension

15.

A decrease in volume leads to a(n) _____ pressure.

1. decrease in
2. equalization of
3. increase in
4. zero

16.

The pressure difference between the intra-alveolar and intrapleural pressures is called _____.

1. atmospheric pressure
2. pulmonary pressure
3. negative pressure
4. transpulmonary pressure

17.

Gas flow decreases as _____ increases.

1. resistance
2. pressure
3. airway diameter
4. friction

18.

Contraction of the external intercostal muscles causes which of the following to occur?

1. The diaphragm moves downward.
2. The rib cage is compressed.

3. The thoracic cavity volume decreases.
4. The ribs and sternum move upward.

19.

Which of the following prevents the alveoli from collapsing?

1. residual volume
2. tidal volume
3. expiratory reserve volume
4. inspiratory reserve volume

20.

Gas moves from an area of _____ partial pressure to an area of _____ partial pressure.

1. low; high
2. low; low
3. high; high
4. high; low

21.

When ventilation is not sufficient, which of the following occurs?

1. The capillary constricts.
2. The capillary dilates.
3. The partial pressure of oxygen in the affected alveolus increases.
4. The bronchioles dilate.

22.

Gas exchange that occurs at the level of the tissues is called _____.

1. external respiration
2. interpulmonary respiration
3. internal respiration
4. pulmonary ventilation

23.

The partial pressure of carbon dioxide is 45 mm Hg in the blood and 40 mm Hg in the alveoli. What happens to the carbon dioxide?

1. It diffuses into the blood.
2. It diffuses into the alveoli.
3. The gradient is too small for carbon dioxide to diffuse.
4. It decomposes into carbon and oxygen.

24.

Oxyhemoglobin forms by a chemical reaction between which of the following?

1. hemoglobin and carbon dioxide
2. carbonic anhydrase and carbon dioxide
3. hemoglobin and oxygen
4. carbonic anhydrase and oxygen

25.

Which of the following factors play a role in the oxygen–hemoglobin saturation/dissociation curve?

1. temperature
2. pH
3. BPG
4. all of the above

26.

Which of the following occurs during the chloride shift?

1. Chloride is removed from the erythrocyte.
2. Chloride is exchanged for bicarbonate.
3. Bicarbonate is removed from the erythrocyte.
4. Bicarbonate is removed from the blood.

27.

A low partial pressure of oxygen promotes hemoglobin binding to carbon dioxide. This is an example of the _____.

1. Haldane effect
2. Bohr effect
3. Dalton’s law
4. Henry’s law

28.

Increased ventilation that results in an increase in blood pH is called _____.

1. hyperventilation
2. hyperpnea
3. acclimatization
4. apnea

29.

Exercise can trigger symptoms of AMS due to which of the following?

1. low partial pressure of oxygen
2. low atmospheric pressure
3. abnormal neural signals
4. small venous reserve of oxygen

30.

Which of the following stimulates the production of erythrocytes?

1. AMS
2. high blood levels of carbon dioxide
3. low atmospheric pressure
4. erythropoietin

31.

The olfactory pits form from which of the following?

1. mesoderm
2. cartilage
3. ectoderm
4. endoderm

32.

A full complement of mature alveoli are present by _____.

1. early childhood, around 8 years of age
2. birth
3. 37 weeks
4. 16 weeks

33.

If a baby is born prematurely before type II cells produce sufficient pulmonary surfactant, which of the following might you expect?

1. difficulty expressing fluid

2. difficulty inflating the lungs
3. difficulty with pulmonary capillary flow
4. no difficulty as type I cells can provide enough surfactant for normal breathing

34.

When do fetal breathing movements begin?

1. around week 20
2. around week 37
3. around week 16
4. after birth

35.

What happens to the fluid that remains in the lungs after birth?

1. It reduces the surface tension of the alveoli.
2. It is expelled shortly after birth.
3. It is absorbed shortly after birth.
4. It lubricates the pleurae.

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CHAPTER OVERVIEW

16: The Digestive System

16.1: Overview of the Digestive System
16.2: Digestive System Processes and Regulation
16.3: The Stomach and the Upper Digestive Organs
16.4: Small and Large Intestines
16.5: Accessory Organs in Digestion- The Liver, Pancreas, and Gallbladder
16.6: Review Questions

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16.1: Overview of the Digestive System

Learning Objectives

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

- Identify the organs of the alimentary canal from proximal to distal, and briefly state their function
- Identify the accessory digestive organs and briefly state their function
- Describe the four fundamental tissue layers of the alimentary canal
- Contrast the contributions of the enteric and autonomic nervous systems to digestive system functioning
- Explain how the peritoneum anchors the digestive organs

The function of the digestive system is to break down the foods you eat, release their nutrients, and absorb those nutrients into the body. Although the small intestine is the workhorse of the system, where the majority of digestion occurs, and where most of the released nutrients are absorbed into the blood or lymph, each of the digestive system organs makes a vital contribution to this process (Figure 16.1.1).

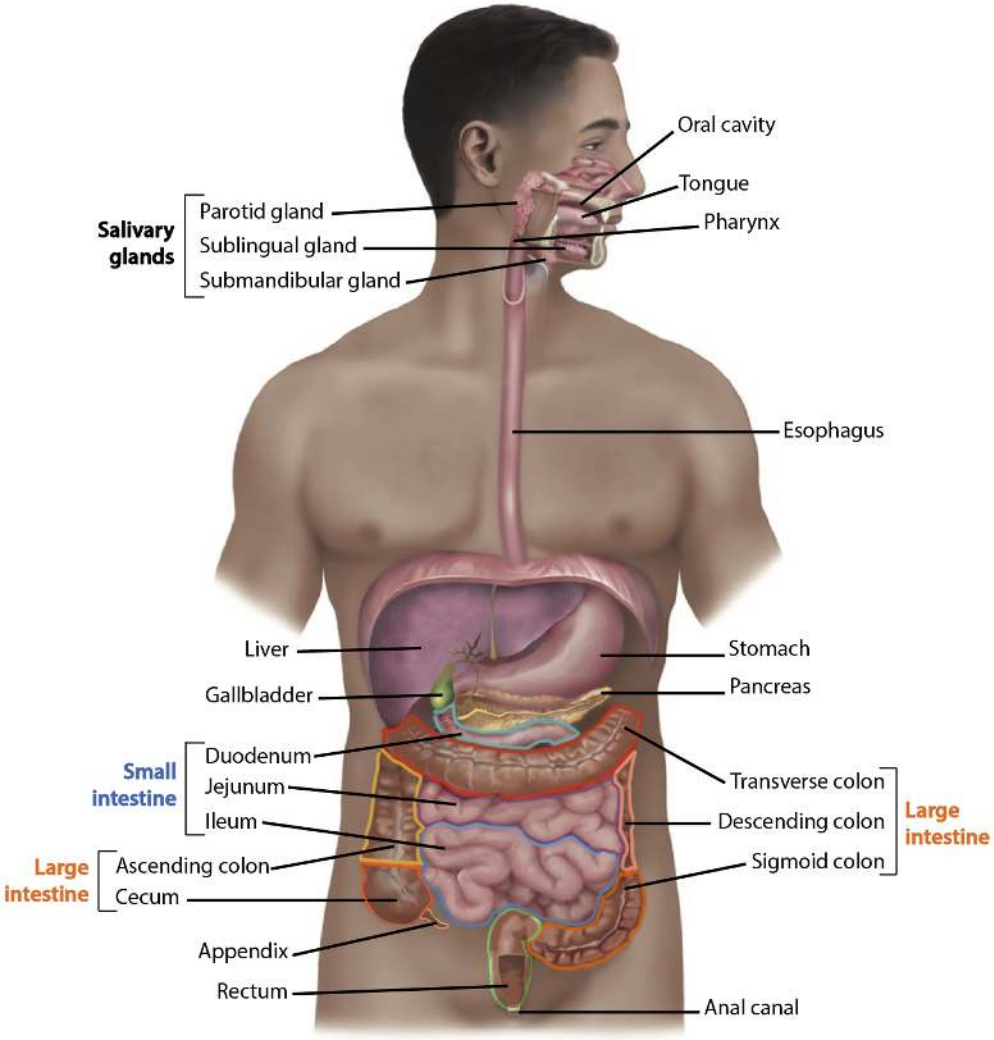


Figure 16.1.1: Organs of the Digestive System. As food moves through the organs of the digestive tract it is broken down into component molecules which are absorbed into the body. The accessory organs (salivary glands, liver, pancreas and gallbladder) secrete digestive enzymes and other substances to assist and regulate the processes. *(Image and caption credit: "Components of the Digestive System" by Jennifer Lange and Gabrielle Spurlock is licensed under CC BY-NC-SA 4.0, modification of original by KnowledgeWorks .)*

As is the case with all body systems, the digestive system does not work in isolation; it functions cooperatively with the other systems of the body. Consider for example, the interrelationship between the digestive and cardiovascular systems. Arteries supply the digestive organs with oxygen and processed nutrients, and veins drain the digestive tract. These intestinal veins, constituting the **hepatic portal system**, are unique; they do not return blood directly to the heart. Rather, this blood is diverted to the liver where its nutrients are off-loaded for processing before blood completes its circuit back to the heart. At the same time, the digestive system provides nutrients to the heart muscle and vascular tissue to support their functioning. The interrelationship of the digestive and endocrine systems is also critical. Hormones secreted by several endocrine glands, as well as endocrine cells of the pancreas, the stomach, and the small intestine, contribute to the control of digestion and nutrient metabolism. In turn, the digestive system provides the nutrients to fuel endocrine function. Table 16.1.1 gives a quick glimpse at how these other systems contribute to the functioning of the digestive system.

Table 16.1.1: Contribution of Other Body Systems to the Digestive System

Body system	Benefits received by the digestive system

Body system	Benefits received by the digestive system
Cardiovascular	Blood supplies digestive organs with oxygen and processed nutrients
Endocrine	Endocrine hormones help regulate secretion in digestive glands and accessory organs
Integumentary	Skin helps protect digestive organs and synthesizes vitamin D for calcium absorption
Lymphatic	Mucosa-associated lymphoid tissue and other lymphatic tissue defend against entry of pathogens; lacteals absorb lipids; and lymphatic vessels transport lipids to bloodstream
Muscular	Skeletal muscles support and protect abdominal organs
Nervous	Sensory and motor neurons help regulate secretions and muscle contractions in the digestive tract
Respiratory	Respiratory organs provide oxygen and remove carbon dioxide
Skeletal	Bones help protect and support digestive organs
Urinary	Kidneys convert vitamin D into its active form, allowing calcium absorption in the small intestine

Digestive System Organs

The easiest way to understand the digestive system is to divide its organs into two main categories. The first group is the organs that make up the **alimentary canal**. **Accessory digestive organs** comprise the second group and are critical for orchestrating the breakdown of food and the assimilation of its nutrients into the body. Accessory digestive organs, despite their name, are critical to the function of the digestive system.

Alimentary Canal Organs

Also called the **gastrointestinal (GI) tract** or gut, the alimentary canal (aliment- = “to nourish”) is a one-way tube about 7.62 meters (25 feet) in length during life and closer to 10.67 meters (35 feet) in length when measured after death, once smooth muscle tone is lost. The main function of the organs of the alimentary canal is to nourish the body. This tube begins at the mouth and terminates at the anus.

The structures of the alimentary canal are:

- mouth
- pharynx
- esophagus
- stomach
- small intestine
- large intestine
- rectum
- anus

Both the mouth and anus are open to the external environment; thus, food and wastes within the alimentary canal are technically considered to be outside the body. Only through the process of absorption do the nutrients in food enter into and nourish the body’s “inner space.”

Accessory Structures

Each accessory digestive organ aids in the breakdown of food (Figure 16.1.1).

The accessory structures are:

- teeth and tongue

- salivary glands
- gallbladder
- liver
- pancreas

Within the mouth, the teeth and tongue begin mechanical digestion, whereas the salivary glands begin chemical digestion. Once food products enter the small intestine, the gallbladder, liver, and pancreas release secretions—such as bile and enzymes—essential for digestion to continue. Together, these are called accessory organs because they sprout from the lining cells of the developing gut (mucosa) and augment its function; indeed, you could not live without their vital contributions, and many significant diseases result from their malfunction. Even after development is complete, they maintain a connection to the gut by way of ducts.

Histology of the Alimentary Canal

Throughout its length, the alimentary tract is composed of the same four tissue layers; the details of their structural arrangements vary to fit their specific functions. Starting from the lumen and moving outwards, these layers are the mucosa, submucosa, muscularis, and serosa, which is continuous with the mesentery (see Figure 16.1.2).

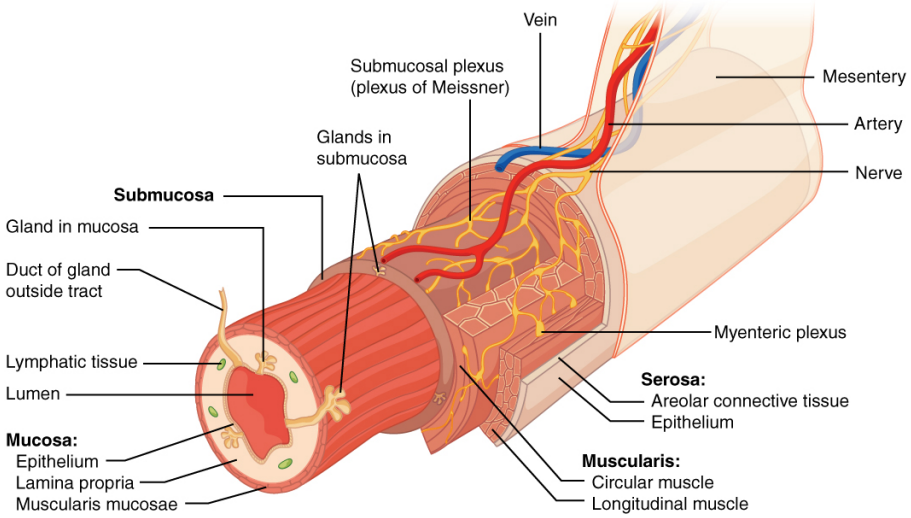


Figure 16.1.2: Layers of the Alimentary Canal The wall of the alimentary canal has four basic tissue layers: the mucosa, submucosa, muscularis, and serosa.

The mucosa is referred to as a mucous membrane, because mucus production is a characteristic feature of gut epithelium. The membrane consists of epithelium, which is in direct contact with ingested food, and the lamina propria, a layer of connective tissue analogous to the dermis. In addition, the mucosa has a thin, smooth muscle layer, called the muscularis mucosae (not to be confused with the muscularis layer, described below).

Epithelium—In the mouth, pharynx, esophagus, and anal canal, the epithelium is primarily a non-keratinized, stratified squamous epithelium. In the stomach and intestines, it is a simple columnar epithelium. Notice that the epithelium is in direct contact with the lumen, the space inside the alimentary canal. Interspersed among its epithelial cells are goblet cells, which secrete mucus and fluid into the lumen, and enteroendocrine cells, which secrete hormones into the interstitial spaces between cells. Epithelial cells have a very brief lifespan, averaging from only a couple of days (in the mouth) to about a week (in the gut). This process of rapid renewal helps preserve the health of the alimentary canal, despite the wear and tear resulting from continued contact with foodstuffs.

Lamina propria—In addition to loose connective tissue, the lamina propria contains numerous blood and lymphatic vessels that transport nutrients absorbed through the alimentary canal to other parts of the body. The lamina propria also serves an immune function by housing clusters of lymphocytes, making up the mucosa-associated lymphoid tissue (MALT). These lymphocyte clusters are particularly substantial in the distal ileum where they are known as Peyer's patches. When you consider that the alimentary canal is exposed to foodborne bacteria and other foreign matter, it is not hard to appreciate why the immune system has evolved a means of defending against the pathogens encountered within it.

Muscularis mucosae—This thin layer of smooth muscle is in a constant state of tension, pulling the mucosa of the stomach and small intestine into undulating folds. These folds dramatically increase the surface area available for digestion and absorption.

As its name implies, the submucosa lies immediately beneath the mucosa. A broad layer of dense connective tissue, it connects the overlying mucosa to the underlying muscularis. It includes blood and lymphatic vessels (which transport absorbed nutrients), and a scattering of submucosal glands that release digestive secretions. Additionally, it serves as a conduit for a dense branching network of nerves, the submucosal plexus, which functions as described below.

The third layer of the alimentary canal is the muscularis (also called the muscularis externa). The muscularis in the small intestine is made up of a double layer of smooth muscle: an inner circular layer and an outer longitudinal layer. The contractions of these layers promote mechanical digestion, expose more of the food to digestive chemicals, and move the food along the canal. In the most proximal and distal regions of the alimentary canal, including the mouth, pharynx, anterior part of the esophagus, and external anal sphincter, the muscularis is made up of skeletal muscle, which gives you voluntary control over swallowing and defecation. The basic two-layer structure found in the small intestine is modified in the organs proximal and distal to it. The stomach is equipped for its churning function by the addition of a third layer, the oblique muscle. While the colon has two layers like the small intestine, its longitudinal layer is segregated into three narrow parallel bands, the tenia coli, which make it look like a series of pouches rather than a simple tube.

The serosa is the portion of the alimentary canal superficial to the muscularis. Present only in the region of the alimentary canal within the abdominal cavity, it consists of a layer of visceral peritoneum overlying a layer of loose connective tissue. Instead of serosa, the mouth, pharynx, and esophagus have a dense sheath of collagen fibers called the adventitia. These tissues serve to hold the alimentary canal in place near the ventral surface of the vertebral column.

The Peritoneum

The digestive organs within the abdominal cavity are held in place by the **peritoneum**, a broad serous membranous sac made up of squamous epithelial tissue surrounded by connective tissue. It is composed of two different regions: the **parietal peritoneum**, which lines the abdominal wall, and the **visceral peritoneum**, which envelopes the abdominal organs (Figure 16.1.3). The **peritoneal cavity** is the space bounded by the visceral and parietal peritoneal surfaces. A few milliliters of watery fluid act as a lubricant to minimize friction between the serosal surfaces of the peritoneum. The visceral peritoneum includes multiple large folds that envelope various abdominal organs, holding them to the dorsal surface of the body wall. Within these folds are blood vessels, lymphatic vessels, and nerves that innervate the organs with which they are in contact, supplying their adjacent organs.

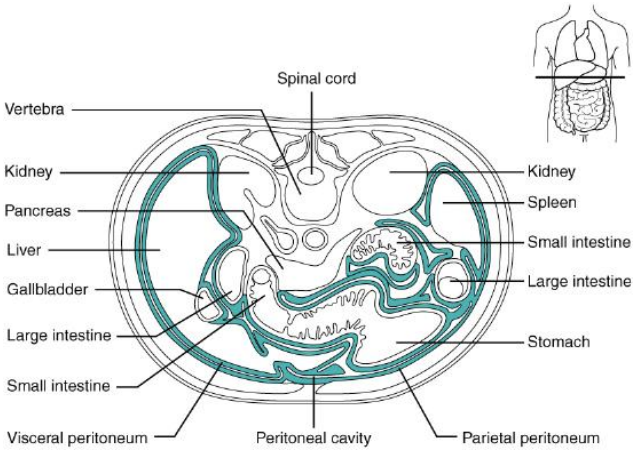


Figure 16.1.3: The Peritoneum A cross-section of the abdomen shows the relationship between abdominal organs and the peritoneum (darker lines).

Disorders of the...

Digestive System: Peritonitis

Inflammation of the peritoneum is called peritonitis. Chemical peritonitis can develop any time the wall of the alimentary canal is breached, allowing the contents of the lumen entry into the peritoneal cavity. For example, when an ulcer perforates the stomach wall, gastric juices spill into the peritoneal cavity. Hemorrhagic peritonitis occurs after a ruptured tubal pregnancy or traumatic injury to the liver or spleen fills the peritoneal cavity with blood. Even more severe peritonitis is associated with bacterial infections seen with appendicitis, colonic diverticulitis, and pelvic inflammatory disease (infection of uterine tubes,

usually by sexually transmitted bacteria). Peritonitis is life threatening and often results in emergency surgery to correct the underlying problem and intensive antibiotic therapy. When your great grandparents and even your parents were young, the mortality from peritonitis was high. Aggressive surgery, improvements in anesthesia safety, the advance of critical care expertise, and antibiotics have greatly improved the mortality rate from this condition. Even so, the mortality rate still ranges from 30 to 40 percent.

Interactive Link



By clicking on this link you can watch a short video of what happens to the food you eat, as it passes from your mouth to your intestine. Along the way, note how the food changes consistency and form. How does this change in consistency facilitate your gaining nutrients from food?

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16.2: Digestive System Processes and Regulation

Learning Objectives

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

- Discuss six fundamental activities of the digestive system, giving an example of each
- Compare and contrast the neural and hormonal controls involved in digestion

The digestive system uses mechanical and chemical activities to break food down into absorbable substances during its journey through the digestive system. Table 16.2.1 provides an overview of the basic functions of the digestive organs.

Interactive Link



Visit this site for an overview of digestion of food in different regions of the digestive tract. Note the route of non-fat nutrients from the small intestine to their release as nutrients to the body.

Table 16.2.1: Functions of the Digestive Organs

Organ	Major functions	Other functions
Mouth	• Ingests food • Chews and mixes food • Begins chemical breakdown of carbohydrates • Moves food into the pharynx • Begins breakdown of lipids via lingual lipase	• Moistens and dissolves food, allowing you to taste it • Cleans and lubricates the teeth and oral cavity • Has some antimicrobial activity
Pharynx	• Propels food from the oral cavity to the esophagus	• Lubricates food and passageways
Esophagus	• Propels food to the stomach	• Lubricates food and passageways
Stomach	• Mixes and churns food with gastric juices to form chyme • Begins chemical breakdown of proteins • Releases food into the duodenum as chyme • Absorbs some fat-soluble substances (for example, alcohol, aspirin) • Possesses antimicrobial functions	• Stimulates protein-digesting enzymes • Secretes intrinsic factor required for vitamin B_{12} absorption in small intestine

Organ	Major functions	Other functions
Small intestine	• Mixes chyme with digestive juices • Propels food at a rate slow enough for digestion and absorption • Absorbs breakdown products of carbohydrates, proteins, lipids, and nucleic acids, along with vitamins, minerals, and water • Performs physical digestion via segmentation	• Provides optimal medium for enzymatic activity
Accessory organs	• Liver: produces bile salts, which emulsify lipids, aiding their digestion and absorption • Gallbladder: stores, concentrates, and releases bile • Pancreas: produces digestive enzymes and bicarbonate	• Bicarbonate-rich pancreatic juices help neutralize acidic chyme and provide optimal environment for enzymatic activity
Large intestine	• Further breaks down food residues • Absorbs most residual water, electrolytes, and vitamins produced by enteric bacteria • Propels feces toward rectum • Eliminates feces	• Food residue is concentrated and temporarily stored prior to defecation • Mucus eases passage of feces through colon

Digestive Processes

The processes of digestion include six activities:

1. **ingestion**
2. **propulsion**
3. **mechanical or physical digestion**
4. **chemical digestion**
5. **absorption**
6. **defecation**.

The first of these processes, **ingestion**, refers to the entry of food into the alimentary canal through the mouth. There, the food is chewed and mixed with saliva, which contains enzymes that begin breaking down the carbohydrates in the food plus some lipid digestion via lingual lipase. Chewing increases the surface area of the food and allows an appropriately sized bolus to be produced.

Food leaves the mouth when the tongue and pharyngeal muscles propel it into the esophagus. This act of swallowing, the last voluntary act until defecation, is an example of **propulsion**, which refers to the movement of food through the digestive tract. It includes both the voluntary process of swallowing and the involuntary process of **peristalsis**. Peristalsis consists of sequential, alternating waves of contraction and relaxation of alimentary wall smooth muscles, which act to propel food along (Figure 16.2.1). These waves also play a role in mixing food with digestive juices. Peristalsis is so powerful that foods and liquids you swallow enter your stomach even if you are standing on your head.

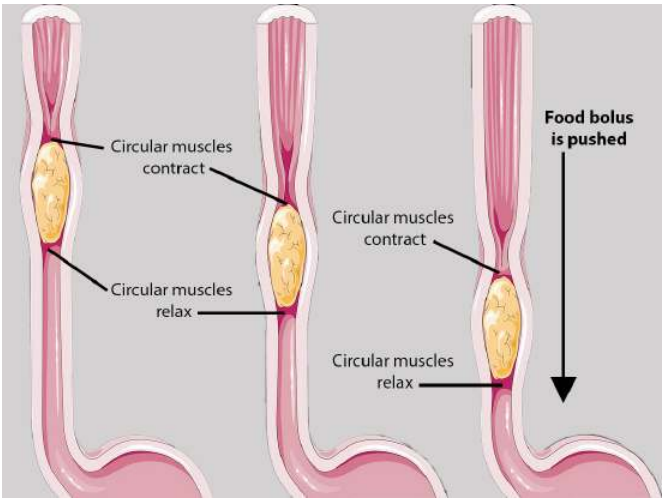


Figure 16.2.1: Peristalsis. Peristalsis moves food through the digestive tract with sliding waves of muscle contraction and relaxation. *(Image credit: "Peristalsis" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of originals by Servier Medical Art under CC BY 2.0.)*

Digestion includes both mechanical and chemical processes. **Mechanical digestion** is a purely physical process that does not change the chemical nature of the food. Instead, it makes the food smaller to increase both surface area and mobility. It includes **mastication**, or chewing, as well as tongue movements that help break food into smaller bits and mix food with saliva. Although there may be a tendency to think that mechanical digestion is limited to the first steps of the digestive process, it occurs after the food leaves the mouth, as well. The mechanical churning of food in the stomach serves to further break it apart and expose more of its surface area to digestive juices, creating an acidic "soup" called chyme. Segmentation, which occurs mainly in the small intestine, consists of localized contractions of circular muscle of the muscularis layer of the alimentary canal. These contractions isolate small sections of the intestine, moving their contents back and forth while continuously subdividing, breaking up, and mixing the contents. By moving food back and forth in the intestinal lumen, segmentation mixes food with digestive juices and facilitates absorption.

In **chemical digestion**, starting in the mouth, digestive secretions break down complex food molecules into their chemical building blocks (for example, proteins into separate amino acids). These secretions vary in composition, but typically contain water, various enzymes, acids, and salts. The process is completed in the small intestine.

Food that has been broken down is of no value to the body unless it enters the bloodstream and its nutrients are put to work. This occurs through the process of **absorption**, which takes place primarily within the small intestine. There, most nutrients are absorbed from the lumen of the alimentary canal into the bloodstream through the epithelial cells that make up the mucosa. Lipids are absorbed into lacteals and are transported via the lymphatic vessels to the bloodstream (the subclavian veins near the heart). The details of these processes will be discussed later.

In **defecation**, the final step in digestion, undigested materials are removed from the body as feces.

Aging and the...

Digestive System: From Appetite Suppression to Constipation

Age-related changes in the digestive system begin in the mouth and can affect virtually every aspect of the digestive system. Taste buds become less sensitive, so food isn't as appetizing as it once was. A slice of pizza is a challenge, not a treat, when you have lost teeth, your gums are diseased, and your salivary glands aren't producing enough saliva. Swallowing can be difficult, and ingested food moves slowly through the alimentary canal because of reduced strength and tone of muscular tissue. Neurosensory feedback is also dampened, slowing the transmission of messages that stimulate the release of enzymes and hormones.

Pathologies that affect the digestive organs—such as hiatal hernia, gastritis, and peptic ulcer disease—can occur at greater frequencies as you age. Problems in the small intestine may include duodenal ulcers, maldigestion, and malabsorption. Problems in the large intestine include hemorrhoids, diverticular disease, and constipation. Conditions that affect the function

of accessory organs—and their abilities to deliver pancreatic enzymes and bile to the small intestine—include jaundice, acute pancreatitis, cirrhosis, and gallstones.

In some cases, a single organ is in charge of a digestive process. For example, ingestion occurs only in the mouth and defecation only in the anus. However, most digestive processes involve the interaction of several organs and occur gradually as food moves through the alimentary canal (Figure 16.2.2).

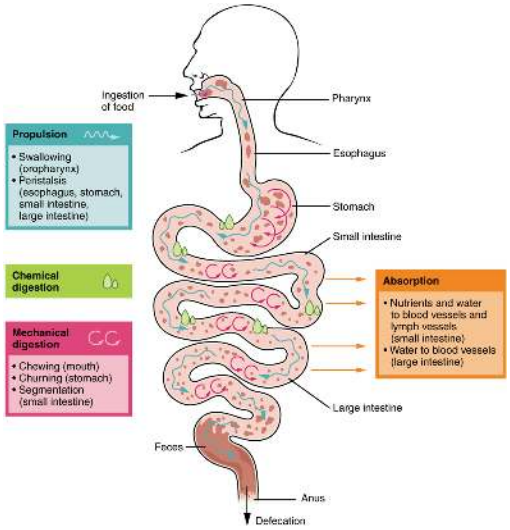


Figure 16.2.2: Digestive Processes The digestive processes are ingestion, propulsion, mechanical digestion, chemical digestion, absorption, and defecation

Some chemical digestion occurs in the mouth. Some absorption can occur in the mouth and stomach, for example, alcohol and aspirin.

Regulatory Mechanisms

Neural and endocrine regulatory mechanisms work to maintain the optimal conditions in the lumen needed for digestion and absorption. These regulatory mechanisms, which stimulate digestive activity through mechanical and chemical activity, are controlled both extrinsically and intrinsically.

Neural Controls

The walls of the alimentary canal contain a variety of sensors that help regulate digestive functions. These include mechanoreceptors, chemoreceptors, and osmoreceptors, which are capable of detecting mechanical, chemical, and osmotic stimuli, respectively. For example, these receptors can sense when the presence of food has caused the stomach to expand, whether food particles have been sufficiently broken down, how much liquid is present, and the type of nutrients in the food (lipids, carbohydrates, and/or proteins). Stimulation of these receptors provokes an appropriate reflex that furthers the process of digestion. This may entail sending a message that activates the glands that secrete digestive juices into the lumen, or it may mean the stimulation of muscles within the alimentary canal, thereby activating peristalsis and segmentation that move food along the intestinal tract.

The walls of the entire alimentary canal are embedded with nerve plexuses that interact with the central nervous system and other nerve plexuses—either within the same digestive organ or in different ones.

Hormonal Controls

A variety of hormones are involved in the digestive process. The main digestive hormone of the stomach is gastrin, which is secreted in response to the presence of food. Gastrin stimulates the secretion of gastric acid by the parietal cells of the stomach mucosa. Other GI hormones are produced and act upon the gut and its accessory organs. Hormones produced by the duodenum include secretin, which stimulates a watery secretion of bicarbonate by the pancreas; cholecystokinin (CCK), which stimulates the secretion of pancreatic enzymes and bile from the liver and release of bile from the gallbladder; and gastric inhibitory peptide, which inhibits gastric secretion and slows gastric emptying and motility. These GI hormones are secreted by specialized epithelial

cells, called endocrinocytes, located in the mucosal epithelium of the stomach and small intestine. These hormones then enter the bloodstream, through which they can reach their target organs.

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16.3: The Stomach and the Upper Digestive Organs

Learning Objectives

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

- List the structures of the upper digestive tract and describe their functions
- Identify the four main types of secreting cells in gastric glands of the stomach, and their important products
- Explain why the stomach does not digest itself
- Describe the mechanical and chemical digestion of food entering the stomach

Upper Digestive Organs

The structures within the upper digestive tract include the mouth (oral cavity), pharynx and esophagus as well as their accessory organs -- the teeth, tongue and salivary glands.

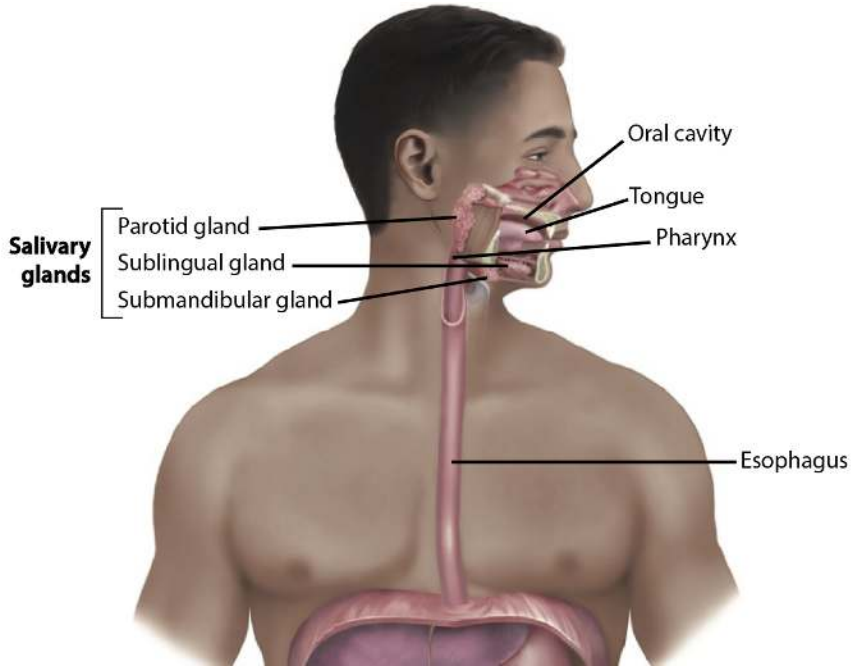


Figure 16.3.1 The structures in the upper digestive tract. *(Image credit: "Components of the Digestive System" by Jennifer Lange and Gabrielle Spurlock is licensed under CC BY-NC-SA 4.0, modification of original by KnowledgeWorks .) / Cropped from original*

Your teeth and tongue aid in chewing, while saliva moistens food and aids in its digestion. Your salivary glands secrete an enzyme called **salivary amylase** that begins to chemically digest your food while chewing begins to mechanically digests it. Salivary amylase aids in the breakdown of carbohydrates (sugars) in your food. Food does not spend enough time in the oral cavity to allow all the carbohydrates to break down, but salivary amylase continues acting until it is inactivated by stomach acids. Saliva also contains an enzyme called lysozyme which can break down the cell walls of certain bacteria, giving saliva antimicrobial properties. The muscles of your tongue convert your chewed food into a **bolus** (rounded mass) which is then swallowed and pushed through the **upper esophageal sphincter** into your esophagus. Peristalsis pushes the bolus down your esophagus until it is then pushed through the **lower esophageal sphincter** into your stomach.

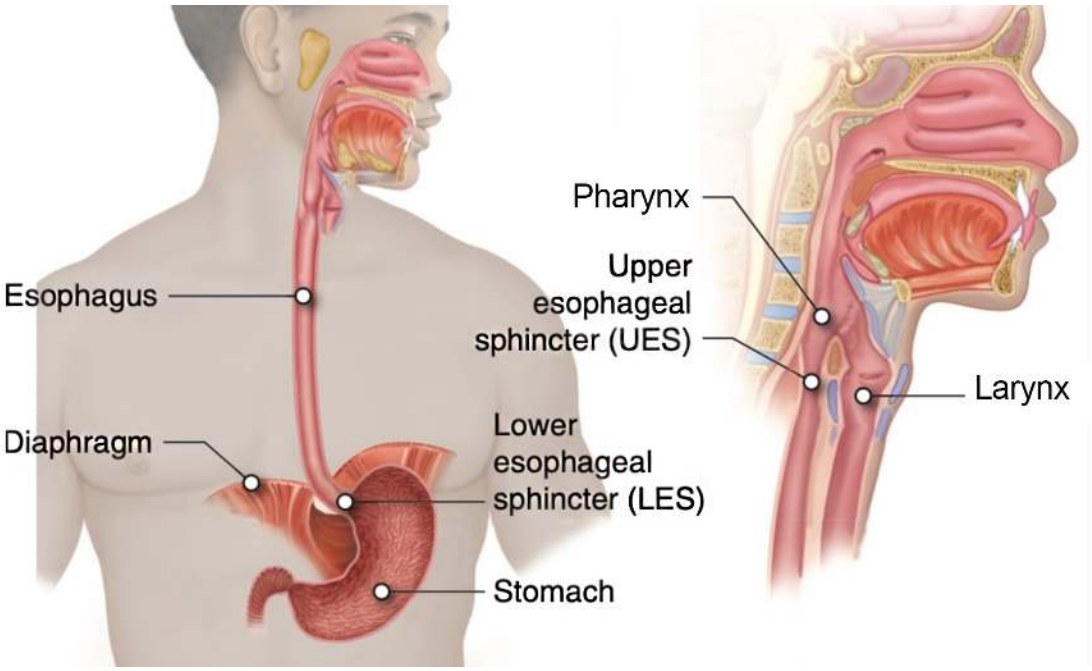


Figure 16.3.2 Esophagus. The upper esophageal sphincter controls the movement of food from the pharynx to the esophagus. The lower esophageal sphincter controls the movement of food from the esophagus to the stomach. *(Image and caption credit: "KnowledgeWorks - Drawing Oesophagus: upper and lower oesophageal sphincters - English labels" by KnowledgeWorks Global Ltd., is licensed under CC BY 4.0. Modifications by Jennifer Lange.)*

The Stomach

Although a minimal amount of carbohydrate digestion occurs in the mouth, chemical digestion really gets underway in the stomach. An expansion of the alimentary canal that lies immediately inferior to the esophagus, the stomach links the esophagus to the first part of the small intestine (the duodenum) and is relatively fixed in place at its esophageal and duodenal ends. In between, however, it can be a highly active structure, contracting and continually changing position and size. These contractions provide mechanical assistance to digestion. The empty stomach is only about the size of your fist, but can stretch to hold as much as 4 liters of food and fluid, or more than 75 times its empty volume, and then return to its resting size when empty. Although you might think that the size of a person's stomach is related to how much food that individual consumes, body weight does not correlate with stomach size. Rather, when you eat greater quantities of food—such as at holiday dinner—you stretch the stomach more than when you eat less.

Popular culture tends to refer to the stomach as the location where all digestion takes place. Of course, this is not true. An important function of the stomach is to serve as a temporary holding chamber. You can ingest a meal far more quickly than it can be digested and absorbed by the small intestine. Thus, the stomach holds food and parses only small amounts into the small intestine at a time. Foods are not processed in the order they are eaten; rather, they are mixed together with digestive juices in the stomach until they are converted into **chyme**, a now liquid mixture of the partially digested food, which is released into the small intestine.

As you will see in the sections that follow, the stomach plays several important roles in chemical digestion, including the continued digestion of carbohydrates and the initial digestion of proteins and triglycerides. Little if any nutrient absorption occurs in the stomach, with the exception of the negligible amount of nutrients in alcohol.

Histology

The wall of the stomach is made of the same four layers as most of the rest of the alimentary canal, but with adaptations to the mucosa and muscularis for the unique functions of this organ. In addition to the typical circular and longitudinal smooth muscle layers, the muscularis has an inner oblique smooth muscle layer (Figure 16.3.2). As a result, in addition to moving food through the canal, the stomach can vigorously churn food, mechanically breaking it down into smaller particles.

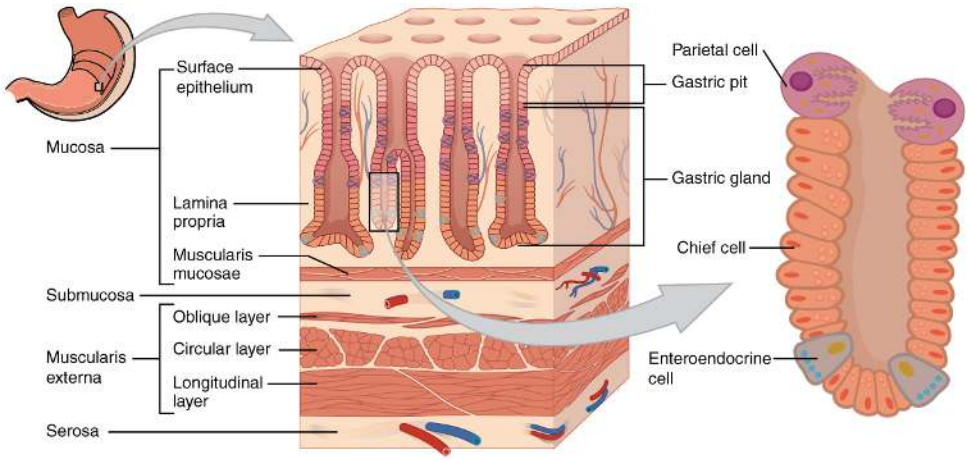


Figure 16.3.3: Histology of the Stomach. The stomach wall is adapted for the functions of the stomach. In the epithelium, gastric pits lead to gastric glands that secrete gastric juice. The gastric glands (one gland is shown enlarged on the right) contain different types of cells that secrete a variety of enzymes, including hydrochloride acid, which activates the protein-digesting enzyme pepsin.

The stomach mucosa's epithelial lining consists only of **surface mucus cells**, which secrete a protective coat of alkaline mucus. A vast number of **gastric pits** dot the surface of the epithelium, giving it the appearance of a well-used pincushion, and mark the entry to each **gastric gland**, which secretes a complex digestive fluid referred to as gastric juice.

Although the walls of the gastric pits are made up primarily of mucus cells, the gastric glands are made up of different types of cells. The glands of the cardia and pylorus are composed primarily of mucus-secreting cells. Cells that make up the pyloric antrum secrete mucus and a number of hormones, including the majority of the stimulatory hormone, gastrin. The much larger glands of the fundus and body of the stomach, the site of most chemical digestion, produce most of the gastric secretions. These glands are made up of a variety of secretory cells. These include parietal cells, chief cells, mucous neck cells, and enteroendocrine cells.

The glands of the gastric glands are the following with their functions:

- **Parietal cells:** Located primarily in the middle region of the gastric glands are parietal cells, which are among the most highly differentiated of the body's epithelial cells. These relatively large cells produce both **hydrochloric acid (HCl)** and intrinsic factor. HCl is responsible for the high acidity (pH 1.5 to 3.5) of the stomach contents and is needed to activate the protein-digesting enzyme, **pepsin**. The acidity also kills much of the bacteria you ingest with food and helps to denature proteins, making them more available for enzymatic digestion. Intrinsic factor is a glycoprotein necessary for the absorption of vitamin B_{12} in the small intestine.
- **Chief cells:** Located primarily in the basal regions of gastric glands are chief cells, which secrete **pepsinogen**, the inactive form of pepsin. HCl is necessary for the conversion of pepsinogen to pepsin.
- **Mucous neck cells:** Gastric glands in the upper part of the stomach contain mucous neck cells that secrete thin, acidic mucus that is much different from the mucus secreted by the goblet cells of the surface epithelium. The role of this mucus is not currently known.
- **Enteroendocrine cells**: Finally, enteroendocrine cells found in the gastric glands secrete various hormones into the interstitial fluid of the lamina propria. These include **gastrin**, which is released mainly by enteroendocrine G cells. Gastrin stimulates further secretion of HCl from parietal cells in the stomach.

Table 16.3.1 describes the digestive functions of important hormones secreted by the stomach.

Interactive Link



Watch this animation that depicts the structure of the stomach and how this structure functions in the initiation of protein digestion. This view of the stomach shows the characteristic rugae. What is the function of these rugae?

Table 16.3.1: Hormones Secreted by the Stomach

Hormone	Production site	Production stimulus	Target organ	Action
Gastrin	Stomach mucosa, mainly G cells of the pyloric antrum	Presence of peptides and amino acids in stomach	Gastrointestinal Tract	1. Increases secretions. 2. Increases motility. 3. Causes mass motions of large intestines.
Ghrelin	Stomach mucosa, mainly fundus	Fasting state (levels increase just prior to meals)	Hypothalamus	Regulates food intake, primarily by stimulating hunger and satiety
Serotonin	Stomach mucosa	Presence of food in the stomach	Stomach	Contracts stomach muscle

The Mucosal Barrier

The mucosa of the stomach is exposed to the highly corrosive acidity of gastric juice. Gastric enzymes that can digest protein can also digest the stomach itself. The stomach is protected from self-digestion by the mucosal barrier. This barrier has several components. First, the stomach wall is covered by a thick coating of bicarbonate-rich mucus. This mucus forms a physical barrier, and its bicarbonate ions neutralize acid. Second, the epithelial cells of the stomach's mucosa meet at tight junctions, which block gastric juice from penetrating the underlying tissue layers. Finally, stem cells located where gastric glands join the gastric pits quickly replace damaged epithelial mucosal cells, when the epithelial cells are shed. In fact, the surface epithelium of the stomach is completely replaced every 3 to 6 days.

Homeostatic Imbalances

Ulcers: When the Mucosal Barrier Breaks Down

As effective as the mucosal barrier is, it is not a “fail-safe” mechanism. Sometimes, gastric juice eats away at the superficial lining of the stomach mucosa, creating erosions, which mostly heal on their own. Deeper and larger erosions are called ulcers.

Why does the mucosal barrier break down? A number of factors can interfere with its ability to protect the stomach lining. The majority of all ulcers are caused by either excessive intake of non-steroidal anti-inflammatory drugs (NSAIDs), including aspirin, or *Helicobacter pylori* infection.

Antacids help relieve symptoms of ulcers such as “burning” pain and indigestion. When ulcers are caused by NSAID use, switching to other classes of pain relievers allows healing. When caused by *H. pylori* infection, antibiotics are effective.

A potential complication of ulcers is perforation: Perforated ulcers create a hole in the stomach wall, resulting in peritonitis (inflammation of the peritoneum). These ulcers must be repaired surgically.

Digestive Functions of the Stomach

The stomach participates in virtually all the digestive activities with the exception of ingestion and defecation. Although almost all absorption takes place in the small intestine, the stomach does absorb some drugs, such as alcohol and aspirin.

Mechanical Digestion

Within a few moments after food enters your stomach, mixing waves begin to occur at intervals of approximately 20 seconds. A mixing wave is a unique type of peristalsis that mixes and softens the food with gastric juices to create chyme. The initial mixing waves are relatively gentle, but these are followed by more intense waves, starting at the body of the stomach and increasing in force as they reach the pylorus. It is fair to say that long before your sushi exits through the pyloric sphincter, it bears little resemblance to the sushi you ate.

The pylorus, which holds around 30 mL (1 fluid ounce) of chyme, acts as a filter, permitting only liquids and small food particles to pass through the mostly, but not fully, closed pyloric sphincter. In a process called gastric emptying, rhythmic mixing waves force about 3 mL of chyme at a time through the pyloric sphincter and into the duodenum. Release of a greater amount of chyme at one time would overwhelm the capacity of the small intestine to handle it. The rest of the chyme is pushed back into the body of the stomach, where it continues mixing. This process is repeated when the next mixing waves force more chyme into the duodenum.

Gastric emptying is regulated by both the stomach and the duodenum. The presence of chyme in the duodenum activates receptors that inhibit gastric secretion. This prevents additional chyme from being released by the stomach before the duodenum is ready to process it. The process of stomach emptying can be seen below in Figure 16.3.4.

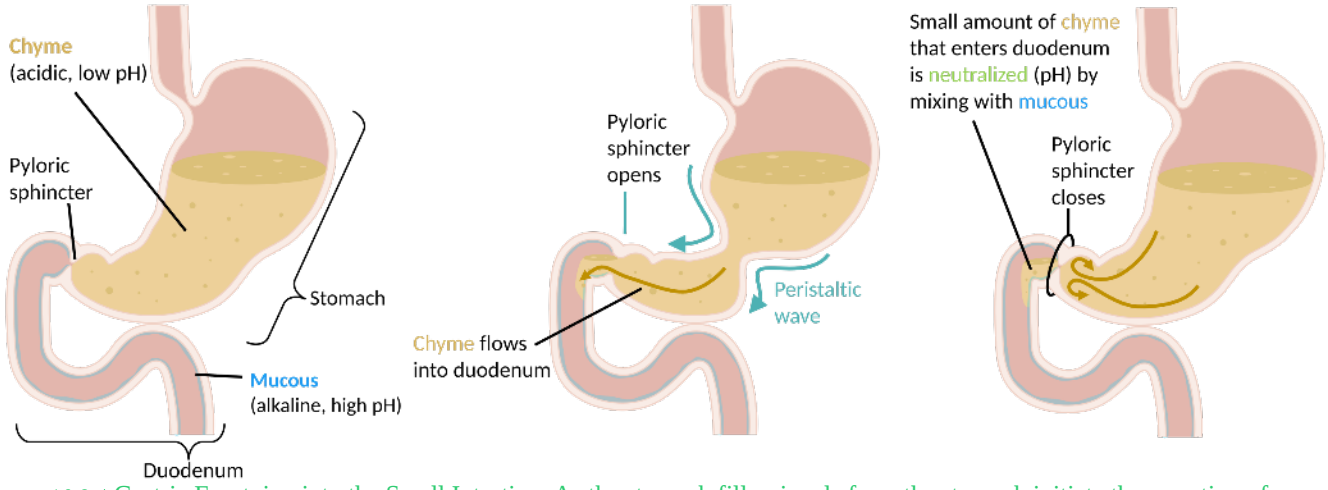


Figure 16.3.4 Gastric Emptying into the Small Intestine: As the stomach fills, signals from the stomach initiate the secretion of alkaline mucous into the duodenum. Peristaltic waves in the stomach then push chyme through the dilated pyloric sphincter into the duodenum of the small intestine. The pH of the small amount of acidic chyme within the duodenum then mixes with the alkaline mucous to neutralize the contents of the intestinal lumen. *(Image and caption credit: "*
Stomach emptying into duodenum
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Chemical Digestion

The fundus, the upper portion of the stomach, plays an important role, because it stores both undigested food and gases that are released during the process of chemical digestion. Food may sit in the fundus of the stomach for a while before being mixed with the chyme. While the food is in the fundus, the digestive activities of salivary amylase continue until the food begins mixing with the acidic chyme. Ultimately, mixing waves incorporate this food with the chyme, the acidity of which inactivates salivary amylase and activates lingual lipase.

The breakdown of protein begins in the stomach through the actions of HCl and the enzyme pepsin.

Its numerous digestive functions notwithstanding, there is only one stomach function necessary to life: the production of intrinsic factor. The intestinal absorption of vitamin B_{12}, which is necessary for both the production of mature red blood cells and normal

neurological functioning, cannot occur without intrinsic factor. People who undergo total gastrectomy (stomach removal)—for life-threatening stomach cancer, for example—can survive with minimal digestive dysfunction if they receive vitamin B_{12} injections.

The contents of the stomach are completely emptied into the duodenum within 2 to 4 hours after you eat a meal. Different types of food take different amounts of time to process. Foods heavy in carbohydrates empty fastest, followed by high-protein foods. Meals with a high triglyceride content remain in the stomach the longest. Since enzymes in the small intestine digest fats slowly, food can stay in the stomach for 6 hours or longer when the duodenum is processing fatty chyme. However, note that this is still a fraction of the 24 to 72 hours that full digestion typically takes from start to finish.

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16.4: Small and Large Intestines

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

- Compare and contrast the location and gross anatomy of the small and large intestines
- Identify three main adaptations of the small intestine wall that increase its absorptive capacity
- Describe the structures responsible for the mechanical and chemical digestion of chyme upon its release into the small intestine
- List three features unique to the wall of the large intestine and identify their contributions to its function
- Identify the beneficial roles of the bacterial flora in digestive system functioning
- Trace the pathway of food waste from its point of entry into the large intestine through its exit from the body as feces

The word intestine is derived from a Latin root meaning “internal,” and indeed, the two organs together nearly fill the interior of the abdominal cavity. In addition, called the small and large bowel, or colloquially the “guts,” they constitute the greatest mass and length of the alimentary canal and, with the exception of ingestion, perform all digestive system functions.

Small Intestine

Chyme released from the stomach enters the **small intestine**, which is the primary digestive organ in the body. Not only is this where most digestion occurs, it is also where practically all absorption occurs. The longest part of the alimentary canal, the small intestine is about 3.05 meters (10 feet) long in a living person (but about twice as long in a cadaver due to the loss of muscle tone). Since this makes it about five times longer than the large intestine, you might wonder why it is called “small.” In fact, its name derives from its relatively smaller diameter of only about 2.54 cm (1 in), compared with 7.62 cm (3 in) for the large intestine. As we’ll see shortly, in addition to its length, the folds and projections of the lining of the small intestine work to give it an enormous surface area, which is approximately 200 m^2, more than 100 times the surface area of your skin. This large surface area is necessary for complex processes of digestion and absorption that occur within it.

Structure

The coiled tube of the small intestine is subdivided into three regions. From proximal (at the stomach) to distal, these are the duodenum, jejunum, and ileum (Figure 16.4.1).

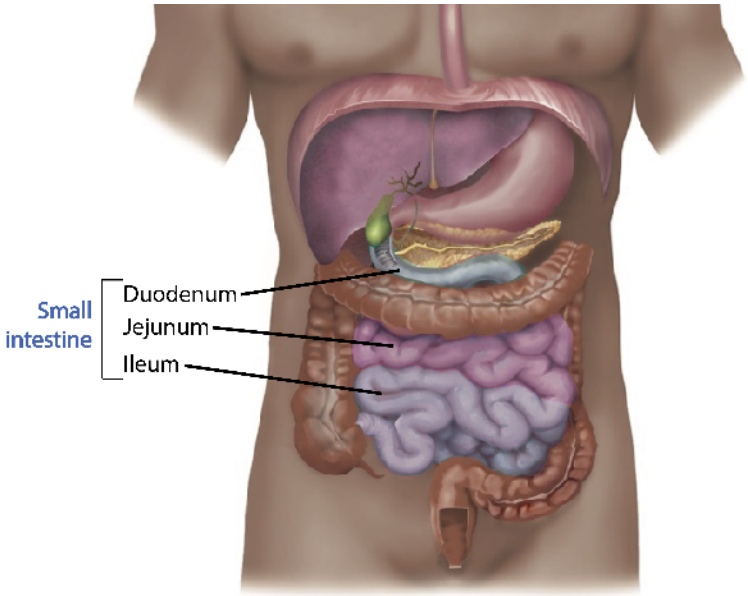


Figure 16.4.1: Small Intestine. The three regions of the small intestine are the duodenum, jejunum, and ileum. *(Image credit: "Regions of the Small Intestine" by Jennifer Lange is licensed under CC BY-NC-SA, modification of original “Drawing of Abdominal Organs” by KnowledgeWorks Global Ltd. and Open Learning Initiative.)*

The shortest region is the 25.4-cm (10-in) **duodenum** (Figure 16.4.2), which begins at the pyloric sphincter. Just past the pyloric sphincter, it bends posteriorly behind the peritoneum, becoming retroperitoneal, and then makes a C-shaped curve around the head

of the pancreas before ascending anteriorly again to return to the peritoneal cavity and join the jejunum. Located in the duodenal wall, the ampulla is where the bile duct (through which bile passes from the liver) and the **main pancreatic duct** join. This ampulla opens into the duodenum at the **major duodenal papilla**.

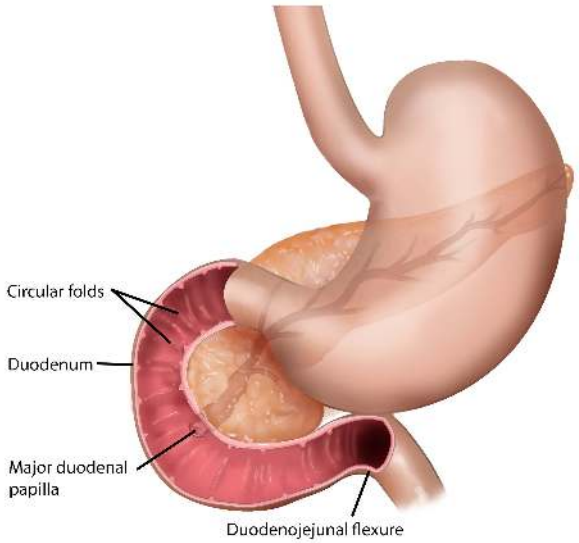


Figure 16.4.2: The Duodenum. The duodenum is the first region of the small intestine. *(Image credit: "Leiden - Drawing Stomach, duodenum, pancreas - no labels" by Ron Slagter is licensed under CC BY-NC-SA; labeled by John Polos.)*

The **jejunum** is about 0.9 meters (3 feet) long (in life) and runs from the duodenum to the ileum. Jejunum means “empty” in Latin and supposedly was so named by the ancient Greeks who noticed it was always empty at death. No clear demarcation exists between the jejunum and the final segment of the small intestine, the ileum.

The **ileum** is the longest part of the small intestine, measuring about 1.8 meters (6 feet) in length. It is thicker, more vascular, and has more developed mucosal folds than the jejunum. The ileum joins the cecum, the first portion of the large intestine, at the **ileocecal sphincter** (or valve). The jejunum and ileum are tethered to the posterior abdominal wall by the mesentery. The large intestine frames these three parts of the small intestine.

Parasympathetic fibers from the vagus nerve and sympathetic nerve fibers provide innervation to the small intestine. The superior mesenteric artery is its main arterial supply. Veins run parallel to the arteries and drain into the superior mesenteric vein. Nutrient-rich blood from the small intestine is then carried to the liver via the hepatic portal vein.

Histology

The wall of the small intestine is composed of the same four layers typically present in the digestive tract wall. However, three features of the mucosa and submucosa are unique. These features, which increase the absorptive surface area of the small intestine more than 600 times, include **circular folds**, **villi**, and **microvilli** (Figure 16.4.3). These adaptations are most abundant in the proximal two-thirds of the small intestine, where the majority of absorption occurs.

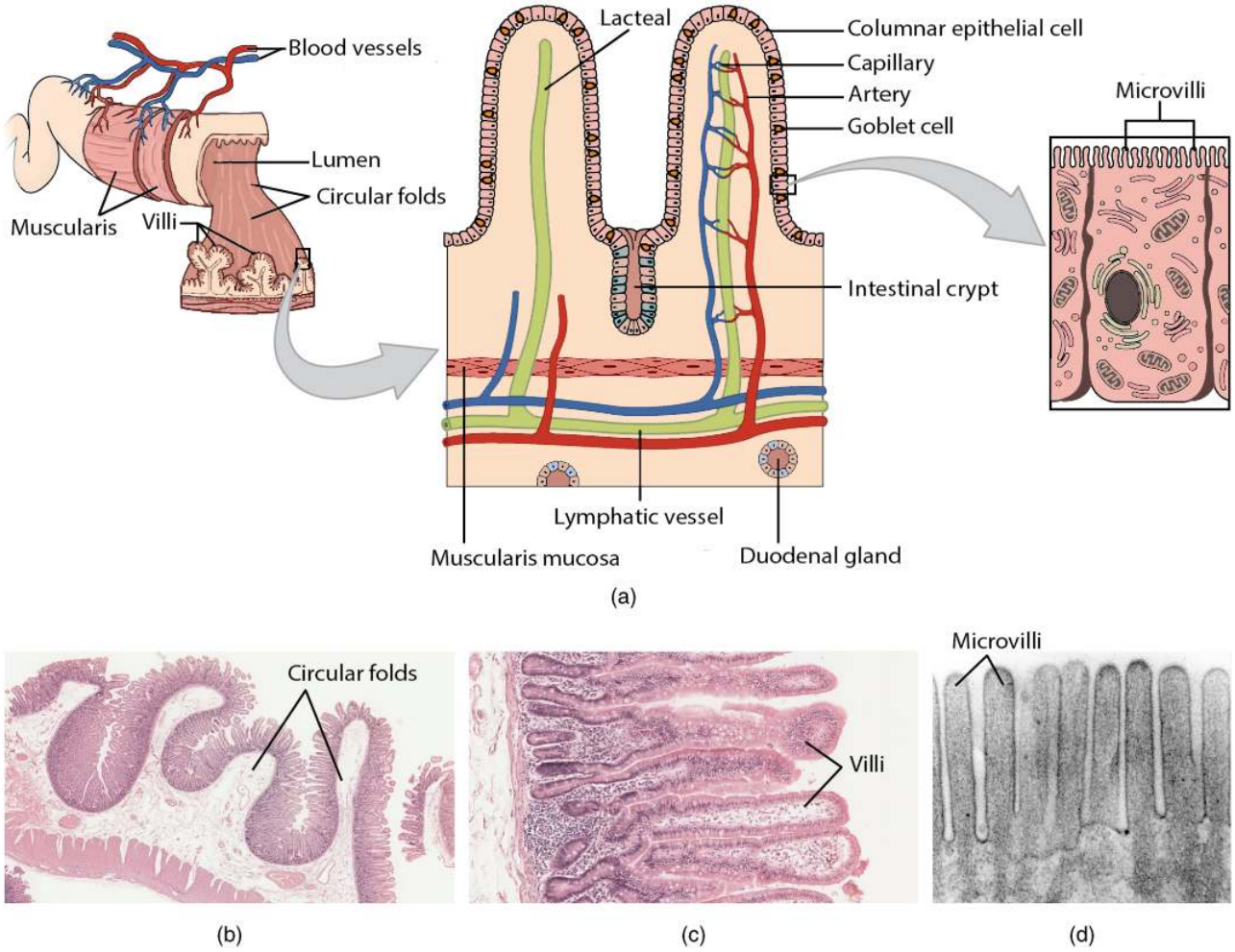


Figure 16.4.3: Histology of the Small Intestine. The absorptive surface of the small intestine is vastly enlarged by the presence of circular folds, villi, and microvilli. (b) Micrograph of the circular folds (LM @ 56x). (c) Micrograph of the villi (LM @ 504x). (d) Electron micrograph of the microvilli (EM @ 196,000x). *(Image credits: "Histology of the Small Intestine Illustration" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original by OpenStax; slides b-d provided by the Regents of the University of Michigan Medical School © 2022.)*

Circular folds

Also called a plica circulare, a **circular fold** is a tall ridge in the mucosa and submucosa (Figure 16.4.3 and Figure 16.4.4). These folds form transverse ridges that can be up to 1 cm in depth and are visible to the naked eye. Beginning near the proximal part of the duodenum and ending near the middle of the ileum, these folds facilitate absorption by increasing the surface area. Additionally, their shape causes the chyme to spiral rather than move in a straight line through the small intestine. This spiraling slows the movement of chyme and provides the time needed for nutrients to be fully absorbed.

Villi

Within the circular folds are small (0.5–1 mm long) hairlike vascularized projections of the epithelium and lamina propria called **villi** (singular = villus) that give the mucosa a furry texture (Figure 16.4.3 and Figure 16.4.4). There are about 20 to 40 villi per square millimeter, increasing the surface area of the epithelium tremendously. The mucosal simple columnar epithelium, primarily composed of absorptive cells, covers the villi. In addition to muscle and connective tissue to support its structure, each villus contains a capillary bed composed of one arteriole and one venule, as well as a lymphatic capillary called a **lacteal**. The breakdown products of carbohydrates and proteins (sugars and amino acids) can enter the bloodstream directly, but lipid breakdown products are absorbed by the lacteals and transported to the bloodstream via the lymphatic system.

Microvilli

As their name suggests, **microvilli** (singular = microvillus) are much smaller (1 μm) than villi (Figure 16.4.3). They are cylindrical apical surface extensions of the plasma membrane of the mucosa's epithelial cells, and are supported by microfilaments within those cells. Although their small size makes it difficult to see each microvillus, their combined microscopic appearance suggests a mass of bristles, which is termed the **brush border**. Fixed to the surface of the microvilli membranes are enzymes that finish digesting carbohydrates and proteins and in some cases transporter proteins to aid in digestion. There are an estimated 200 million microvilli per square millimeter of small intestine, greatly expanding the surface area of the plasma membrane and thus greatly enhancing absorption.

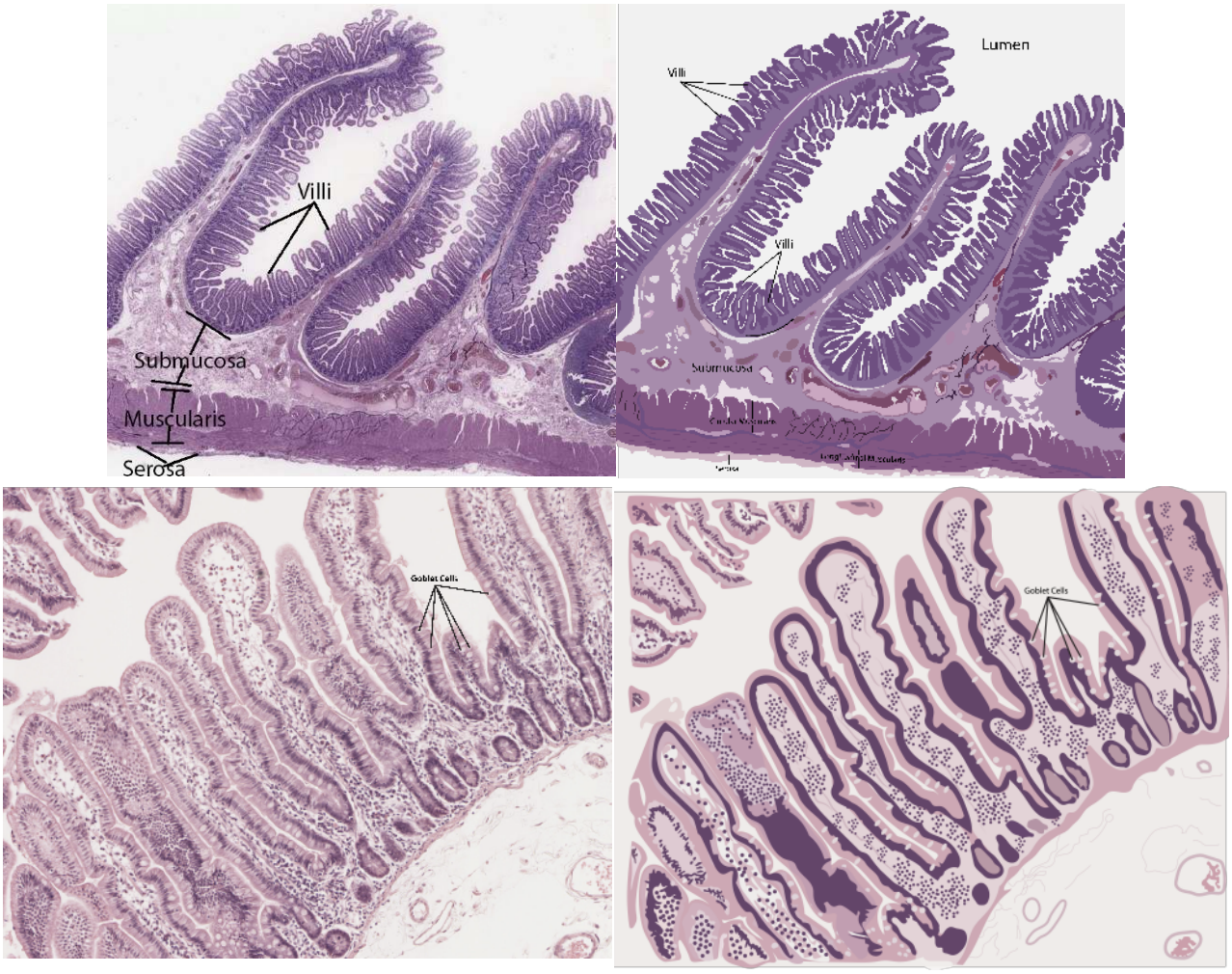


Figure 16.4.4: Jejunum histology. Under scanning power you can clearly see the layers of the wall of the jejunum and the prominent villi. When you magnify to high power you can see mucus producing goblet cells mixed in with the columnar cells of the epithelium. *(Image Credit: Histology photographs (left, top and bottom) provided by the Regents of the University of Michigan under a BY-SA-NC Creative Commons license 4.0. Illustration (right top and bottom) original work by Gabrielle Spurlock.)*

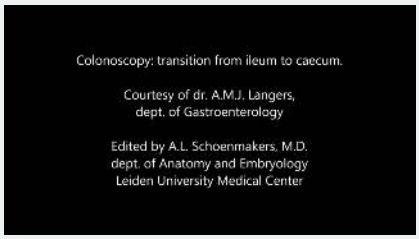
Intestinal Glands

In addition to the three specialized absorptive features just discussed, the mucosa between the villi is dotted with deep crevices that each lead into a tubular **intestinal gland** (crypt of Lieberkühn), which is formed by cells that line the crevices. These produce **intestinal juice**, a slightly alkaline (pH 7.4 to 7.8) mixture of water and mucus. Each day, about 0.95 to 1.9 liters (1 to 2 quarts) are secreted in response to the distention of the small intestine or the irritating effects of chyme on the intestinal mucosa. In addition to the exocrine glands making intestinal juice, there are enteroendocrine cells to secrete many regulatory hormones that communicate with other digestive organs including the pancreas and gallbladder.

The submucosa of the duodenum is the only site of the complex mucus-secreting **duodenal glands** (Brunner's glands), which produce a bicarbonate-rich alkaline mucus that buffers the acidic chyme as it enters from the stomach.

Visualizing the Intestine: Colonoscopy

This video shows a part of a colonoscopy, with normal anatomy: it starts in the terminal ileum, where the circular folds and the intestinal villi can be seen and are clearly indicated. Then the scope is gradually retracted, passing the ileocaecal junction to arrive in the caecum. In the ascending colon the semilunar folds can be seen and are indicated, one can also see the absence of villi here.



("Leiden - Video Colonoscopy: transition from ileum to caecum - English labels" by Alexandra M.J. Langers, LUMC and Alieke L. Schoenmakers, LUMC, license: CC BY-NC-SA.)

Digestive Functions of the Small Intestine

Mechanical Digestion

The movement of intestinal smooth muscles includes both **segmentation** and a form of peristalsis called **migrating motility complexes**. The kind of peristaltic mixing waves seen in the stomach are not observed here.

If you could see into the small intestine when it was going through segmentation, it would look as if the contents were being shoved incrementally back and forth, as the rings of smooth muscle repeatedly contract and then relax. Segmentation in the small intestine does not force chyme through the tract. Instead, it combines the chyme with digestive juices and pushes food particles against the mucosa to be digested and absorbed. The duodenum is where the most rapid segmentation occurs, at a rate of about 12 times per minute. In the ileum, segmentations are only about eight times per minute.

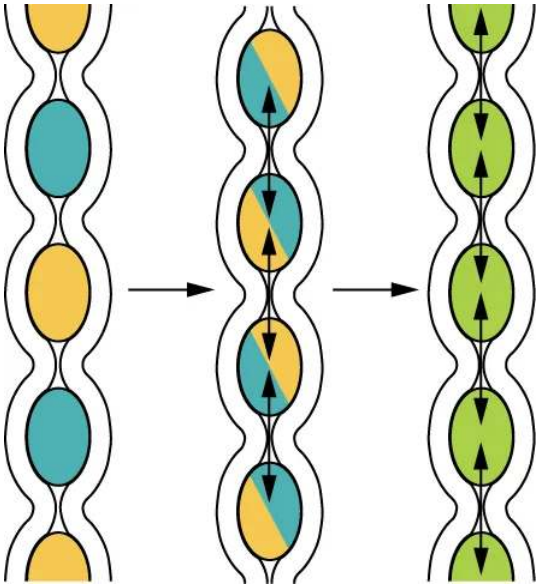


Figure 16.4.5: Segmentation separates chyme and then pushes it back together, mixing it and providing time for digestion and absorption.

When most of the chyme has been absorbed, the small intestinal wall becomes less distended. At this point, the localized segmentation process is replaced by transport movements. The duodenal mucosa secretes the hormone **motilin**, which initiates

peristalsis in the form of a **migrating motility complex**. These complexes, which begin in the duodenum, force chyme through a short section of the small intestine and then stop. The next contraction begins a little bit farther down than the first, forces chyme a bit farther through the small intestine, then stops. These complexes move slowly down the small intestine, forcing chyme on the way, taking around 90 to 120 minutes to finally reach the end of the ileum. At this point, the process is repeated, starting in the duodenum.

The ileocecal valve, a sphincter, is usually in a constricted state, but when motility in the ileum increases, this sphincter relaxes, allowing food residue to enter the first portion of the large intestine, the cecum. After chyme passes through, backward pressure helps close the sphincter, preventing backflow into the ileum. Because of this reflex, your lunch is completely emptied from your stomach and small intestine by the time you eat your dinner. It takes about 3 to 5 hours for all chyme to leave the small intestine.

Chemical Digestion

For optimal chemical digestion, chyme must be delivered from the stomach slowly and in small amounts. This is because chyme from the stomach is typically hypertonic (higher solute concentration than the content in small intestine). If large quantities of chyme were forced all at once into the small intestine, the resulting osmotic water loss from the blood into the intestinal lumen to dilute the chyme would result in potentially life-threatening low blood volume. In addition, the acidic pH of chyme from the stomach must be neutralized before it further progress through the small intestine, as the digestive enzymes in the small intestine function most optimally at less acidic pH. Both processes take time, so the pumping action of the pylorus must be carefully controlled to prevent the duodenum from being overwhelmed with chyme.

The digestion of proteins and carbohydrates, which partially occurs in the stomach, is completed in the small intestine with the aid of intestinal and pancreatic secretions:

- enzymes secreted by the pancreas break the fragmented amino acid chains into peptides, which are then split into amino acids by brush border enzymes present in the plasma membrane of the epithelial cells;
- lipids arrive in the duodenum coarsely emulsified (a mixture of water and fat globules), so bile from the liver and gallbladder create a fine emulsion which allows the lipases from the pancreas to break the lipid molecules into free fatty acids and monoglycerides.

DISORDERS OF THE...

Digestive System: Lactose Intolerance

Lactose intolerance is a condition characterized by indigestion caused by dairy products. It occurs when the absorptive cells of the small intestine do not produce enough lactase, the enzyme that digests the milk sugar lactose. In most mammals, lactose intolerance increases with age. In contrast, some human populations, most notably Caucasians, are able to maintain the ability to produce lactase as adults.

In people with lactose intolerance, the lactose in chyme is not digested. Bacteria in the large intestine ferment the undigested lactose, a process that produces gas. In addition to gas, symptoms include abdominal cramps, bloating, and diarrhea. Symptom severity ranges from mild discomfort to severe pain; however, symptoms resolve once the lactose is eliminated in feces.

The hydrogen breath test is used to help diagnose lactose intolerance. Lactose-tolerant people have very little hydrogen in their breath. Those with lactose intolerance exhale hydrogen, which is one of the gases produced by the bacterial fermentation of lactose in the colon. After the hydrogen is absorbed from the intestine, it is transported through blood vessels into the lungs. There are a number of lactose-free dairy products available in grocery stores. In addition, dietary supplements are available. Taken with food, they provide lactase to help digest lactose.

Large Intestine

The **large intestine** is the terminal part of the alimentary canal. The primary function of this organ is to finish absorption of nutrients and water, synthesize certain vitamins, form feces, and eliminate feces from the body.

Structure

The large intestine runs from the appendix to the anus (Figure 16.4.6). It frames the small intestine on three sides. Despite its being about one-half as long as the small intestine, it is called large because it has a diameter that is more than twice the diameter of the small intestine, about 3 inches. The large intestine is subdivided into four main regions: the cecum, the colon, the rectum, and the

anus. The ileocecal valve, located at the opening between the ileum and the large intestine, controls the flow of chyme from the small intestine to the large intestine.

Cecum

The first part of the large intestine is the **cecum**, a sac-like structure that is suspended inferior to the ileocecal valve. It is about 6 cm (2.4 in) long, receives the contents of the ileum, and continues the absorption of water and salts. The **appendix** (or vermiform appendix) is a winding, dead-end tube that attaches to the cecum. Although the 7.6-cm (3-in) long appendix contains lymphoid tissue, suggesting an immunologic function, this organ is generally considered vestigial (a structure present in our ancestors that has over time lost its original function). However, at least one recent report postulates a survival advantage conferred by the appendix: in diarrheal illness, the appendix may serve as a bacterial reservoir to repopulate the enteric bacteria for those surviving the initial phases of the illness. Moreover, its twisted anatomy provides a haven for the accumulation and multiplication of enteric bacteria.

Colon

The cecum blends seamlessly with the **colon**. The small intestine is faintly superimposed to show the location of both the large and small intestines. Upon entering the colon, the food residue first travels up the **ascending colon** on the right side of the abdomen. At the inferior surface of the liver, the colon bends to form the **right colic flexure** (hepatic flexure) and becomes the **transverse colon**. The region defined as hindgut begins with the last third of the transverse colon and continues on. Food residue passing through the transverse colon travels across to the left side of the abdomen, where the colon angles sharply immediately inferior to the spleen, at the **left colic flexure** (splenic flexure). From there, food residue passes through the **descending colon**, which runs down the left side of the posterior abdominal wall. After entering the pelvis inferiorly, it becomes the s-shaped **sigmoid colon**, which extends medially to the midline (Figure 16.4.6). The ascending and descending colon, and the rectum (discussed next) are located in the retroperitoneum.

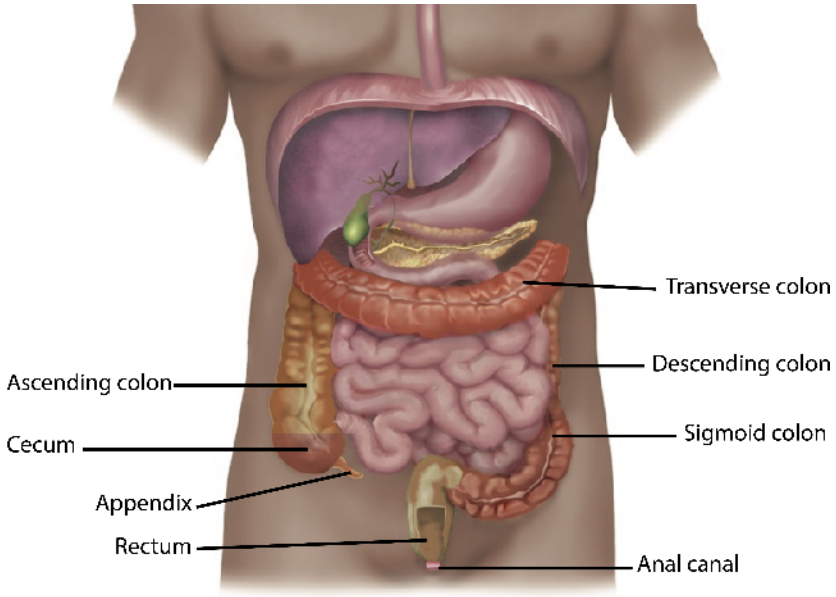


Figure 16.4.6: Large Intestine. The large intestine includes the cecum, colon, and rectum. *(Image credit: "Regions of the Large Intestine" by Jennifer Lange is licensed under CC BY-NC-SA, modification of original "Drawing of Abdominal Organs" by KnowledgeWorks Global Ltd. and Open Learning Initiative.)*

DISORDER OF THE...

Digestive System: Colorectal Cancer

Each year, approximately 140,000 Americans are diagnosed with colorectal cancer, and another 49,000 die from it, making it one of the most deadly malignancies. People with a family history of colorectal cancer are at increased risk. Smoking, excessive alcohol consumption, and a diet high in animal fat and protein also increase the risk. Despite popular opinion to the contrary, studies support the conclusion that dietary fiber and calcium do not reduce the risk of colorectal cancer.

Colorectal cancer may be signaled by constipation or diarrhea, cramping, abdominal pain, and rectal bleeding. Bleeding from the rectum may be either obvious or occult (hidden in feces). Since most colon cancers arise from benign mucosal growths called polyps, cancer prevention is focused on identifying these polyps. The colonoscopy is both diagnostic and therapeutic. Colonoscopy not only allows identification of precancerous polyps, the procedure also enables them to be removed before they become malignant. Screening for fecal occult blood tests and colonoscopy is recommended for those over 50 years of age.

Rectum

Food residue leaving the sigmoid colon enters the **rectum** in the pelvis, near the third sacral vertebra. The final 20.3 cm (8 in) of the alimentary canal, the rectum extends anterior to the sacrum and coccyx. Even though rectum is Latin for "straight," this structure follows the curved contour of the sacrum and has three lateral bends that create a trio of internal transverse folds called the **rectal valves**. These valves help separate the feces from gas to prevent the simultaneous passage of feces and gas.

Anal Canal

Finally, food residue reaches the last part of the large intestine, the **anal canal**, which is located in the perineum, completely outside of the abdominopelvic cavity. This 3.8–5 cm (1.5–2 in) long structure opens to the exterior of the body at the anus. The anal canal includes two sphincters. The **internal anal sphincter** is made of smooth muscle, and its contractions are involuntary. The **external anal sphincter** is made of skeletal muscle, which is under voluntary control. Except when defecating, both usually remain closed.

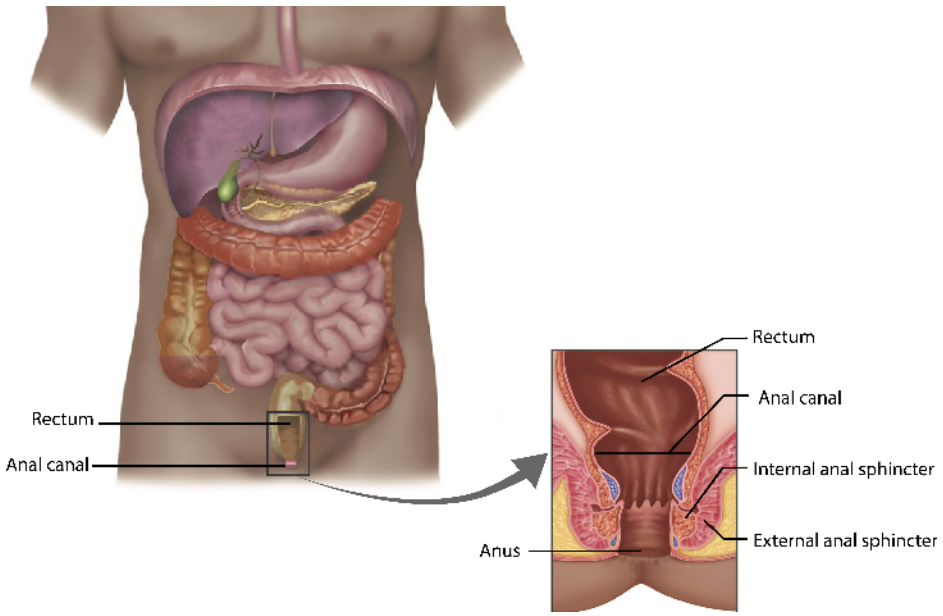
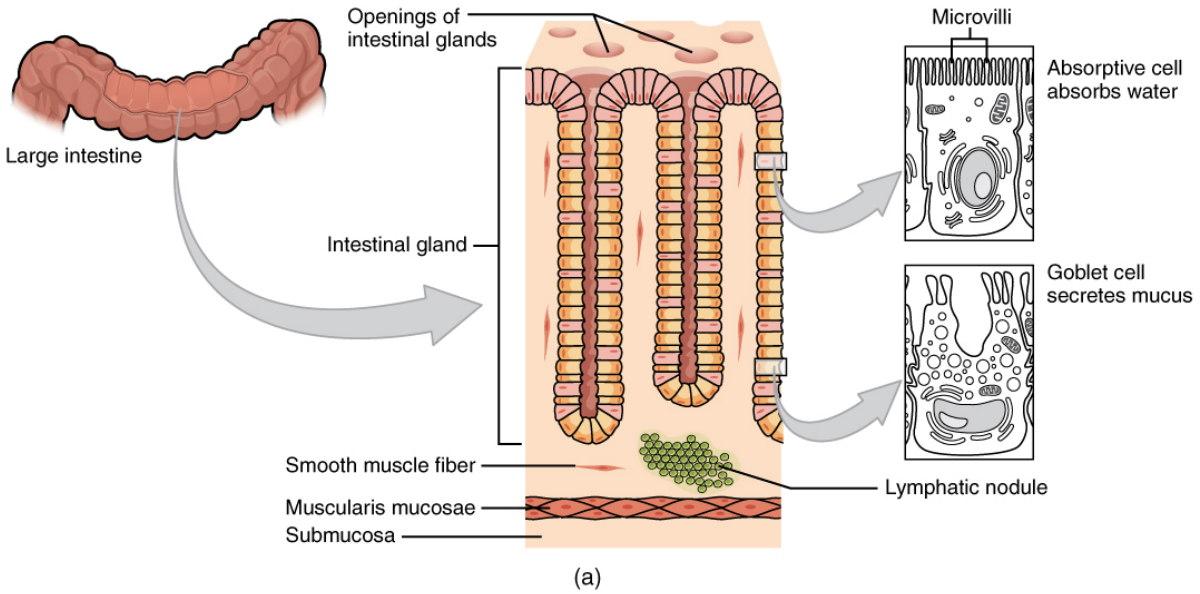
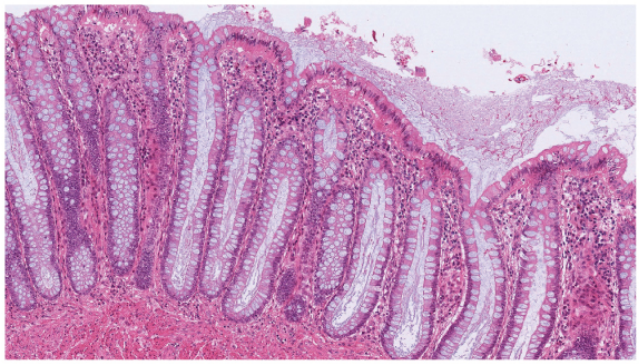


Figure 16.4.7: Anal Canal. The anal canal has two sphincters that regulate its opening. The external anal sphincter contains voluntary skeletal muscle while the internal anal sphincter contains involutatary smooth muscle. *(Image credit: "Anal Canal" by Jennifer Lange is licensed under CC BY-NC-SA, modification of original "Drawing of Abdominal Organs" by KnowledgeWorks Global Ltd. and Open Learning Initiative.)*

Histology

There are several notable differences between the walls of the large and small intestines (Figure 16.4.8 and Figure 16.4.9). For example, few enzyme-secreting cells are found in the wall of the large intestine, and there are no circular folds or villi. Other than in the anal canal, the mucosa of the colon is simple columnar epithelium made mostly of absorptive enterocytes with microvilli and goblet cells. In addition, the mucosa has far more intestinal glands, which contain a vast population of enterocytes and goblet cells. These goblet cells secrete mucus that eases the movement of feces and protects the intestine from the effects of the acids and gases produced by enteric bacteria. The enterocytes absorb water and salts as well as vitamins produced by your intestinal bacteria.





(b)

Figure 16.4.8: Histology of the large Intestine. (a) The histologies of the large intestine and small intestine (not shown) are adapted for the digestive functions of each organ. (b) This micrograph shows the colon's simple columnar epithelium and goblet cells. LM x 464. Micrograph provided by the Regents of University of Michigan Medical School © 2012. (Image credit: "Histology of Large Intestine" by OpenStax is licensed under CC BY 3.0)

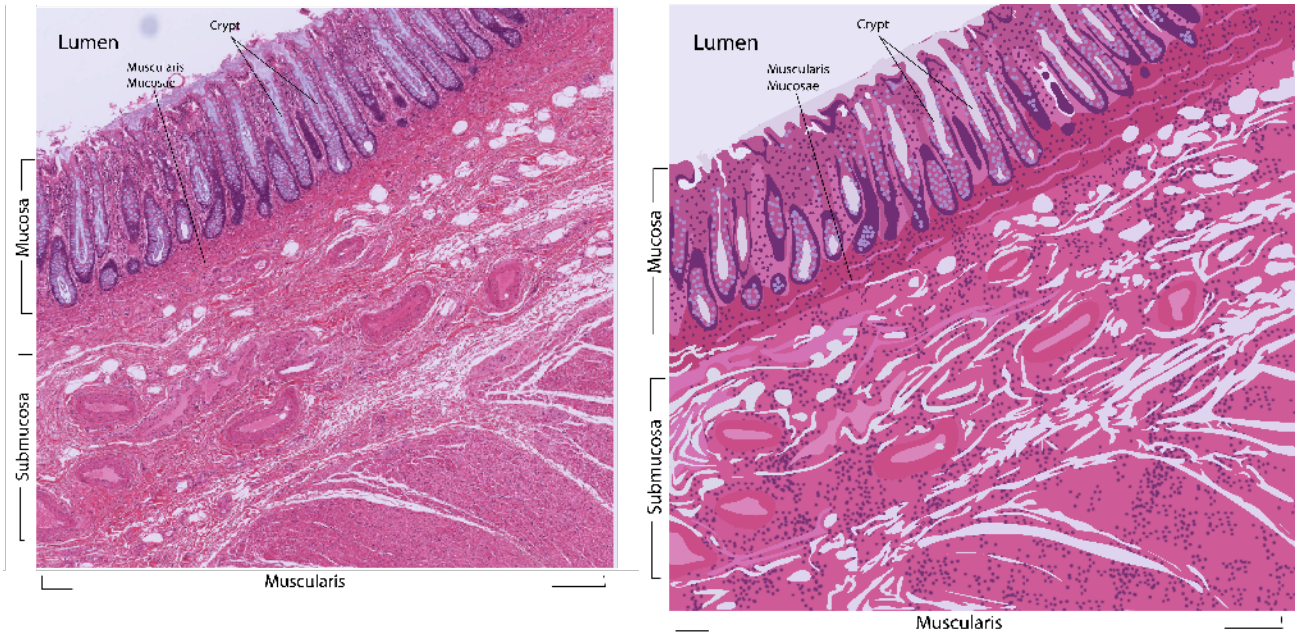


Figure 16.4.9: Low Power Histology of Large Intestine. (Left) Histology photgraph showing the colon and (right) illustration of the colon. The muscularis has deep crypts that are lined with goblet cells. The goblet cells produce a lot of mucus which help lubricate/clump the fecal matter. The crypts also have stem cells in the crypts replace cells lost due to friction from the mucosal layer. Numerous blood vessels and nerves are found in the sub mucosa. Lymph nodules can be observed in the submucosa as well. The muscularis sits below the submucosa. However, the longitudinal layer may be missing depending on where the slide was taken from. (*Micrograph provided by the Regents of University of Michigan Medical School © 2012. (Image credit: "Histology of Large Intestine" by OpenStax is licensed under CC BY 3.0. Illustration of colon histology original work by Gabrielle Spurlock.)*

Structural Features

The **teniae coli** (also spelled taenia) are three bands of smooth muscle that make up the longitudinal muscle layer of the muscularis of the large intestine, except at its terminal end (Figure 16.4.10). The bands are spaced equidistantly around the circumference of the tube. Tonic contractions of the teniae coli bunch up the colon into a succession of pouches called **haustra** (singular = hostrum), which creates the wrinkled, lumpy appearance of the colon. Attached to the teniae coli are small, fat-filled sacs of visceral peritoneum. The purpose of these is unknown. Although the rectum and anal canal have neither teniae coli nor haustra, they do have well-developed layers of muscularis that create the strong contractions needed for defecation.

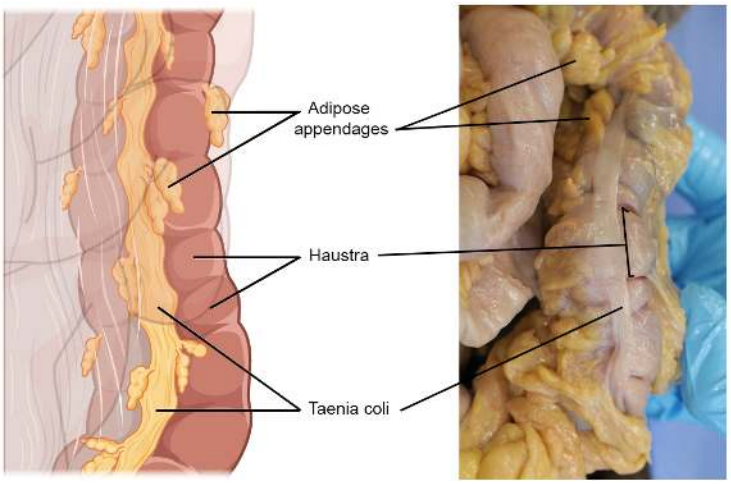


Figure 16.4.10: Structural Features of the Large Intestine. On the surface of the colon, there are fatty projections, bulges (haustra), and remnants of longitudinal smooth muscles (teniae coli). *(Image credit: "Large Intestine Structural Features by Jennifer Lange is licensed under CC BY-NC-SA 4.0 , modification of originals "Teniae Coli, Haustra, Epiploic Appendage" by OpenStax and "Leiden MOOC - Reader Anatomy on the Table - The Large Intestine" by O. Paul Gobée, LUMC.)*

The stratified squamous epithelial mucosa of the anal canal connects to the skin on the outside of the anus. This mucosa varies considerably from that of the rest of the colon to accommodate the high level of abrasion as feces pass through. Depressions within

the canal's wall secrete mucus that facilitates defecation.

Bacterial Flora

Most bacteria that enter the alimentary canal are killed by lysozyme, defensins, hydrochloric acid, or protein-digesting enzymes. However, trillions of bacteria live within the large intestine and are referred to as the **bacterial flora** or gut microbiome. Most of the more than 700 species of these bacteria are nonpathogenic commensal organisms that cause no harm as long as they stay in the gut lumen.

Some of the benefits that your gut microbiome provides include:

- Synthesis of vitamins such as biotin and vitamin K. Vitamin K is especially important for blood clotting.
- Metabolizing undigested materials such as carbohydrates
  - However, this can lead to the sometimes painful effect of gas in the colon
- Deterring the growth of harmful bacteria.
  - Your gut microbiome compete for nutrients harmful bacteria would use and also produce chemicals that harm pathogens.
- Stimulating your immune system

Digestive Functions of the Large Intestine

The residue of chyme that enters the large intestine contains few nutrients except water, which is reabsorbed as the residue lingers in the large intestine, typically for 12 to 24 hours. Thus, it may not surprise you that the large intestine can be completely removed without significantly affecting digestive functioning. For example, in severe cases of inflammatory bowel disease, the large intestine can be removed by a procedure known as a colectomy. Often, a new fecal pouch can be crafted from the small intestine and sutured to the anus, but if not, an ileostomy can be created by bringing the distal ileum through the abdominal wall, allowing the watery chyme to be collected in a bag-like adhesive appliance.

Absorption, Feces Formation, and Defecation

The small intestine absorbs about 90 percent of the water you ingest (either as liquid or within solid food). The large intestine absorbs most of the remaining water, a process that converts the liquid chyme residue into semisolid **feces** (“stool”). Feces is composed of undigested food residues, unabsorbed digested substances, millions of bacteria, old epithelial cells from the GI mucosa, inorganic salts, other waste products, and enough water to let it pass smoothly out of the body. Of every 500 mL (17 ounces) of food residue that enters the cecum each day, about 150 mL (5 ounces) become feces.

The process of defecation begins when mass movements force feces from the colon into the rectum, stretching the rectal wall and provoking the defecation reflex, which eliminates feces from the rectum. This parasympathetic reflex is mediated by the spinal cord. It contracts the sigmoid colon and rectum, relaxes the internal anal sphincter, and initially contracts the external anal sphincter. The presence of feces in the anal canal sends a signal to the brain, which gives you the choice of voluntarily opening the external anal sphincter (defecating) or keeping it temporarily closed. If you decide to delay defecation, it takes a few seconds for the reflex contractions to stop and the rectal walls to relax. The next mass movement will trigger additional defecation reflexes until you defecate.

If defecation is delayed for an extended time, additional water is absorbed, making the feces firmer and potentially leading to constipation. On the other hand, if the waste matter moves too quickly through the intestines, not enough water is absorbed, and diarrhea can result. This can be caused by the ingestion of foodborne pathogens. In general, diet, health, and stress determine the frequency of bowel movements. The number of bowel movements varies greatly between individuals, ranging from two or three per day to three or four per week.

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

Learning Objectives

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

- State the main digestive roles of the liver, pancreas, and gallbladder
- Identify three main features of liver histology that are critical to its function
- Discuss the composition and function of bile
- Identify the major types of enzymes and buffers present in pancreatic juice

Chemical digestion in the small intestine relies on the activities of three accessory digestive organs: the liver, pancreas, and gallbladder (Figure 16.5.1). The digestive role of the liver is to produce bile and export it to the duodenum. The gallbladder primarily stores, concentrates, and releases bile. The pancreas produces pancreatic juice, which contains digestive enzymes and bicarbonate ions, and delivers it to the duodenum.

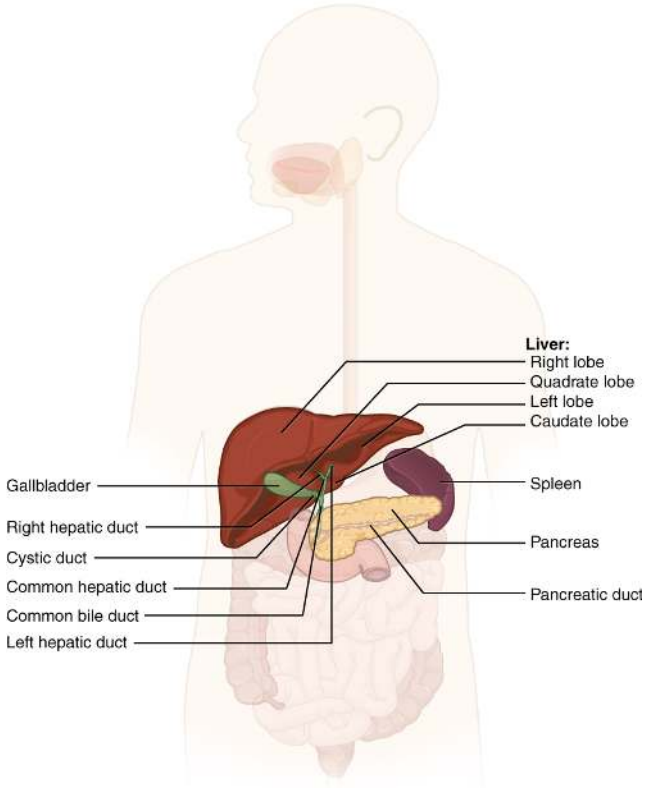


Figure 16.5.1: Accessory Organs The liver, pancreas, and gallbladder are considered accessory digestive organs, but their roles in the digestive system are vital.

The Liver

The liver is the largest gland in the body, weighing about three pounds in an adult. It is also one of the most important organs. In addition to being an accessory digestive organ, it plays a number of roles in metabolism and regulation. The liver lies inferior to the diaphragm in the right upper quadrant of the abdominal cavity and receives protection from the surrounding ribs.

The liver is divided into two primary lobes: a large right lobe and a much smaller left lobe. In the right lobe, some anatomists also identify an inferior quadrate lobe and a posterior caudate lobe, which are defined by internal features. The liver is connected to the abdominal wall and diaphragm by five peritoneal folds referred to as ligaments.

The **porta hepatis** (“gate to the liver”) is where the hepatic artery and hepatic portal vein enter the liver. As shown in Figure 16.5.2, the hepatic artery delivers oxygenated blood from the heart to the liver. The hepatic portal vein delivers partially deoxygenated

blood containing nutrients absorbed from the small intestine and actually supplies more oxygen to the liver than do the much smaller hepatic arteries. In addition to nutrients, drugs and toxins are also absorbed. After processing the bloodborne nutrients and toxins, the liver releases nutrients needed by other cells back into the blood, which drains into the central vein and then through the hepatic vein to the inferior vena cava. With this hepatic portal circulation, all blood from the alimentary canal passes through the liver. This largely explains why the liver is the most common site for the metastasis of cancers that originate in the alimentary canal.

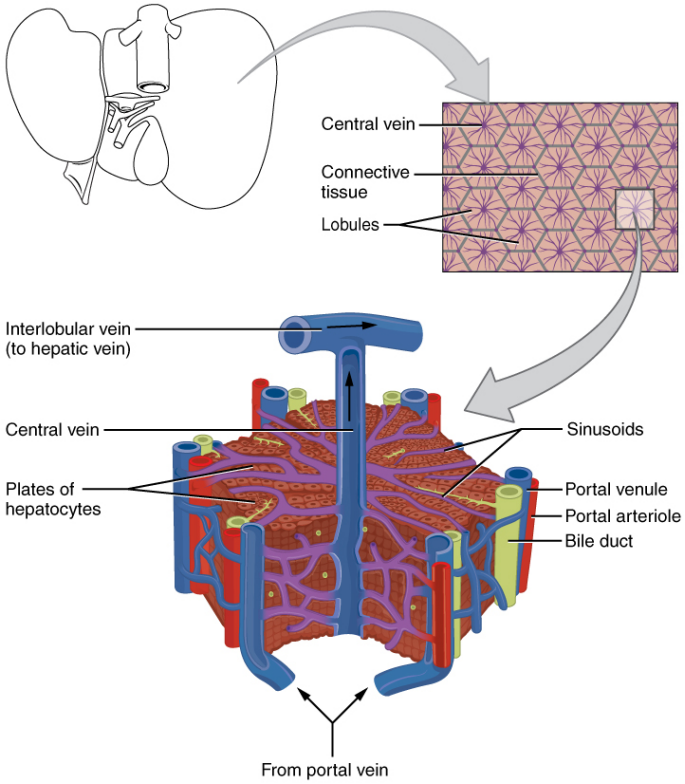


Figure 16.5.2: Microscopic Anatomy of the Liver The liver receives oxygenated blood from the hepatic artery and nutrient-rich deoxygenated blood from the hepatic portal vein.

Histology

The liver has three main components: **hepatocytes**, **bile canaliculi**, and hepatic sinusoids. A hepatocyte is the liver's main cell type, accounting for around 80 percent of the liver's volume. These cells play a role in a wide variety of secretory, metabolic, and endocrine functions. Plates of hepatocytes called hepatic laminae radiate outward from the portal vein in each hepatic lobule.

Between adjacent hepatocytes, grooves in the cell membranes provide room for each bile canaliculus (plural = canaliculi). These small ducts accumulate the bile produced by hepatocytes. From here, bile flows first into bile ductules and then into bile ducts. The bile ducts unite to form the larger right and left hepatic ducts, which themselves merge and exit the liver as the common hepatic duct. This duct then joins with the cystic duct from the gallbladder, forming the common bile duct through which bile flows into the small intestine.

A hepatic sinusoid is an open, porous blood space formed by fenestrated capillaries from nutrient-rich hepatic portal veins and oxygen-rich hepatic arteries. Hepatocytes are tightly packed around the fenestrated endothelium of these spaces, giving them easy access to the blood. From their central position, hepatocytes process the nutrients, toxins, and waste materials carried by the blood.

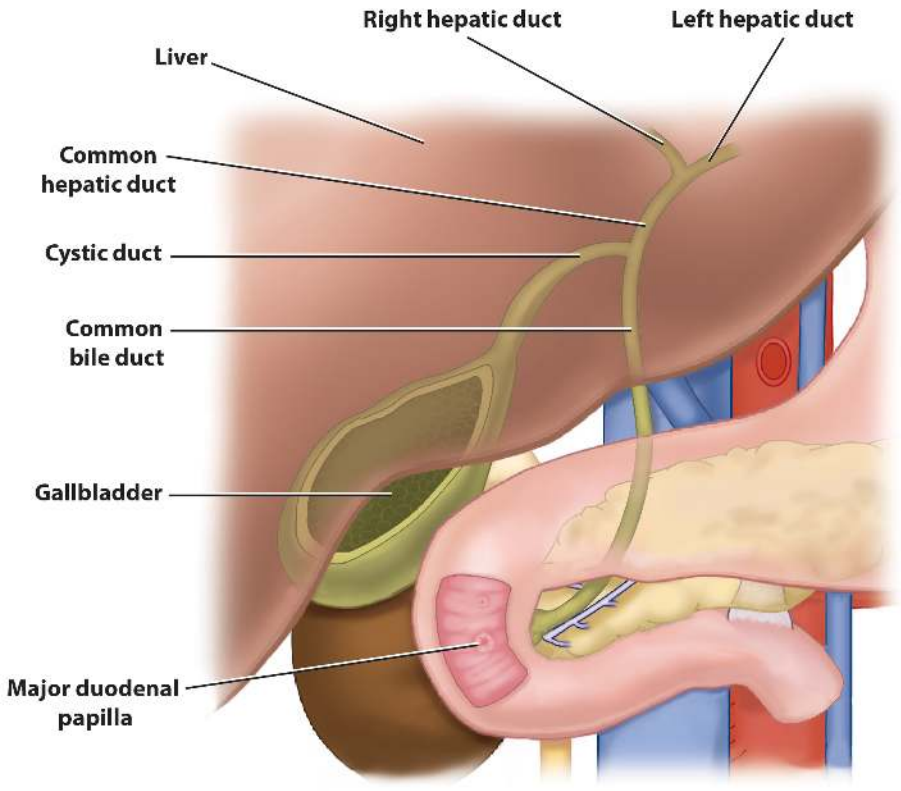


Figure 16.5.3 Bile Ducts. The ducts carrying bile from the liver and the gallbladder unite and release bile into the duodenum. *(Image and caption credit: "Bile Ducts" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original from BlueLink.)*

Bile

Recall that lipids are hydrophobic, that is, they do not dissolve in water. Thus, before they can be digested in the watery environment of the small intestine, large lipid globules must be broken down into smaller lipid globules, a process called **emulsification**. Bile is a mixture secreted by the liver to accomplish the emulsification of lipids in the small intestine.

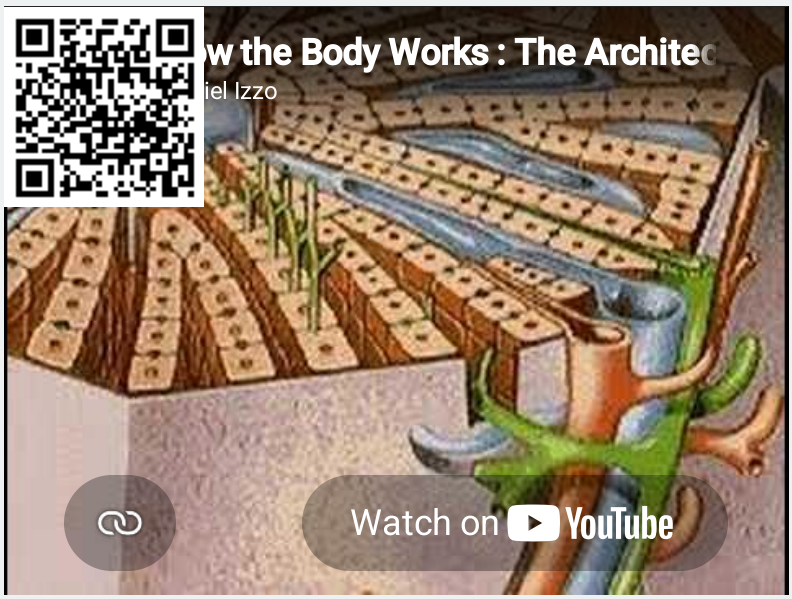
Hepatocytes secrete about one liter of bile each day. A yellow-brown or yellow-green alkaline solution (pH 7.6 to 8.6), bile is a mixture of water, bile salts, bile pigments, phospholipids, electrolytes, cholesterol, and triglycerides. The components most critical to emulsification are bile salts and phospholipids, which have a nonpolar (hydrophobic) region as well as a polar (hydrophilic) region. The hydrophobic region interacts with the large lipid molecules, whereas the hydrophilic region interacts with the watery chyme in the intestine. This results in the large lipid globules being pulled apart into many tiny lipid fragments of about 1 μm in diameter. This change dramatically increases the surface area available for lipid-digesting enzyme activity. This is the same way dish soap works on fats mixed with water.

Bile salts act as emulsifying agents, so they are also important for the absorption of digested lipids. While most constituents of bile are eliminated in feces, bile salts are reclaimed by the enterohepatic circulation. Once bile salts reach the ileum, they are absorbed and returned to the liver in the hepatic portal blood. The hepatocytes then excrete the bile salts into newly formed bile. Thus, this precious resource is recycled.

Bilirubin, the main bile pigment, is a waste product produced when the spleen removes old or damaged red blood cells from the circulation. These breakdown products, including proteins, iron, and toxic bilirubin, are transported to the liver via the splenic vein of the hepatic portal system. In the liver, proteins and iron are recycled, whereas bilirubin is excreted in the bile. It accounts for the green color of bile. Bilirubin is eventually transformed by intestinal bacteria into stercobilin, a brown pigment that gives your stool its characteristic color! In some disease states, bile does not enter the intestine, resulting in white (‘acholic’) stool with a high fat content, since virtually no fats are broken down or absorbed.

Hepatocytes work non-stop, but bile production increases when fatty chyme enters the duodenum and stimulates the secretion of the gut hormone secretin. Between meals, bile is produced but conserved. The valve-like hepatopancreatic ampulla closes, allowing bile to divert to the gallbladder, where it is concentrated and stored until the next meal.

Interactive Link



Watch this video to see the structure of the liver and how this structure supports the functions of the liver, including the processing of nutrients, toxins, and wastes. At rest, about 1500 mL of blood per minute flow through the liver. What percentage of this blood flow comes from the hepatic portal system?

The Pancreas

The soft, oblong, glandular pancreas lies transversely in the retroperitoneum behind the stomach. Its head is nestled into the "c-shaped" curvature of the duodenum with the body extending to the left about 15.2 cm (6 in) and ending as a tapering tail in the hilum of the spleen. It is a curious mix of exocrine (secreting digestive enzymes) and endocrine (releasing hormones into the blood) functions (Figure 16.5.3).

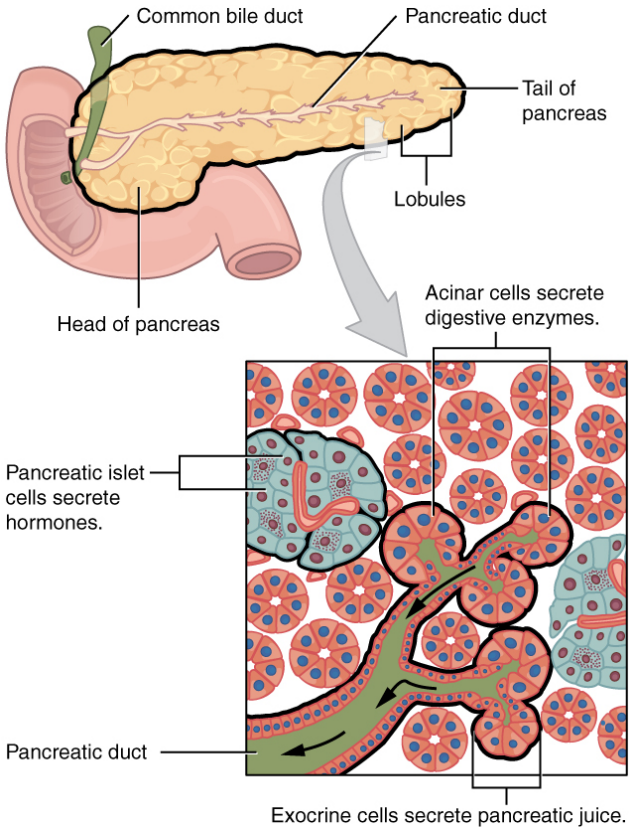


Figure 16.5.3: Exocrine and Endocrine Pancreas The pancreas has a head, a body, and a tail. It delivers pancreatic juice to the duodenum through the pancreatic duct.

The exocrine part of the pancreas arises as little grape-like cell clusters, each called an **acinus** (plural = acini), located at the terminal ends of pancreatic ducts. These acinar cells secrete enzyme-rich pancreatic juice into tiny merging ducts that form two dominant ducts. The larger duct fuses with the common bile duct (carrying bile from the liver and gallbladder) just before entering the duodenum via a common opening (the hepatopancreatic ampulla).

Scattered through the sea of exocrine acini are small islands of endocrine cells, the islets of Langerhans. These vital cells produce the hormones pancreatic polypeptide, insulin, glucagon, and somatostatin.

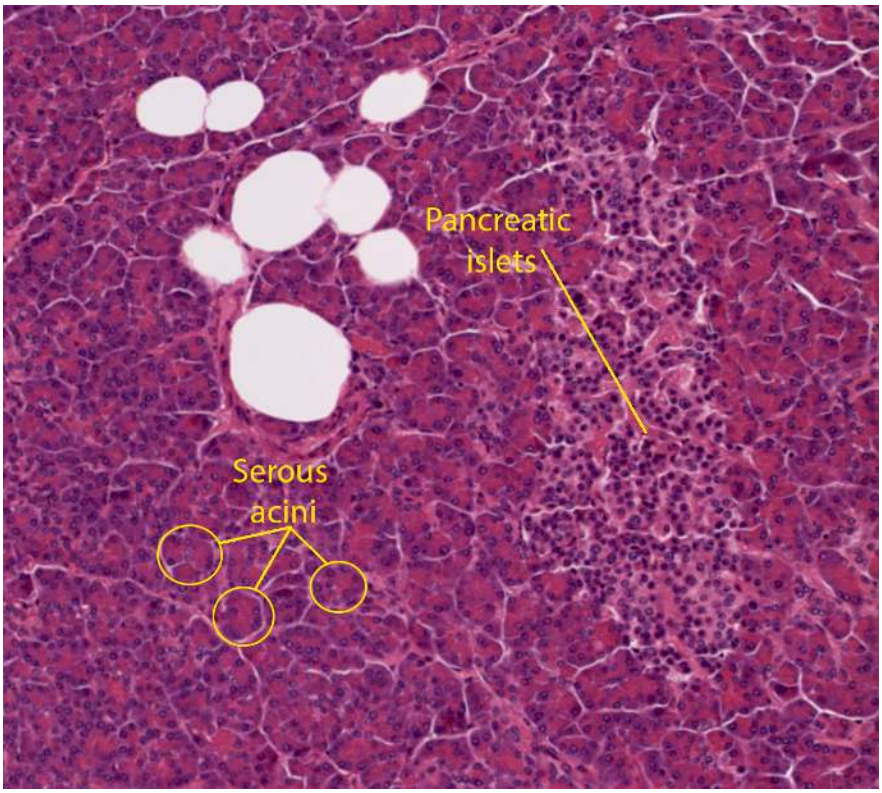


Figure 16.5.4 Pancreatic Islet Histology @ 400x. You can see the serous cells are clumped into the grape light acini. The lighter colored pancreatic islet is also more clear under this magnification. *(Image Credit :"Pancreatic Islet Histology @ 400x" micrograph provided by the Regents of University of Michigan Medical School © 2012.)*

Pancreatic Juice

The pancreas produces over a liter of pancreatic juice each day. Unlike bile, it is clear and composed mostly of water along with some salts, sodium bicarbonate, and several digestive enzymes. Sodium bicarbonate is responsible for the slight alkalinity of pancreatic juice (pH 7.1 to 8.2), which serves to buffer the acidic gastric juice in chyme, inactivate pepsin from the stomach, and create an optimal environment for the activity of pH-sensitive digestive enzymes in the small intestine. Pancreatic enzymes are active in the digestion of sugars, proteins, and fats.

The pancreas produces protein-digesting enzymes in their inactive forms. These enzymes are activated in the duodenum. If produced in an active form, they would digest the pancreas (which is exactly what occurs in the disease, pancreatitis). The intestinal brush border enzyme enteropeptidase stimulates the activation of trypsin from trypsinogen of the pancreas, which in turn changes the pancreatic enzymes procarboxypeptidase and chymotrypsinogen into their active forms, carboxypeptidase and chymotrypsin. These enzymes will then continue protein digestion in the small intestine.

The enzymes that digest starch (amylase), fat (lipase), and nucleic acids (nuclease) are secreted in their active forms, since they do not attack the pancreas as do the protein-digesting enzymes.

Pancreatic Secretion

Regulation of pancreatic secretion is the job of hormones and the parasympathetic nervous system. The entry of acidic chyme into the duodenum stimulates the release of **secretin**, which in turn causes the duct cells to release bicarbonate-rich pancreatic juice. The presence of proteins and fats in the duodenum stimulates the secretion of cholecystokinin (**CCK)**, which then stimulates the acini to secrete enzyme-rich pancreatic juice and enhances the activity of secretin. Parasympathetic regulation occurs mainly during the cephalic and gastric phases of gastric secretion, when vagal stimulation prompts the secretion of pancreatic juice.

Usually, the pancreas secretes just enough bicarbonate to counterbalance the amount of HCl produced in the stomach. Hydrogen ions enter the blood when bicarbonate is secreted by the pancreas. Thus, the acidic blood draining from the pancreas neutralizes the alkaline blood draining from the stomach, maintaining the pH of the venous blood that flows to the liver.

The Gallbladder

The gallbladder is 8–10 cm (~3–4 in) long and is nested in a shallow area on the posterior aspect of the right lobe of the liver. This muscular sac stores, concentrates, and, when stimulated, propels the bile into the duodenum via the common bile duct. The cystic duct is 1–2 cm (less than 1 in) long and turns inferiorly as it bridges the neck and hepatic duct.

The simple columnar epithelium of the gallbladder mucosa is organized in rugae, similar to those of the stomach. The gallbladder's wall contains a middle, muscular coat made of smooth muscle fibers. When these fibers contract, the gallbladder's contents are ejected through the cystic duct and into the bile duct (Figure 16.5.5). Visceral peritoneum reflected from the liver capsule holds the gallbladder against the liver and forms the outer coat of the gallbladder. The gallbladder's mucosa absorbs water and ions from bile, concentrating it by up to 10-fold.

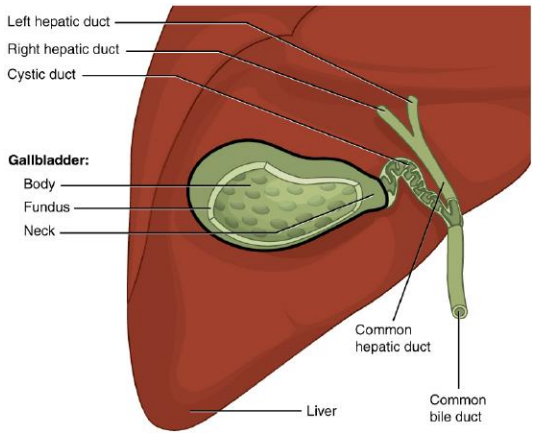


Figure 16.5.5: Gallbladder The gallbladder stores and concentrates bile, and releases it into the two-way cystic duct when it is needed by the small intestine.

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16.6: Review Questions

8.

Which of these organs is not considered an accessory digestive structure?

1. mouth
2. salivary glands
3. pancreas
4. liver

9.

Which of the following organs is supported by a layer of adventitia rather than serosa?

1. esophagus
2. stomach
3. small intestine
4. large intestine

10.

Which of the following membranes covers the stomach?

1. falciform ligament
2. mesocolon
3. parietal peritoneum
4. visceral peritoneum

11.

Which of these processes occurs in the mouth?

1. ingestion
2. mechanical digestion
3. chemical digestion
4. all of the above

12.

Which of these processes occurs throughout most of the alimentary canal?

1. ingestion
2. propulsion
3. segmentation
4. absorption

13.

Which of the following stimuli activates sensors in the walls of digestive organs?

1. breakdown products of digestion
2. distension
3. pH of chyme
4. all of the above

14.

Which of these statements about reflexes in the GI tract is false?

1. Short reflexes are provoked by nerves near the GI tract.
2. Short reflexes are mediated by the enteric nervous system.
3. Food that distends the stomach initiates long reflexes.
4. Long reflexes can be provoked by stimuli originating outside the GI tract.

15.

Which of these ingredients in saliva is responsible for activating salivary amylase?

1. mucus
2. phosphate ions
3. chloride ions
4. urea

16.

Which of these statements about the pharynx is true?

1. It extends from the nasal and oral cavities superiorly to the esophagus anteriorly.
2. The oropharynx is continuous superiorly with the nasopharynx.
3. The nasopharynx is involved in digestion.
4. The laryngopharynx is composed partially of cartilage.

17.

Which structure is located where the esophagus penetrates the diaphragm?

1. esophageal hiatus
2. cardiac orifice
3. upper esophageal sphincter
4. lower esophageal sphincter

18.

Which phase of deglutition involves contraction of the longitudinal muscle layer of the muscularis?

1. voluntary phase
2. buccal phase
3. pharyngeal phase
4. esophageal phase

19.

Which of these cells secrete hormones?

1. parietal cells
2. mucous neck cells
3. enteroendocrine cells
4. chief cells

20.

Where does the majority of chemical digestion in the stomach occur?

1. fundus and body
2. cardia and fundus
3. body and pylorus
4. body

21.

During gastric emptying, chyme is released into the duodenum through the _____.

1. esophageal hiatus
2. pyloric antrum
3. pyloric canal
4. pyloric sphincter

22.

Parietal cells secrete _____.

1. gastrin
2. hydrochloric acid

3. pepsin
4. pepsinogen

23.

In which part of the alimentary canal does most digestion occur?

1. stomach
2. proximal small intestine
3. distal small intestine
4. ascending colon

24.

Which of these is most associated with villi?

1. haustra
2. lacteals
3. bacterial flora
4. intestinal glands

25.

What is the role of the small intestine’s MALT?

1. secreting mucus
2. buffering acidic chyme
3. activating pepsin
4. preventing bacteria from entering the bloodstream

26.

Which part of the large intestine attaches to the appendix?

1. cecum
2. ascending colon
3. transverse colon
4. descending colon

27.

Which of these statements about bile is true?

1. About 500 mL is secreted daily.
2. Its main function is the denaturation of proteins.
3. It is synthesized in the gallbladder.
4. Bile salts are recycled.

28.

Pancreatic juice _____.

1. deactivates bile.
2. is secreted by pancreatic islet cells.
3. buffers chyme.
4. is released into the cystic duct.

29.

Where does the chemical digestion of starch begin?

1. mouth
2. esophagus
3. stomach
4. small intestine

30.

Which of these is involved in the chemical digestion of protein?

1. pancreatic amylase
2. trypsin
3. sucrase
4. pancreatic nuclease

31.

Where are most fat-digesting enzymes produced?

1. small intestine
2. gallbladder
3. liver
4. pancreas

32.

Which of these nutrients is absorbed mainly in the duodenum?

1. glucose
2. iron
3. sodium
4. water

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CHAPTER OVERVIEW

17: The Urinary System

17.1: Introduction to the Urinary System
17.2: Overview of the Kidney
17.3: Microscopic Anatomy of the Kidney
17.4: Urine Formation and Glomerular Filtration Rate (GFR)
17.5: Tubular Reabsorption and Secretion
17.6: Endocrine Regulation of Kidney Function
17.7: Review Questions

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17.1: Introduction to the Urinary System

Chapter Learning Objectives

- Name the organs of the urinary system
- Explain the major function(s) of each organ of the urinary system
- Describe the macroscopic and microscopic structures of the kidney
- Trace the flow of blood and urine through the kidney
- Trace the flow of urine through the urinary tract

The Urinary or Renal System consists of two kidneys and the pathway, two ureters, urinary bladder, and one urethra, for urine to exit the body. The kidneys' primary function is to make urine by first filtering out many of the electrolytes, solutes, and water in the blood, forming the filtrate. As the filtrate passes through microscopic units called **nephrons**, certain solutes and water molecules are reabsorbed back to the blood because they are too precious to waste and other molecules are secreted because the body does not need them. As the filtrate moves through the nephrons, it becomes more concentrated as water will be reabsorbed from it and returned to the blood. As the filtrate reaches the end of the nephrons, it has now become urine, which will leave the body as waste. Another perspective on the function of the kidneys is to monitor the level of certain solutes in the blood to maintain homeostasis. The kidneys' secondary function is to make hormones such erythropoietin, discussed in the chapter on the endocrine system.

The two ureters will carry urine from the kidneys down to the urinary bladder by peristalsis for storage. As the urinary bladder fills with urine, nerve endings will detect the stretched bladder to signal emptying. With sphincters relaxing, urine will flow out of the urinary bladder through the urethra to be expelled.

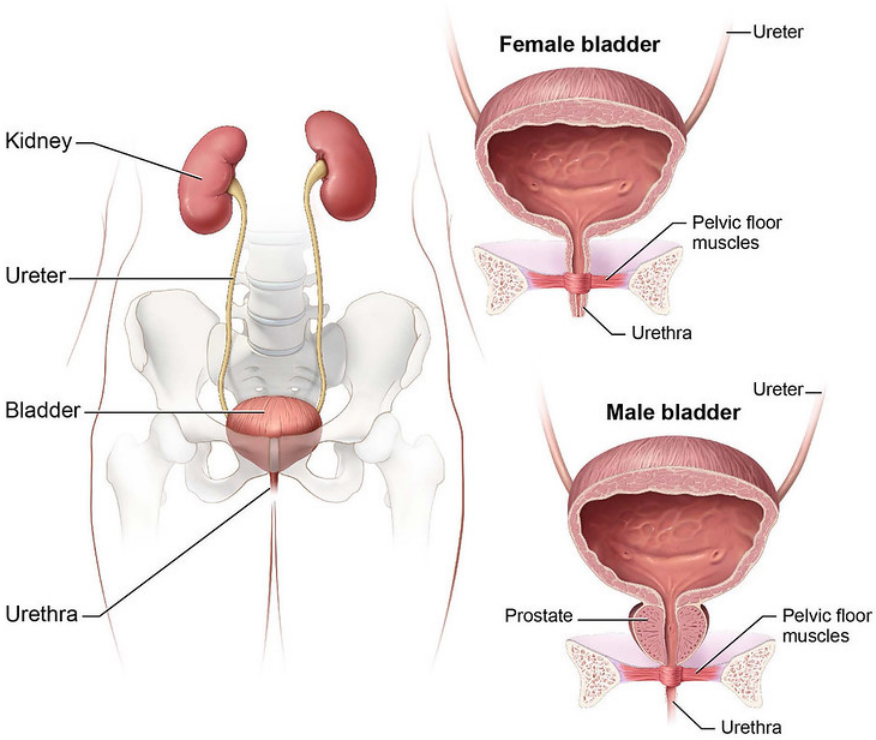


Figure 22.1.1: Organs of the Urinary System. The male and female human urinary system, including kidneys, bladder, ureter and urethra, pelvic floor muscles and the prostate. *(Image credit: "Organs of the Urinary System" by NIH Medial Arts is licensed under CC-BY-NC 2.0.)*

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17.2: Overview of the Kidney

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

- Describe the external structure and the locations of the kidney
- Identify the major internal divisions and structures of the kidney
- Name the regions in a nephron

The kidneys lie laterally to the spine in the retroperitoneal space between the parietal peritoneum and the posterior abdominal wall, well protected by muscle, fat, and ribs. Each kidney weighs about 125–175 g in males and 115–155 g in females. They are about 11–14 cm in length, 6 cm wide, and 4 cm thick. This makes them roughly the size of your fist, with the male kidney typically a bit larger than the female kidney. The kidneys are well vascularized, receiving about 25 percent of the cardiac output at rest.

External Anatomy

The left kidney is located at about the level of the T12 to L3 vertebrae, whereas the right is slightly lower due to slight displacement by the liver. Superior portions of the kidneys are somewhat protected by the eleventh and twelfth ribs (Figure 17.2.1). They are directly covered by a **fibrous capsule,** composed of dense irregular connective tissue that helps to hold their shape, and are surrounded by a shock-absorbing layer of adipose tissue called the **renal fat pad.** This adipose tissues is, in turn, encompassed by a tough **renal fascia**. The fascia and, to a lesser extent, the overlying peritoneum serve to firmly anchor the kidneys to the posterior abdominal wall.

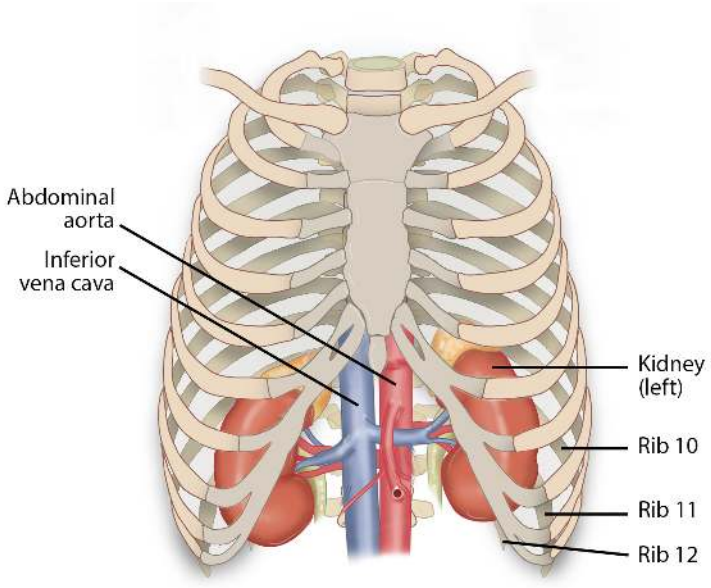


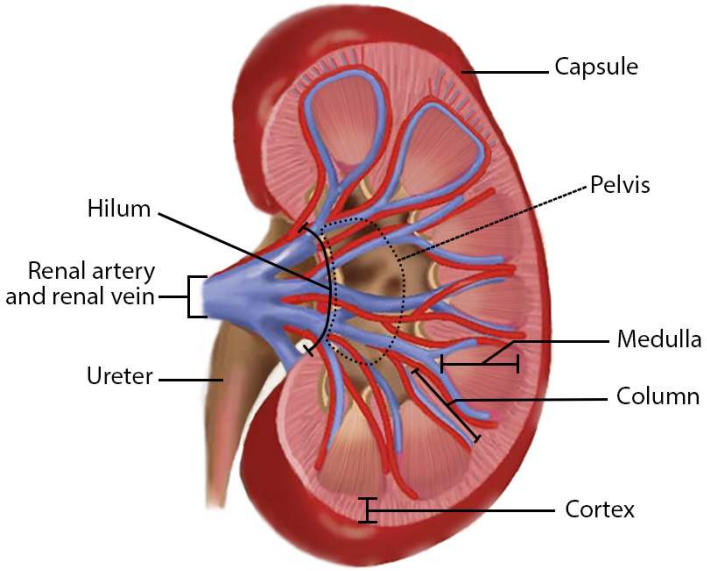
Figure 17.2.1: Kidney Position. The kidneys are located deep to the floating ribs, which provide protection for the kidneys. *(Image credit: "Kidney Position Relative to the Thoracic Cage" by Jennifer Lange is licensed under CC BY-NC-SA 4.0; modification of "Slagter - Drawing and Chest X-ray of the ribs and clavicula - no labels" by Ron Slagter, and "Slagter - Drawing Anatomy of the kidney, adrenal glands and bladder - no labels" by Ron Slagter.)*

Internal Anatomy

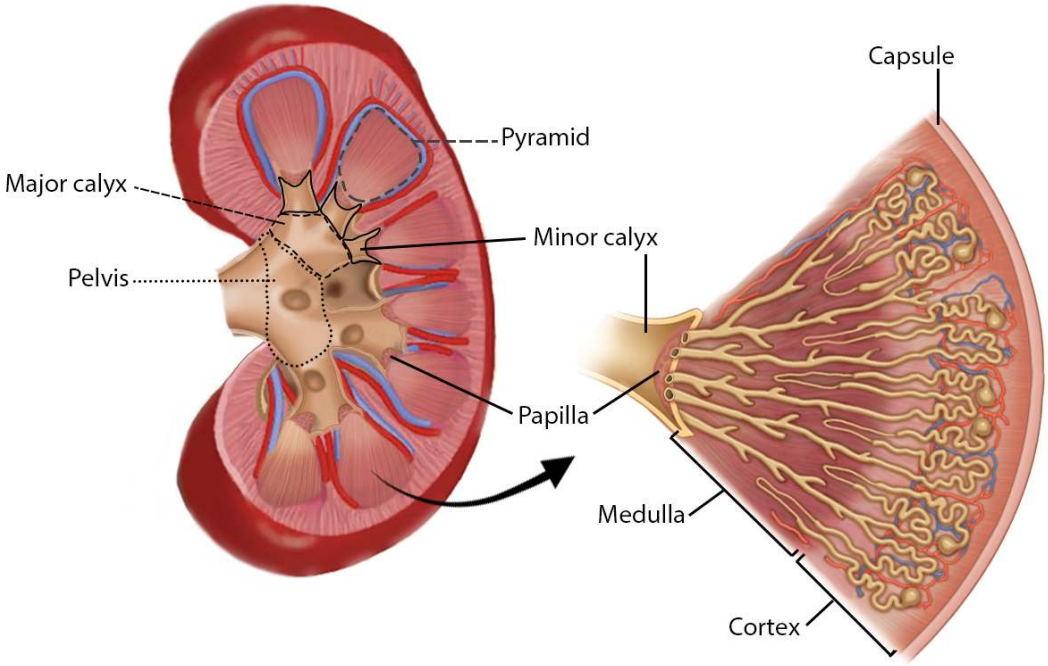
A frontal section through the kidney reveals a thin outer region called the **renal cortex** and an inner region called the **medulla** (Figure 17.2.2*A*). The **renal columns** are connective tissue extensions that pass through the medulla to separate the most characteristic features of the medulla: the **renal pyramids**. Each of the 8-18 lobes within the human kidney contain a pyramid and the cortex immediately superficial to it, and these can be delineated by following the column radiations to the surface of the kidney. The renal columns also provide a supportive framework for vessels that enter and exit the cortex.

Each renal lobe contains microscopic tubules, called **nephrons**, that filter the blood and produce urine. This urine is gathered by **collecting ducts** passing from the cortex, through the pyramid and terminating in the renal papilla. The **renal papilla** is the apex of the pyramid, located at the boundary between the renal medulla and the minor calyx of the renal collecting system (Figure 17.2.2*B*).

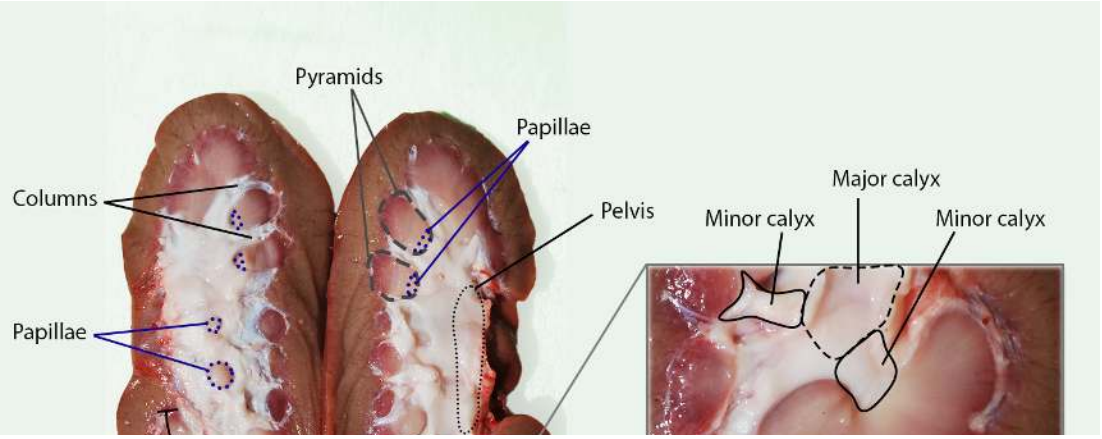
A **minor calyx** surrounds the renal papilla of each pyramid and collects urine from that pyramid. Several minor calyces converge to form a major calyx and the **major calyces** merge to form the **renal pelvis**. The smooth muscle in the renal pelvis funnels urine via peristalsis out of the kidney and into the ureter.

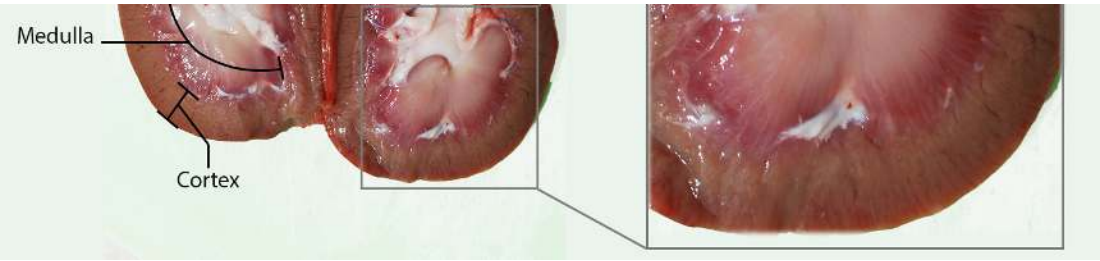


A. Major regions of the kidney



B. Urine collecting structures from each renal lobe





C. Dissected Pig Kidney

Figure 17.2.2: Kidney Sections. These sectional images reveals the outer cortex and inner medulla of the kidney. Located at the hilum are the renal artery, renal vein, and ureter. Urine produced within a single pyramid drains into a minor calyx. Multiple minor calyxes merge to form a major calyx and the multiple major calyces merge to form the renal pelvis. *(Image credits: A. "Kidney Regions and Major Structures" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original "Slagter - Drawing Anatomy of the urinary system - no labels" by Ron Slagter. B. "Urine Collecting Structures" by Jennifer Lange is -licensed under CC BY-NC-SA 4.0, modification of originals "Slagter - Drawing Anatomy of the urinary system - no labels" by Ron Slagter and "KnowledgeWorks - Drawing Kidney anatomy and detail - English labels" by KnowledgeWorks Global Ltd.. C. "Dissected Pig Kidney" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of photo by John Campbell.)*

Blood Vessels

The renal artery enters the kidney medially, first divides into **segmental arteries** moving toward the medulla, followed by further branching to form **interlobar arteries** that pass through the renal columns to reach the cortex (Figure 17.2.3). The interlobar arteries, in turn, branch into **arcuate arteries** lying between the renal cortex and renal medulla. Arcuate arteries will branch further to form **interlobular** or **cortical radiate arteries** that extends into the cortex, and then branch into **afferent arterioles**. Afferent arterioles lead blood to the beginning of the nephron.

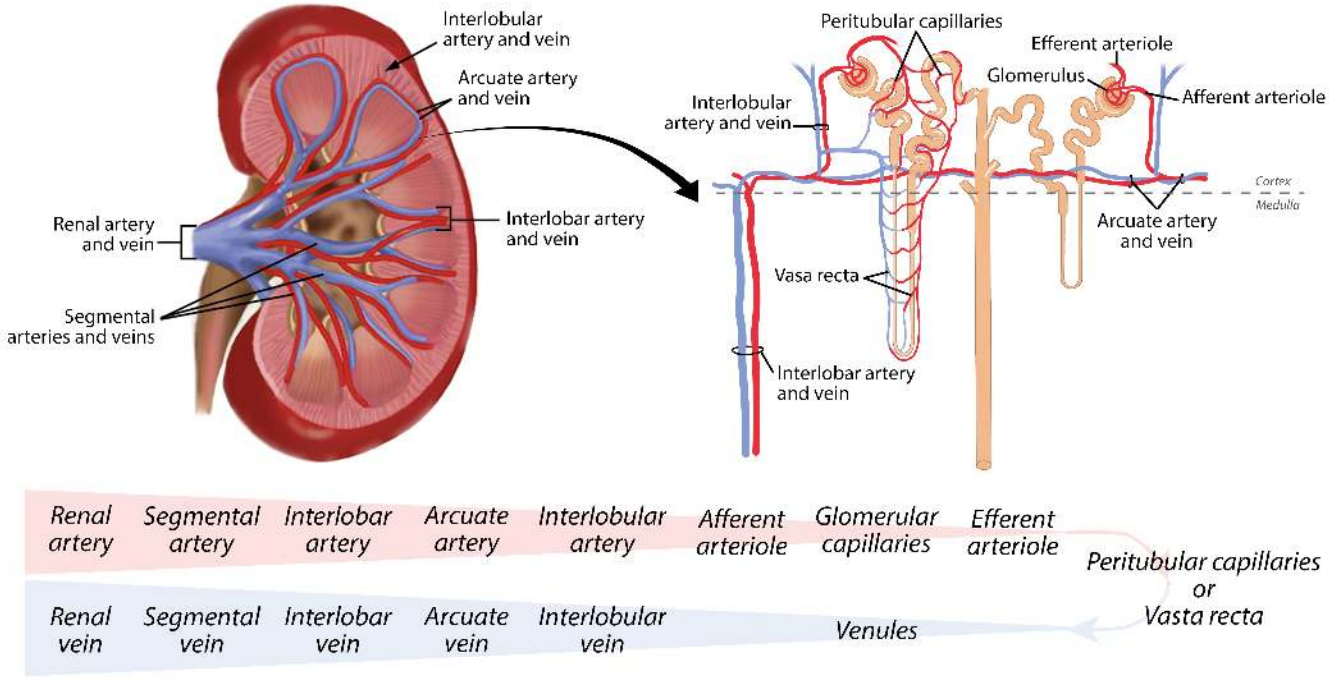


Figure 17.2.3: Blood Flow in the Kidney. Oxygenated blood with waste materials enters the kidney through the renal artery and deoxygenated blood with fewer waste materials exits the kidney in the renal vein. Renal circulation is unique because it will pass through two arterioles and two capillary beds before entering the venous system. *(Image credit: "Renal Vasculature" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of originals "Slagter - Drawing Anatomy of the urinary system - no labels" by Ron Slagter and "Slagter - Drawing Kidney macroscopic and microscopic anatomy - no labels" by Ron Slagter.)*

Nephrons are the "functional units" of the kidney; they cleanse the blood and balance its plasma constituents. The afferent arterioles have higher blood pressure than typical arterioles, and thus have more muscle tissue in their walls. Each afferent arteriole leads to a tuft of fenestrated capillaries about 200 µm in diameter, called the **glomerulus** (Figure 17.2.3). At their distal end the glomerular capillaries form a second arteriole, the **efferent arteriole** that will next form another capillary network around the more distal portions of the nephron tubule, the **peritubular capillaries** (in the cortex) and **vasa recta** (in the medulla). As the glomerular

filtrate progresses through the nephron, these capillary networks recover most of the solutes and water and return them to the circulation. Blood from the second capillary beds then empty into venules. These merge to form **interlobular veins**, then **arcuate veins, interlobar veins,** and **segmental veins,** which finally merge to become the **renal vein**. (Figure 17.2.3).

Nephrons

Nephrons are microscopic structures to make urine, thus they are the "functional" units in the kidneys. Each kidney has over 1 million nephrons. Figure 17.2.4 and Figure 17.2.5 show two nephrons and the blood vessels running around them. Each nephron starts in the cortex with the **renal corpuscle**, which has the glomerular capsule surrounding the glomerulus (capillary bed). The glomerular capsule continues as the **proximal convoluted tubule (PCT)** which then straightens out and enters the renal medulla as the **descending limb of the nephron loop.** At various depths within the medulla the nephron loops make a U-turn to become the **ascending limb**. The nephron loop is also called the loop of Henle. The loop will enter the cortex and become the **distal convoluted tubule (DCT)**, the end of the nephron. The content inside, soon to be urine, will continue from the DCT to a collecting duct.

In a dissected kidney identifying the cortex and medulla is easy, as they have different colors and patterns (Figure 17.2.2*C*). Different parts of the nephrons are found in the two regions. All of the renal corpuscles as well as both the proximal convoluted tubules (PCTs) and distal convoluted tubules are found in the cortex. Some nephrons have a short nephron loop that does not dip much beyond the cortex. These nephrons are called **cortical nephrons**. About 15 percent of nephrons have long nephron loops that extend deep into the medulla and are called **juxtamedullary nephrons**. Figure 17.2.4 shows two types of nephrons, cortical and juxtamedullary nephrons, named according to their locations. Details of nephron structure will be discussed in the next section, Section 22.3.

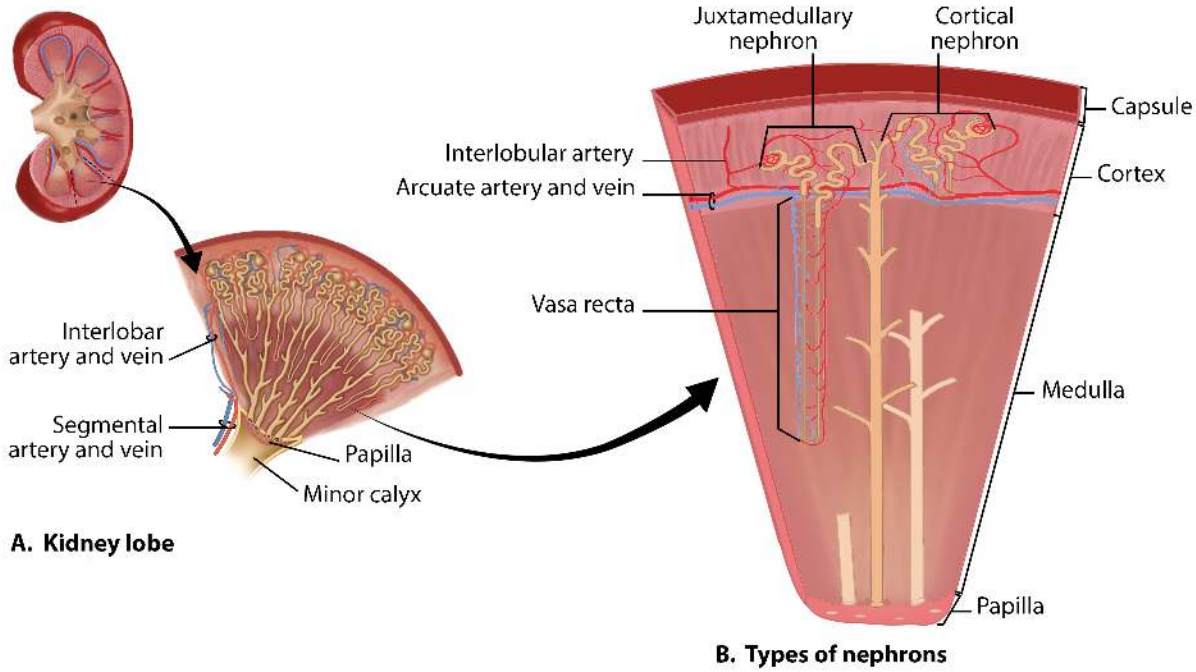


Figure 17.2.4: Renal Lobe and Nephron Types. Each minor calyx receives urine produced within the nephron of a single renal lobe. Within each lobe are thousands of nephrons with varying positions across the cortex and medulla. *(Image credit: "Renal Lobe and Nephron Types" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of originals A. "Slagter - Drawing Anatomy of the urinary system - no labels" by Ron Slagter and "KnowledgeWorks - Drawing Kidney anatomy and detail - English labels" by KnowledgeWorks Global Ltd.; B. "Slagter - Drawing Kidney macroscopic and microscopic anatomy - no labels" by Ron Slagter.)*

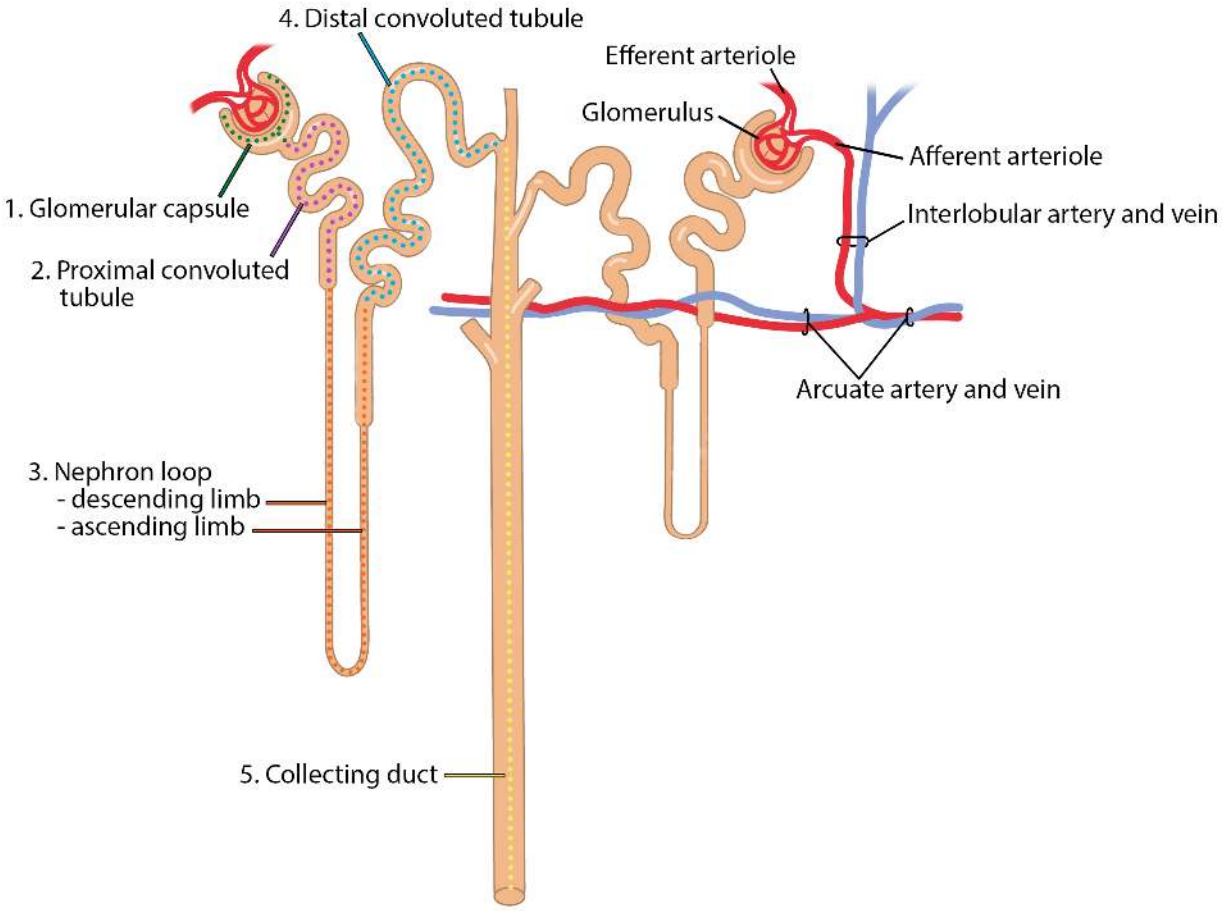


Figure 17.2.5: Nephron Structure. Blood in the glomerular capillaries is filtered into the glomerular capsule. This filtrate is modified as it flows through the nephron regions (in order - proximal convoluted tubule, nephron loop, distal convoluted tubule) and the collecting duct. *(Image credit: "Nephron Structure" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original "Slagter - Drawing Kidney macroscopic and microscopic anatomy - no labels" by Ron Slagter.)*

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17.3: Microscopic Anatomy of the Kidney

Learning Objectives

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

- Distinguish the histological differences between the renal cortex and medulla
- Describe the structure of the filtration membrane
- Identify the major structures and subdivisions of the renal corpuscles, renal tubules, and renal capillaries
- Discuss the function of the peritubular capillaries and vasa recta
- Identify the location of the juxtaglomerular apparatus and describe the cells that line it
- Describe the histology of the proximal convoluted tubule, loop of Henle, distal convoluted tubule, and collecting ducts

The renal structures that conduct the essential work of the kidney cannot be seen by the naked eye. Only a light or electron microscope can reveal these structures. Even then, serial sections and computer reconstruction are necessary to give us a comprehensive view of the functional anatomy of the nephron and its associated blood vessels.

Nephrons: The Functional Unit

Nephrons take a simple filtrate of the blood and modify it into urine. Many changes take place in the different parts of the nephron before urine is created for disposal. The term forming urine will be used hereafter to describe the filtrate as it is modified into true urine. The principle task of the nephron population is to balance the plasma to homeostatic set points and excrete potential toxins in the urine. They do this by accomplishing three principle functions—**filtration**, **reabsorption**, and **secretion**. They also have additional secondary functions that exert control in three areas: blood pressure (via production of **renin**), red blood cell production (via the hormone EPO), and calcium absorption (via conversion of calcidiol into calcitriol, the active form of vitamin D).

Different parts of the nephron are found in different regions. The renal cortex is easily distinguished from the renal medulla by the presence of renal corpuscles. These easily visualized balls contain the glomerular capillaries and the glomerular capsule. Around the corpuscles, the arrangement of the tubules in the cortex appears to be random. That is because the convoluted tubules twist, turn, and wrap around themselves and the renal corpuscles. Filtrate leaves the glomerular capillaries and enters the capsular space and then flows into the proximal convoluted tubule.

- **Proximal convoluted tubules** (PCT) are the larger tubules in the region composed of simple cuboidal epithelium. The cells of the PCT are larger and have abundant microvilli making up a brush border.
- The **distal convoluted tubule** is also composed of simple cuboidal epithelium. It has a smaller diameter and smaller cells than the PCT and the cells have few microvilli.

The renal medulla lacks renal corpuscles, so visually it only contains long tubules that run mostly parallel to each other. The two regions of the tubule found here both have two types of epithelial tissue in their walls.

- The **nephron loop** is a part of the nephron that has thin and thick limbs. The thin descending nephron loop and the thin ascending nephron loop will be made up of simple squamous epithelium. The thick ascending nephron loop is made of simple cuboidal epithelium that lacks a brush border. The nephron loop is also called the loop of Henle.
- The **collecting duct** (technically not part of the nephron - see below) starts as a simple cuboidal epithelium and transitions to become a simple columnar epithelium as it nears the renal papilla.

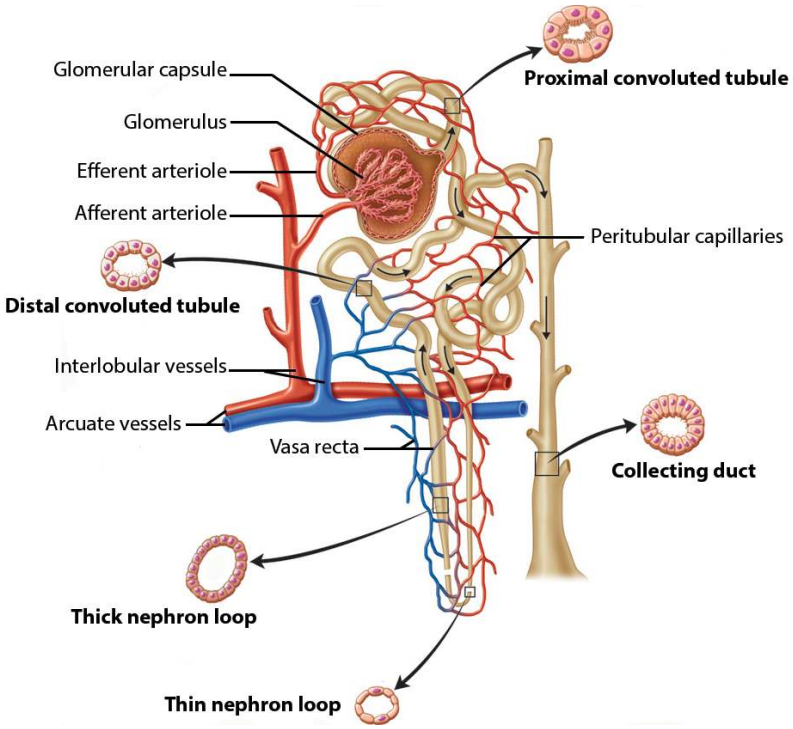


Figure \(\PageIndex{1}\): The Nephron. Nephrons have specialized regions for filtering the blood and then modifying that filtrate into urine. Along the nephron, each region has a slightly different epithelium that reflects the functional role of that region. *(Image credit: "Nephron Structure with Histology Illustration" by Jennifer Lange is licensed under CC BY-SA-NC 4.0, modification of original by Cenveo.)*

Renal Corpuscle

As discussed earlier, the renal corpuscle consists of a tuft of capillaries called the glomerulus that is largely surrounded by the **glomerular capsule** (Bowman's capsule). The **glomerulus** is a high-pressure capillary bed between **afferent** and **efferent arterioles**. The glomerular capsule surrounds the glomerulus to form a lumen, and captures and directs this filtrate to the **proximal convoluted tubule** (PCT). The outermost part of the glomerular capsule, the parietal layer, is a simple squamous epithelium. It transitions onto the glomerular capillaries to form the visceral layer of the capsule. Here, the cells are not squamous, but uniquely shaped cells (**podocytes**) extending finger-like arms (**pedicels**) to cover the glomerular capillaries (Figure 17.3.2). These projections interdigitate to form **filtration slits**, leaving small gaps between the digits to form a sieve. As blood passes through the glomerulus, 10 to 20 percent of the plasma filters between these sieve-like fingers to be captured by the glomerular capsule and funneled to the PCT. The pedicels of the podocytes form a mesh like slit over the basement membrane. The fenestrated capillaries within the glomerulus, the basement membrane and the pedicels of the podocytes create the **filtration membrane** that surrounds the glomerulus. This filtration membrane is size selective, allowing only small molecules to pass through such as water and ions, while larger molecules such as proteins and cells remain in the blood.

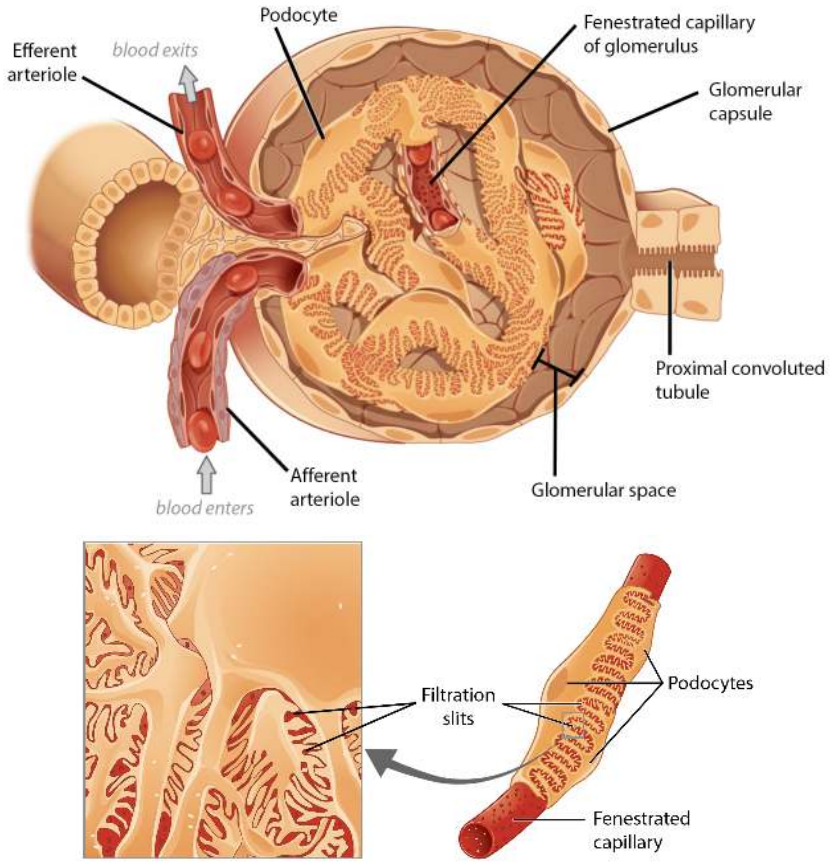


Figure \(\PageIndex{2}\): Filtration Membrane. Filtration of the blood occurs across the filtration membrane, consisting of the fenestrated capillaries and the filtration slits between the podocytes (the visceral layer of the glomerular capsule). Substances can diffuse from the blood into the nephron based on size and electrical charge. *(Image credit: "Filtration Membrane" by Jennifer Lange is licensed under CC BY-SA-NC 4.0, modification of originals Podocytes and Juxtaglomerular Apparatus and Glomerulus by OpenStax.)*

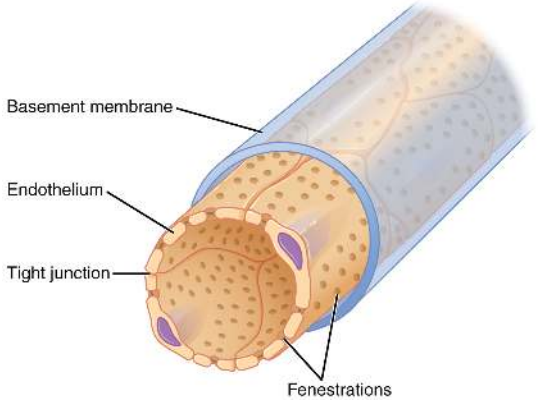


Figure 17.3.3: Fenestrated Capillary Fenestrations allow many substances to diffuse from the blood based primarily on size.

An additional factor affecting the ability of substances to cross this barrier is their electric charge. The proteins associated with these pores are negatively charged, so they tend to repel negatively charged substances and allow positively charged substances to pass more readily. The basement membrane prevents filtration of medium-to-large proteins such as globulins. Overall, filtration is regulated by fenestrations in capillary endothelial cells, podocytes with filtration slits, membrane charge, and the basement

membrane between capillary cells. The result is the creation of a filtrate that does not contain cells or large proteins, and has a slight predominance of positively charged substances.

Lying just outside the glomerular capsule and the glomerulus is the **juxtaglomerular apparatus** (JGA) (Figure 17.3.4). At the juncture where the afferent and efferent arterioles enter and leave Bowman's capsule, the initial part of the **distal convoluted tubule** (DCT) comes into direct contact with the arterioles. The wall of the DCT at that point forms a part of the JGA known as the **macula densa**. This cluster of cuboidal epithelial cells monitors the fluid composition of fluid flowing through the DCT. In response to the concentration of Na^+ in the fluid flowing past them, these cells release signals that alter filtration at the glomerulus.

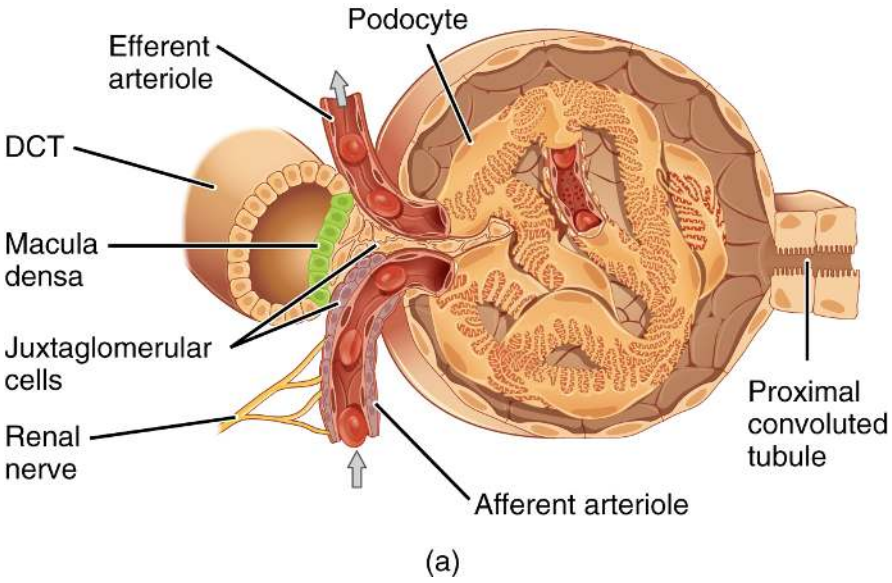


Figure 17.3.4: Juxtaglomerular Apparatus and Glomerulus (a) The JGA allows specialized cells to monitor the composition of the fluid in the DCT and adjust the glomerular filtration rate. (b) This micrograph shows the glomerulus and surrounding structures. LM × 1540. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

A second cell type in this apparatus is the **juxtaglomerular cell**. This is a modified, smooth muscle cell lining the afferent arteriole that can contract or relax in response to ATP or adenosine released by the macula densa. Such contraction and relaxation regulate blood flow to the glomerulus. If the osmolarity (**the concentration of solutes**) of the filtrate is too high (hyperosmotic), the juxtaglomerular cells will contract, decreasing the **glomerular filtration rate** (GFR) so less plasma is filtered, leading to less urine formation and greater retention of fluid. This will ultimately decrease blood osmolarity toward the normal set point. If the osmolarity of the filtrate is too low, the juxtaglomerular cells will relax, increasing the GFR and enhancing the loss of water to the urine, causing blood osmolarity to rise. In other words, when the concentration of solutes in the blood goes up, filtration and urine formation decrease and water is retained. When the concentration of solutes in the blood goes down, filtration and urine formation increase and water is lost by way of the urine. The net result of these opposing actions is to keep the rate of filtration relatively constant. A second function of the macula densa cells is to regulate renin release from the juxtaglomerular cells of the afferent arteriole (Figure 17.3.5). Renin sets off a cascading series of events that affect blood pressure and water reabsorption. The function of the renin-angiotensin-aldosterone mechanism is discussed in greater detail later in this chapter

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17.4: Urine Formation and Glomerular Filtration Rate (GFR)

Learning Objectives

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

- Describe glomerular filtration rate (GFR), state the average value of GFR, and explain how clearance rate can be used to measure GFR
- List common symptoms of kidney failure
- Describe the myogenic and tubuloglomerular feedback mechanisms and explain how they affect urine volume and composition
- Describe the function of the juxtaglomerular apparatus

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

Failure of the renal anatomy and/or physiology can lead suddenly or gradually to renal failure. In this event, a number of symptoms, signs, or laboratory findings point to the diagnosis.

The following is a brief list of the symptoms of kidney failure:

- weakness
- lethargy
- shortness of breath
- widespread edema (swelling due to fluid retention)
- metabolic acidosis or alkalosis
- heart arrhythmias
- loss of appetite
- uremia (high levels of urea, a metabolic waste, in the blood)
- fatigue
- excessive or too little urination

Glomerular Filtration Rate (GFR)

The volume of filtrate formed by both kidneys per minute is termed the **glomerular filtration rate** (**GFR**). The heart pumps about 5 L blood per min under resting conditions. Approximately 20 percent or one liter enters the kidneys to be filtered. On average, this liter results in the production of about 125 mL/min filtrate produced in males (range of 90 to 140 mL/min) and 105 mL/min filtrate produced in females (range of 80 to 125 mL/min). This amount equates to a volume of about 180 L/day in males and 150 L/day in females. Ninety-nine percent of this filtrate is returned to the circulation by reabsorption so that only about 1–2 liters of urine are produced per day (Table 17.4.2).

Table 17.4.2: Calculating Urine Formation per Day

	Flow per minute (mL)	Calculation
Renal blood flow	1050	Cardiac output is about 5000 mL/minute, of which 21 percent flows through the kidney. 5000*0.21 = 1050 mL blood/min
Renal plasma flow	578	Renal plasma flow equals the blood flow per minute times the hematocrit. If a person has a hematocrit of 45, then the renal plasma flow is 55 percent. 1050*0.55 = 578 mL plasma/min

	Flow per minute (mL)	Calculation
Glomerular filtration rate	110	The GFR is the amount of plasma entering Bowman's capsule per minute. It is the renal plasma flow times the fraction that enters the renal capsule (19 percent). 578*0.19 = 110 mL filtrate/min
Urine	1296 ml/day	The filtrate not recovered by the kidney is the urine that will be eliminated. It is the GFR times the fraction of the filtrate that is not reabsorbed (0.8 percent). 110*.008 = 0.9 mL urine /min Multiply urine/min times 60 minutes times 24 hours to get daily urine production. 0.9*60*24 = 1296 mL/day urine

It is vital that the flow of blood through the kidney be at a suitable rate to allow for filtration. This rate determines how much solute is retained or discarded, how much water is retained or discarded, and ultimately, the osmolarity of blood and the blood pressure of the body.

Regulation of Glomerular Filtration Rate

GFR needs to be maintained at a constant level as too much or too little filtration can have negative effects on the body. Too much filtration may result in excessive fluid loss, while too little filtration may result in wastes building up in the blood. The following describes the variety of ways the body regulates the GFR.

Sympathetic Nerves

The kidneys are innervated by the sympathetic neurons of the autonomic nervous system via the celiac plexus and splanchnic nerves. Reduction of sympathetic stimulation results in vasodilation and increased blood flow through the kidneys during resting conditions. When the frequency of sympathetic stimulation increases, the smooth muscles surrounding the afferent arteriole constricts (vasoconstriction), resulting in diminished blood flow into the glomerulus, so less filtration occurs. Under conditions of stress, sympathetic nervous activity increases, resulting in the direct vasoconstriction of afferent arterioles (norepinephrine effect) as well as stimulation of the adrenal medulla. The adrenal medulla, in turn, produces a generalized vasoconstriction through the release of epinephrine. This includes vasoconstriction of the afferent arterioles, further reducing the volume of blood flowing through the kidneys. This process redirects blood to other organs with more immediate needs. If blood pressure falls, the sympathetic nerves will also stimulate the release of renin, an enzyme that leads to the increase of blood pressure.

Autoregulation

The kidneys are very effective at regulating the rate of blood flow over a wide range of blood pressures. Your blood pressure will decrease when you are relaxed or sleeping. It will increase when exercising. Yet, despite these changes, the filtration rate through the kidney will change very little. This is due to two internal autoregulatory mechanisms that operate without outside influence: the **myogenic mechanism** and the **tubuloglomerular feedback mechanism.**

Arteriole Myogenic Mechanism

The myogenic mechanism regulating blood flow within the kidney depends upon a characteristic shared by most smooth muscle cells of the body. When you stretch a smooth muscle cell, it contracts; when you stop, it relaxes, restoring its resting length. This mechanism works in the afferent arteriole that supplies the glomerulus. GFR must be maintained at a constant rate, it must not be too high or too low. If GFR went up every time your blood pressure went up, excessive filtrate would be produced. The myogenic mechanism acts to counteract this. When blood pressure increases, smooth muscle cells in the wall of the arteriole are stretched and

respond by contracting which constricts the blood vessels. This reduces blood flow into the glomerulus. By reducing blood flow into the glomerulus, GFR can be maintained at a constant rate, rather than it increasing due to an increase in systemic blood pressure. When blood pressure drops after an increase, the same smooth muscle cells relax, allowing the afferent arteriole to dilate, allowing a continued even flow of blood.

Tubuloglomerular Feedback

The tubuloglomerular feedback mechanism involves the JGA and a signaling mechanism between its components. Recall that the JGA is made up of the juxtaglomerular cells, the macula densa and the afferent arteriole as seen in Figure 17.4.1. This mechanism stimulates either constriction or dilation of the afferent arteriole (Table 17.4.1. Recall that the distal convoluted tubule (DCT) is in intimate contact with the afferent and efferent arterioles of the glomerulus. Specialized macula densa cells in this segment of the tubule respond to changes in the fluid flow rate and Na^+ concentration. As GFR increases, there is less time for NaCl to be reabsorbed (returned to the blood) in the proximal convoluted tubule (PCT), resulting in higher osmolarity in the filtrate. This increased solute concentration of the forming urine, and the greater flow rate within the DCT, activates macula densa cells to respond by releasing signaling molecules. These signaling molecules stimulate the afferent arteriole to constrict, slowing blood flow and reducing GFR. Conversely, when GFR decreases, less Na^+ is in the forming urine, and most will be reabsorbed before reaching the macula densa, which will result in decreased signaling molecules, allowing the afferent arteriole to dilate and increase GFR.

Table \(\PageIndex{1}\: Paracrine Mechanisms Controlling Glomerular Filtration Rate

Change in GFR	NaCl Absorption	Effect on GFR
Increased GFR	Tubular NaCl increases	Vasoconstriction slows GFR
Decreased GFR	Tubular NaCl decreases	Vasodilation increases GFR

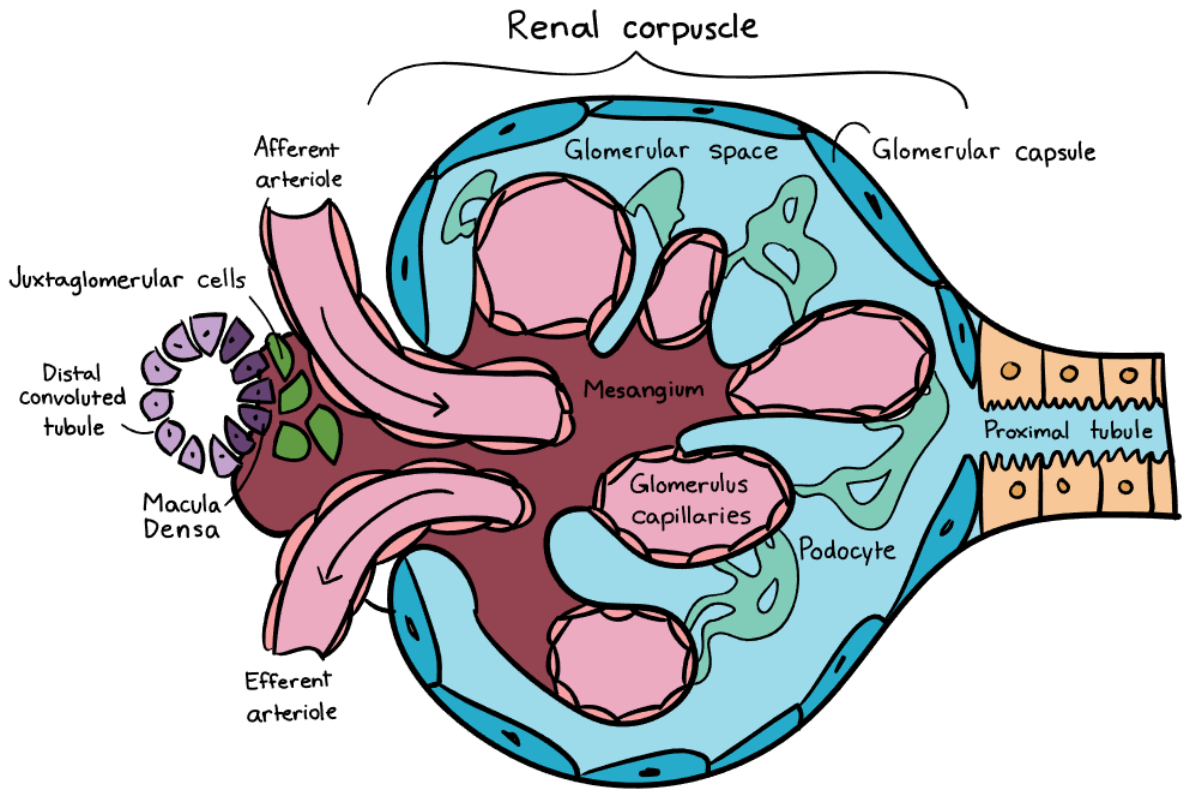


Figure 17.4.1 The juxtaglomerular apparatus: The juxtaglomerular apparatus consists of the juxtaglomerular cells, cells within the distal convoluted tubule called the macula densa, and the afferent arteriole. Concentrations of solutes within the filtrate will be detected by cells of the macula densa which will then signal to the juxtaglomerular cells. This signaling process results either in the constriction of the afferent arteriole and decrease in GFR in the glomerulus or dilation of the afferent arteriole and increase in GFR. *(Image credit: "Renal Corpuscle" by KhanAcademy, licensed under CC BY-NC-SA 3.0 US.* All Khan Academy content is available for free at www.khanacademy.org*)*

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17.5: Tubular Reabsorption and Secretion

Learning Objectives

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

- List specific transport mechanisms occurring in different parts of the nephron, including active transport, osmosis, facilitated diffusion, and passive electrochemical gradients
- Describe how and where water, organic compounds, and ions are reabsorbed in the nephron
- List the locations in the nephron where tubular secretion occurs

With up to 180 liters per day passing through the nephrons of the kidney, it is quite obvious that most of that fluid and its contents must be reabsorbed. That recovery occurs in the PCT, loop of Henle, DCT, and the collecting ducts (Table 17.5.1 and Figure 17.5.1). Various portions of the nephron differ in their capacity to reabsorb water and specific solutes. While much of the reabsorption and secretion occur passively based on concentration gradients, the amount of water that is reabsorbed or lost is tightly regulated. This control is exerted directly by ADH and aldosterone, and indirectly by renin. Most water is recovered in the PCT, loop of Henle, and DCT. About 10 percent (about 18 L) reaches the collecting ducts. The collecting ducts, under the influence of ADH, can recover almost all of the water passing through them, in cases of dehydration, or almost none of the water, in cases of over-hydration.

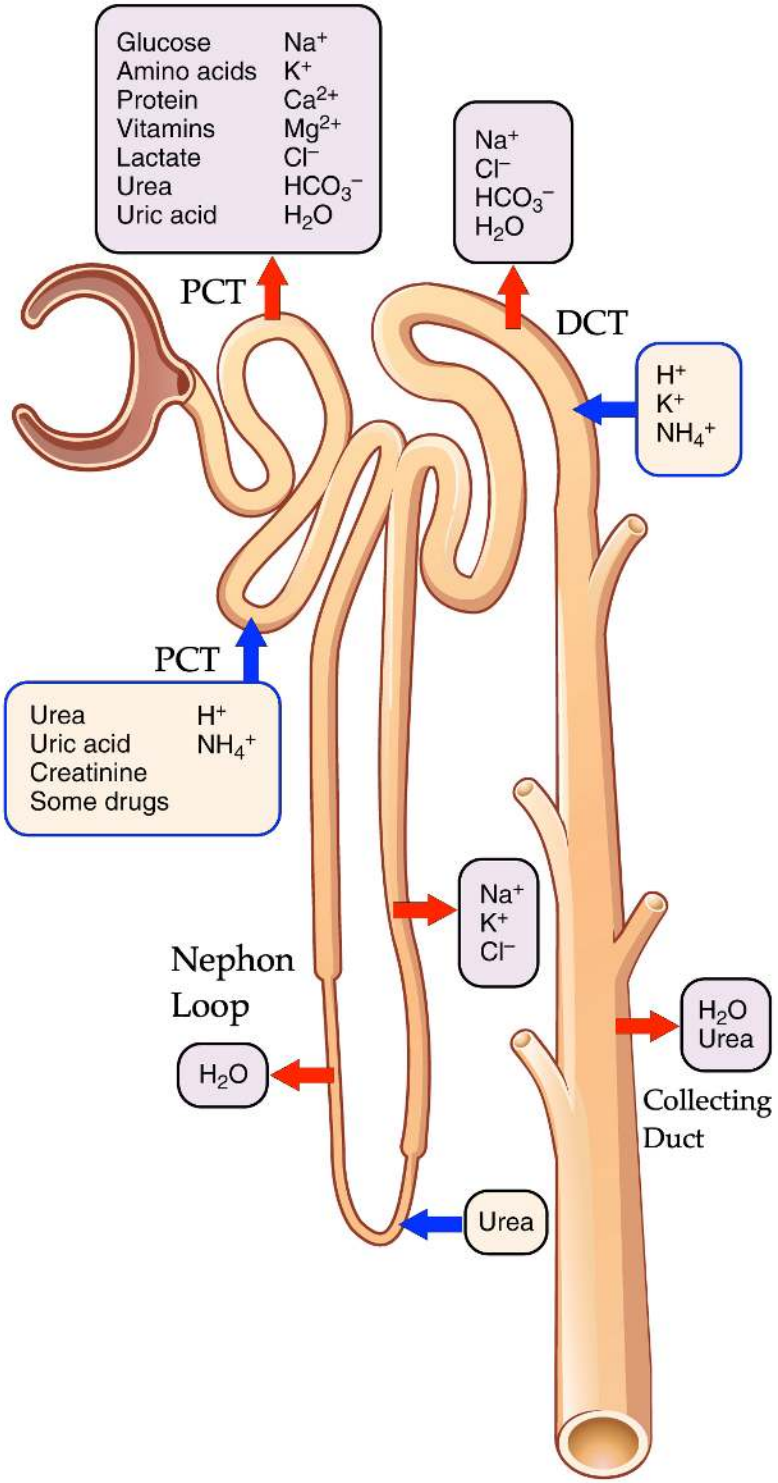


Figure 17.5.1: Locations of Secretion and Reabsorption in the Nephron. Red arrows indicate reabsorption and blue arrows indicate secretion. *(Image credit: "Locations of Secretion and Reabsorption in the Nephron" by OpenStax is licensed under CC BY 4.0) / Modified by Harmony Folse*

Table 17.5.1: Substances Secreted or Reabsorbed in the Nephron and Their Locations

Substance	PCT	Loop of Henle	DCT	Collecting ducts

Substance	PCT	Loop of Henle	DCT	Collecting ducts
Glucose	Almost 100 percent reabsorbed; secondary active transport with Na^+			
Oligopeptides, proteins, amino acids	Almost 100 percent reabsorbed; symport with Na^+			
Vitamins	Reabsorbed			
Lactate	Reabsorbed			
Creatinine	Secreted			
Urea	50 percent reabsorbed by diffusion; also secreted	Secretion, diffusion in descending limb		Reabsorption in medullary collecting ducts; diffusion
Sodium	65 percent actively reabsorbed	25 percent reabsorbed in thick ascending limb; active transport	5 percent reabsorbed; active	5 percent reabsorbed, stimulated by aldosterone; active
Chloride	Reabsorbed, symport with Na^+, diffusion	Reabsorbed in thin and thick ascending limb; diffusion in ascending limb	Reabsorbed; diffusion	Reabsorbed; symport
Water	67 percent reabsorbed osmotically with solutes	15 percent reabsorbed in descending limb; osmosis	8 percent reabsorbed if ADH; osmosis	Variable amounts reabsorbed, controlled by ADH, osmosis
HCO_3^-	80–90 percent symport reabsorption with Na^+	Reabsorbed, symport with Na^+ and antiport with $Cl^–$; in ascending limb		Reabsorbed antiport with $Cl^–$
H^+	Secreted; diffusion		Secreted; active	Secreted; active
NH_4^+	Secreted; diffusion		Secreted; diffusion	Secreted; diffusion
Some drugs	Secreted		Secreted; active	Secreted; active
Potassium	65 percent reabsorbed; diffusion	20 percent reabsorbed in thick ascending limb; symport	Secreted; active	Secretion controlled by aldosterone; active
Calcium	Reabsorbed; diffusion	Reabsorbed in thick ascending limb; diffusion		Reabsorbed if parathyroid hormone present; active
Magnesium	Reabsorbed; diffusion	Reabsorbed in thick ascending limb; diffusion	Reabsorbed	
Phosphate	85 percent reabsorbed, inhibited by parathyroid hormone, diffusion		Reabsorbed; diffusion	

Mechanisms of Recovery

Mechanisms by which substances move across membranes for reabsorption or secretion include active transport, diffusion, facilitated diffusion, and osmosis. These were discussed in an earlier chapter, and you may wish to review them.

Active transport utilizes energy, usually the energy found in a phosphate bond of ATP, to move a substance across a membrane from a low to a high concentration. It is very specific and must have an appropriately shaped receptor for the substance to be transported. An example would be the active transport of Na^+ out of a cell and K^+ into a cell by the Na^+/K^+ pump. Both ions are moved in opposite directions from a lower to a higher concentration.

Simple diffusion moves a substance from a higher to a lower concentration down its concentration gradient. It requires no energy and only needs to be soluble.

Facilitated diffusion is similar to diffusion in that it moves a substance down its concentration gradient. The difference is that it requires specific membrane receptors or channel proteins for movement. The movement of glucose and, in certain situations, Na^+ ions, is an example of facilitated diffusion. In some cases of mediated transport, two different substances share the same channel protein port; these mechanisms are described by the terms symport and antiport.

Most of the Ca^{++}, Na^+, glucose, and amino acids must be reabsorbed by the nephron to maintain homeostatic plasma concentrations. Other substances, such as urea, K^+, ammonia (NH_3), creatinine, and some drugs are secreted into the filtrate as waste products. Acid–base balance is maintained through actions of the lungs and kidneys: The lungs rid the body of H^+, whereas the kidneys secrete or reabsorb H^+ and bicarbonate ion (HCO_3^-) (Table 17.5.2). In the case of urea, about 50 percent is passively reabsorbed by the PCT. More is recovered by in the collecting ducts as needed. ADH induces the insertion of urea transporters and aquaporin channel proteins.

Table 17.5.2: Substances Filtered and Reabsorbed by the Kidney per 24 Hours

Substance	Amount filtered (grams)	Amount reabsorbed (grams)	Amount in urine (grams)
Water	180 L	179 L	1 L
Proteins	10–20	10–20	0
Chlorine	630	625	5
Sodium	540	537	3
Bicarbonate	300	299.7	0.3
Glucose	180	180	0
Urea	53	28	25
Potassium	28	24	4
Uric acid	8.5	7.7	0.8
Creatinine	1.4	0	1.4

Reabsorption and Secretion in the PCT

The renal corpuscle (the glomerulus plus the glomerular capsule) filters the blood to create a filtrate that differs from blood mainly in the absence of cells and large proteins. From this point to the ends of the collecting ducts, the filtrate or forming urine is undergoing modification through secretion and reabsorption before true urine is produced. The first point at which the forming urine is modified is in the PCT. Here, some substances are reabsorbed, whereas others are secreted. Note the use of the term “reabsorbed.” All of these substances were “absorbed” in the digestive tract—99 percent of the water and most of the solutes filtered by the nephron must be reabsorbed. Water and substances that are reabsorbed are returned to the circulation by the peritubular and vasa recta capillaries. It is important to understand the difference between the glomerulus and the peritubular and vasa recta capillaries. The glomerulus has a relatively high pressure inside its capillaries and can sustain this by dilating the afferent arteriole while constricting the efferent arteriole. This assures adequate filtration pressure even as the systemic blood pressure varies. Movement of water into the peritubular capillaries and vasa recta will be influenced primarily by osmolarity and concentration gradients. Sodium is actively pumped out of the PCT into the interstitial spaces between cells and diffuses down its concentration gradient into the peritubular capillary. As it does so, water will follow passively to maintain an isotonic fluid

environment inside the capillary. This is called obligatory water reabsorption, because water is "obliged" to follow the Na^+ (Figure 17.5.2).

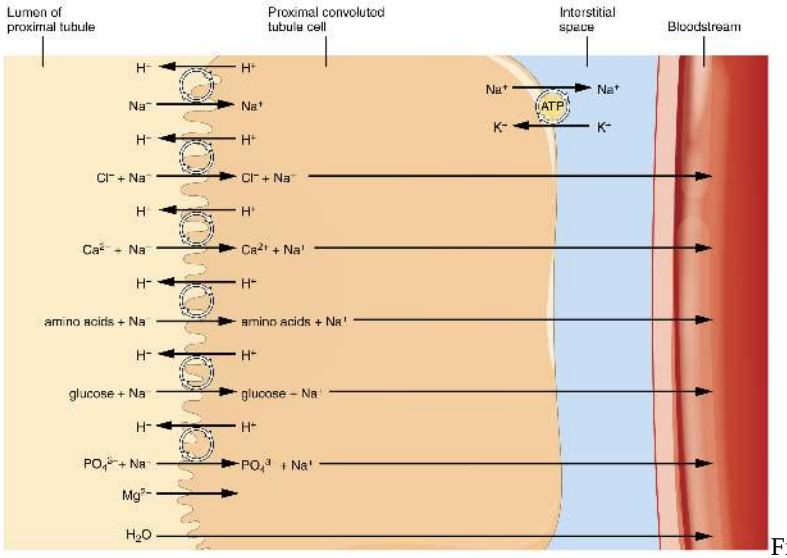


Figure 17.5.2: Substances Reabsorbed and Secreted by the PCT

More substances move across the membranes of the PCT than any other portion of the nephron. Recall that cells have two surfaces: apical and basal. The apical surface is the one facing the lumen or open space of a cavity or tube, in this case, the inside of the PCT. The basal surface of the cell faces the connective tissue base to which the cell attaches (basement membrane) or the cell membrane closer to the basement membrane if there is a stratified layer of cells. In the PCT, there is a single layer of simple cuboidal endothelial cells against the basement membrane.

About 67 percent of the water, Na^+, and K^+ entering the nephron is reabsorbed in the PCT and returned to the circulation. Almost 100 percent of glucose, amino acids, and other organic substances such as vitamins are normally recovered here. Some glucose may appear in the urine if circulating glucose levels are high enough that all the glucose transporters in the PCT are saturated, so that their capacity to move glucose is exceeded (transport maximum, or T_m). In males, the maximum amount of glucose that can be recovered is about 375 mg/min, whereas in females, it is about 300 mg/min. This recovery rate translates to an arterial concentration of about 200 mg/dL. Though an exceptionally high sugar intake might cause sugar to appear briefly in the urine, the appearance of glycosuria usually points to type I or II diabetes mellitus. Fifty percent of $Cl^–$ and variable quantities of Ca^{++}, Mg^{++}, and $HPO_4^{2–}$ are also recovered in the PCT.

Recovery of bicarbonate ($HCO_3^–$) is vital to the maintenance of acid–base balance, since it is a very powerful and fast-acting buffer. An important enzyme is used to catalyze this mechanism: carbonic anhydrase (CA). This same enzyme and reaction is used in red blood cells in the transportation of CO_2, in the stomach to produce hydrochloric acid, and in the pancreas to produce $HCO_3^–$ to buffer acidic chyme from the stomach.

The significant recovery of solutes from the PCT lumen to the interstitial space creates an osmotic gradient that promotes water recovery. As noted before, water moves through channels created by the aquaporin proteins. These proteins are found in all cells in varying amounts and help regulate water movement across membranes and through cells by creating a passageway across the hydrophobic lipid bilayer membrane. Changing the number of aquaporin proteins in membranes of the collecting ducts also helps to regulate the osmolarity of the blood. The movement of many positively charged ions also creates an electrochemical gradient. This charge promotes the movement of negative ions toward the interstitial spaces and the movement of positive ions toward the lumen.

Reabsorption and Secretion in the Loop of Henle

The loop of Henle consists of two sections: descending and ascending sections. Primarily water is reabsorbed at the thin descending limp of the loop and only ions are reabsorbed at the thick ascending limb. The thick ascending limb is completely impermeable to water due to the absence of aquaporin proteins. The descending and ascending portions of the loop are highly specialized to enable recovery of much of the Na^+ and water that were filtered by the glomerulus. As the forming urine moves through the loop, the osmolarity will change from isosmotic with blood (about 278–300 mOsmol/kg) to both a very hypertonic solution of about 1200

mOsmol/kg and a very hypotonic solution of about 100 mOsmol/kg. These changes are accomplished by osmosis in the descending limb and active transport in the ascending limb. Solutes and water recovered from these loops are returned to the circulation by way of the vasa recta.

Reabsorption and Secretion in the Distal Convoluted Tubule

Approximately 80 percent of filtered water has been recovered by the time the dilute forming urine enters the DCT. The DCT will recover another 10–15 percent before the forming urine enters the collecting ducts. Aldosterone affects ion reabsorption in the DCT. The movement of Na^+ out of the lumen of the collecting duct creates a negative charge that promotes the movement of Cl^- out of the lumen into the interstitial space. Peritubular capillaries receive the solutes and water, returning them to the circulation.

Cells of the DCT also recover Ca^{++} from the filtrate. Receptors for parathyroid hormone (PTH) are found in DCT cells and when bound to PTH, induce the insertion of calcium channels on their luminal surface. The channels enhance Ca^{++} recovery from the forming urine. Finally, calcitriol (the active form of vitamin D) is very important for calcium recovery. It induces the production of calcium-binding proteins that transport Ca^{++} into the cell. Any Ca^{++} not reabsorbed at this point is lost in the urine.

Collecting Ducts and Recovery of Water

Regulation of urine volume and osmolarity are major functions of the collecting ducts. By varying the amount of water that is recovered, the collecting ducts play a major role in maintaining the body's normal osmolarity. If plasma osmolarity rises (solute concentration in the blood rises), more water is recovered and urine volume decreases; if plasma osmolarity decreases (solute concentration in the blood decreases), less water is recovered and urine volume increases. This function is regulated by the posterior pituitary hormone antidiuretic hormone (ADH, also known as vasopressin). With mild dehydration, plasma osmolarity rises slightly. This increase is detected by osmoreceptors in the hypothalamus, which stimulates the release of ADH from the posterior pituitary. If plasma osmolarity decreases slightly, the opposite occurs. The mechanism of how ADH affects water reabsorption is discussed later in this chapter.

In addition to receptors for ADH, cells within the collecting duct have receptors for the steroid hormone aldosterone. While ADH is primarily involved in the regulation of water recovery, aldosterone regulates Na^+ recovery. When aldosterone output increases, more Na^+ is recovered from the forming urine and water follows the Na^+ passively. Aldosterone also increases secretion of K^+ from the blood into the forming urine. When aldosterone decreases, more Na^+ remains in the forming urine and more K^+ is recovered in the circulation.

Collecting duct cells play significant roles in regulating blood pH. Intercalated cells reabsorb K^+ and HCO_3^- while secreting H^+. This function lowers the acidity of the plasma while increasing the acidity of the urine.

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17.6: Endocrine Regulation of Kidney Function

Learning Objectives

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

- Describe how each of the renin–angiotensin mechanism functions in the extrinsic control of GFR
- Describe how each of the following works to regulate reabsorption and secretion, so as to affect urine volume and composition: renin–angiotensin system, aldosterone, and antidiuretic hormone

Several hormones have specific, important roles in regulating kidney function. They act to stimulate or inhibit blood flow. Some of these are endocrine, acting from a distance, whereas others are paracrine, acting locally.

Renin–Angiotensin–Aldosterone

Renin is an enzyme that is produced by the juxtaglomerular (JG) cells of the afferent arteriole at the juxtaglomerular apparatus (JGA). It enzymatically converts angiotensinogen (made by the liver, freely circulating) into angiotensin I. Its release is stimulated by the JGA in response to decreased extracellular fluid (ECF) volume.

Angiotensin-converting enzyme (**ACE**) is not a hormone but it is functionally important in regulating systemic blood pressure and kidney function. It is produced in the lungs but binds to the surfaces of endothelial cells in the afferent arterioles and glomerulus. It enzymatically converts inactive angiotensin I into active angiotensin II. ACE is important in raising blood pressure. People with high blood pressure are sometimes prescribed ACE inhibitors to lower their blood pressure.

Angiotensin II is a potent vasoconstrictor that plays an immediate role in the regulation of blood pressure. It acts systemically to cause vasoconstriction as well as constriction of both the afferent and efferent arterioles of the glomerulus. In instances of blood loss or dehydration, it reduces both GFR and renal blood flow, thereby limiting fluid loss and preserving blood volume. Its release is usually stimulated by decreases in blood pressure, and so the preservation of adequate blood pressure is its primary role.

Aldosterone, often called the “salt-retaining hormone,” is released from the adrenal cortex in response to angiotensin II or directly in response to increased plasma K^+. It promotes Na^+ reabsorption by the nephron, promoting the retention of water. When Na+ is reabsorbed into the blood, it increases the solute concentration of the blood. Water will then follow and be reabsorbed, as water moves towards an area of higher concentration of solutes via osmosis. Aldosterone is also important in regulating K^+, promoting its excretion. As a result, renin has an immediate effect on blood pressure due to angiotensin II–stimulated vasoconstriction and a prolonged effect through Na^+ recovery due to aldosterone. At the same time that aldosterone causes increased recovery of Na^+, it also causes greater loss of K^+. Progesterone is a steroid that is structurally similar to aldosterone. It binds to the aldosterone receptor and weakly stimulates Na^+ reabsorption and increased water recovery. This process is unimportant in males due to low levels of circulating progesterone. It may cause increased retention of water during some periods of the menstrual cycle in females when progesterone levels increase.

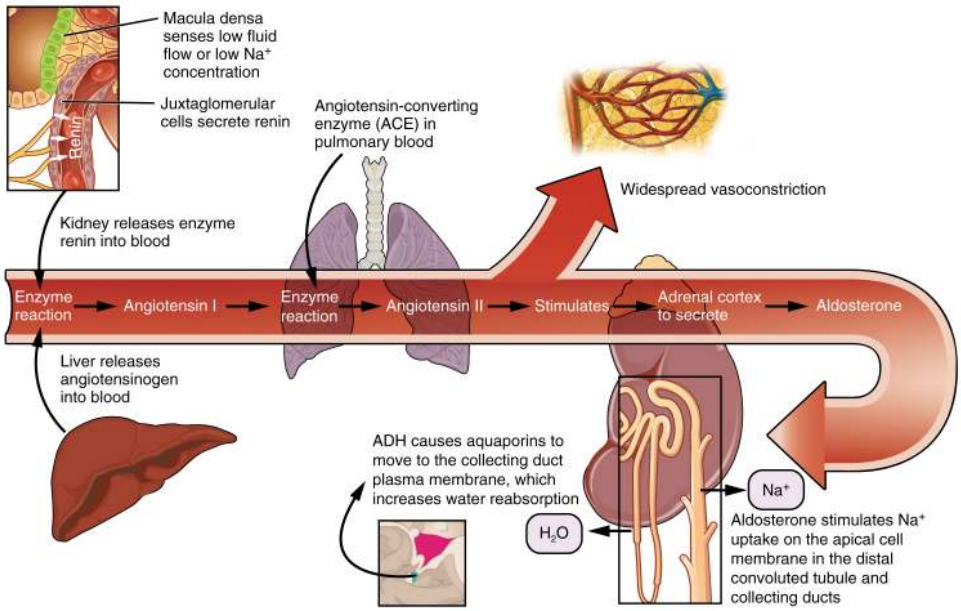


Figure 17.6.1 Conversion of Angiotensin I to Angiotensin II The enzyme renin converts the pro-enzyme angiotensin I; the lung-derived enzyme ACE converts angiotensin I into active angiotensin II.

Antidiuretic Hormone (ADH)

Diuretics are drugs that can increase water loss by interfering with the recapture of solutes and water from the forming urine. They are often prescribed to lower blood pressure. Coffee, tea, and alcoholic beverages are familiar diuretics. **ADH**, a hormone released by the posterior pituitary, works to do the exact opposite. It promotes the recovery of water, decreases urine volume, and maintains plasma osmolarity and blood pressure. When stimulated by ADH, the cells of the collecting duct will insert aquaporin channel proteins into their membranes, which as their name suggests, allow water to pass from the collecting duct lumen through the cells and into the interstitial spaces to be recovered by the vasa recta and returned to the blood. This process allows for the recovery of large amounts of water from the filtrate back into the blood. In the absence of ADH, these channels are not inserted, resulting in the excretion of water in the form of dilute urine. Most, if not all, cells of the body contain aquaporin molecules, whose channels are so small that only water can pass. At least 10 types of aquaporins are known in humans, and six of those are found in the kidney. The function of all aquaporins is to allow the movement of water across the lipid-rich, hydrophobic cell membrane (Figure 17.6.2).

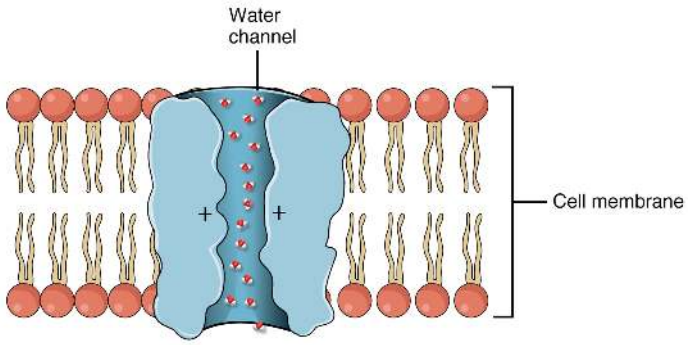


Figure 17.6.2 Aquaporin Water Channel Positive charges inside the channel prevent the leakage of electrolytes across the cell membrane, while allowing water to move due to osmosis.

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17.7: Review Questions

Use the following questions to test your knowledge of the Urinary System.

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CHAPTER OVERVIEW

18: The Reproductive System

18.1: Anatomy and Physiology of the Male Reproductive System
18.2: Anatomy and Physiology of the Female Reproductive System

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18.1: Anatomy and Physiology of the Male Reproductive System

Learning Objectives

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

- Describe the structure and function of the organs of the testicular reproductive system
- Describe the structure and function of the sperm cell
- Explain the events during spermatogenesis that produce haploid sperm from diploid cells
- Identify the importance of testosterone in reproductive function

People often use the words "female" and "male" to describe two different concepts: our sense of gender identity, and our biological sex as determined by our X/Y chromosomes, hormones, sex organs, and other physical characteristics. For some people, gender identity is different from biological sex or their sex assigned at birth. In this chapter and the next chapter, "female" and "male" refer to sex only, and the typical reproductive anatomy of XX and XY individuals is discussed.

Unique for its role in reproduction, a gamete is a specialized sex cell, which in humans carries 23 chromosomes—one half the number in body cells. In almost all sexually reproducing species, these two haploid cells differ in size; the smaller gamete is called the male gamete and the larger one is called the female gamete. At fertilization, the chromosomes in one male gamete, called a sperm (or spermatozoon), combine with the chromosomes in one female gamete, called an ovum. The function of the male, or testicular, reproductive system (Figure 18.1.1) is to produce sperm and transfer them to the female reproductive tract. The paired testes are a crucial component in this process, as they produce both sperm and androgens, the hormones that support male reproductive physiology. In male humans, the most important androgen is testosterone. For people with a penis, several accessory organs and ducts aid the process of sperm maturation and transport the sperm and other seminal components to the penis, which may deliver sperm to the female reproductive tract. In this section, we examine each of these different structures, and discuss the process of sperm production and transport.

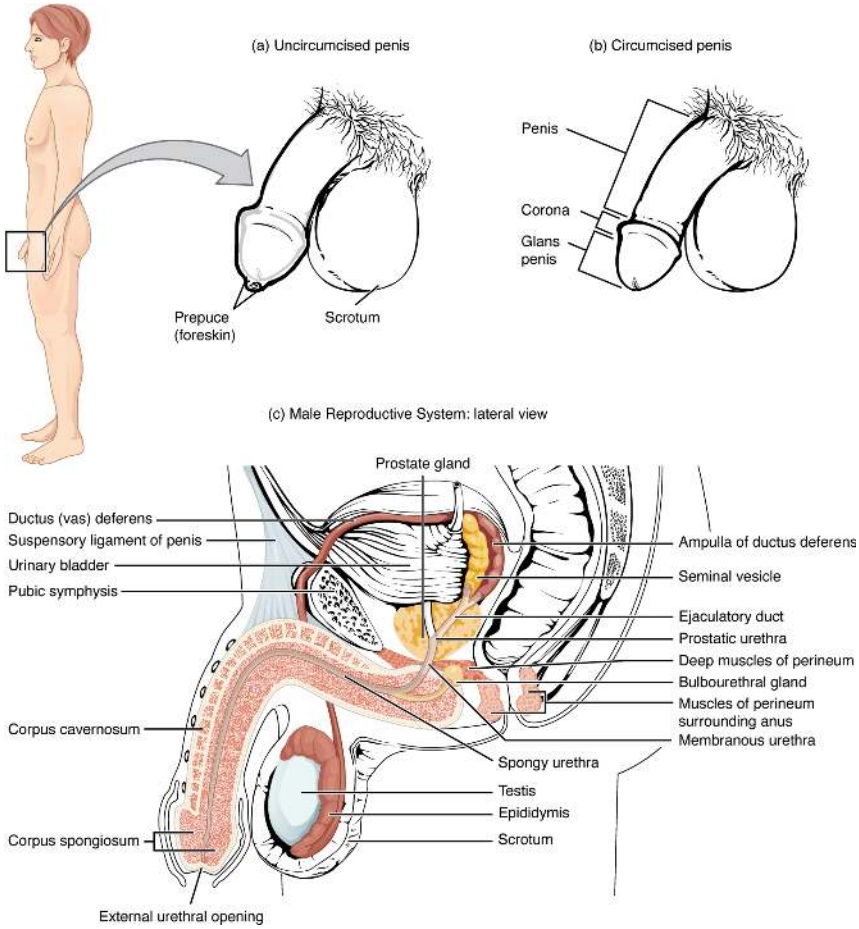


Figure 18.1.1: Testicular Reproductive System The structures of the testicular reproductive system include the testes, the epididymides, the penis, and the ducts and glands that produce and carry semen. Sperm exit the scrotum through the ductus deferens, which is bundled in the spermatic cord. The seminal vesicles and prostate gland add fluids to the sperm to create semen.

Scrotum

The testes are located in a skin-covered, highly pigmented, muscular sack called the scrotum that extends from the body behind the penis (see Figure 18.1.1). This location is important in sperm production, which occurs within the testes, and proceeds more efficiently when the testes are kept 2 to 4°C below core body temperature.

The dartos muscle makes up the subcutaneous muscle layer of the scrotum (Figure 18.1.2). It continues internally to make up the scrotal septum, a wall that divides the scrotum into two compartments, each housing one testis. Descending from the internal oblique muscle of the abdominal wall are the two cremaster muscles, which cover each testis like a muscular net. By contracting simultaneously, the dartos and cremaster muscles can elevate the testes in cold weather (or water), moving the testes closer to the body and decreasing the surface area of the scrotum to retain heat. Alternatively, as the environmental temperature increases, the scrotum relaxes, moving the testes farther from the body core and increasing scrotal surface area, which promotes heat loss. Externally, the scrotum has a raised medial thickening on the surface called the raphae.

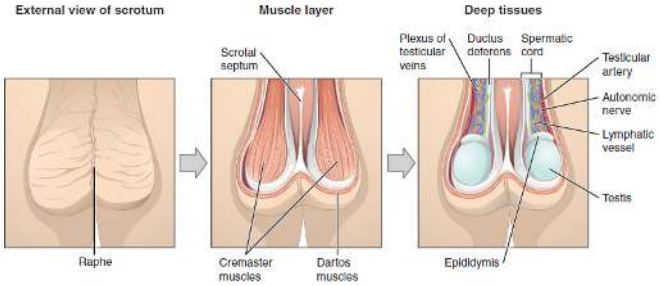


Figure 18.1.2: The Scrotum and Testes This anterior view shows the structures of the scrotum and testes.

Testes

The testes (singular = testis) are the male gonads—that is, the male reproductive organs. They produce both sperm and androgens, such as testosterone, and are active throughout the reproductive lifespan.

Paired ovals, adult testes are each approximately 4 to 5 cm in length and are housed within the scrotum (see Figure 18.1.2). They are surrounded by two distinct layers of protective connective tissue (Figure 18.1.3). The outer tunica vaginalis is a serous membrane that has both a parietal and a thin visceral layer. Beneath the tunica vaginalis is the tunica albuginea, a tough, white, dense connective tissue layer covering the testis itself. Not only does the tunica albuginea cover the outside of the testis, it also invaginates to form septa that divide the testis into 300 to 400 structures called lobules. Within the lobules, sperm develop in structures called seminiferous tubules. During the seventh month of the developmental period of a male fetus, each testis moves through the abdominal musculature to descend into the scrotal cavity. This is called the “descent of the testis.” Cryptorchidism is the clinical term used when one or both of the testes fail to descend into the scrotum prior to birth.

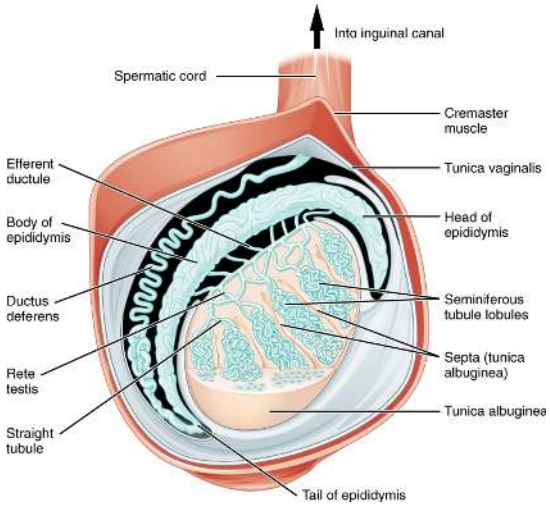


Figure 18.1.3: Anatomy of the Testis This sagittal view shows the seminiferous tubules, the site of sperm production. Formed sperm are transferred to the epididymis, where they mature. They leave the epididymis during an ejaculation via the ductus deferens.

The tightly coiled seminiferous tubules form the bulk of each testis. They are composed of developing sperm cells surrounding a lumen, the hollow center of the tubule, where formed sperm are released into the duct system of the testis. Specifically, from the lumens of the seminiferous tubules, sperm move into the straight tubules (or tubuli recti), and from there into a fine meshwork of tubules called the rete testes. Sperm leave the rete testes, and the testis itself, through the 15 to 20 efferent ductules that cross the tunica albuginea.

Inside the seminiferous tubules are six different cell types. These include supporting cells called sustentacular cells, as well as five types of developing sperm cells called germ cells. Germ cell development progresses from the basement membrane—at the perimeter of the tubule—toward the lumen. Let’s look more closely at these cell types.

Sertoli Cells

Surrounding all stages of the developing sperm cells are elongate, branching Sertoli cells. Sertoli cells are a type of supporting cell called a sustentacular cell, or sustentocyte, that are typically found in epithelial tissue. Sertoli cells secrete signaling molecules that promote sperm production and can control whether germ cells live or die. They extend physically around the germ cells from the peripheral basement membrane of the seminiferous tubules to the lumen. Tight junctions between these sustentacular cells create the blood–testis barrier, which keeps bloodborne substances from reaching the germ cells and, at the same time, keeps surface antigens on developing germ cells from escaping into the bloodstream and prompting an autoimmune response.

Germ Cells

The least mature cells, the spermatogonia (singular = spermatogonium), line the basement membrane inside the tubule. Spermatogonia are the stem cells of the testis, which means that they are still able to differentiate into a variety of different cell types throughout adulthood. Spermatogonia divide to produce primary and secondary spermatocytes, then spermatids, which finally produce formed sperm. The process that begins with spermatogonia and concludes with the production of sperm is called spermatogenesis.

Spermatogenesis

As just noted, spermatogenesis occurs in the seminiferous tubules that form the bulk of each testis (see Figure 18.1.3). The process begins at puberty, after which time sperm are produced constantly throughout a male's life. One production cycle, from spermatogonia through formed sperm, takes approximately 64 days. A new cycle starts approximately every 16 days, although this timing is not synchronous across the seminiferous tubules. Sperm counts—the total number of sperm a person produces—slowly decline after age 35, and some studies suggest that smoking can lower sperm counts irrespective of age.

The process of spermatogenesis begins with mitosis of the diploid spermatogonia (Figure 18.1.4). Because these cells are diploid ($2n$), they each have a complete copy of the person's genetic material, or 46 chromosomes. However, mature gametes are haploid ($1n$), containing 23 chromosomes—meaning that daughter cells of spermatogonia must undergo a second cellular division through the process of meiosis.

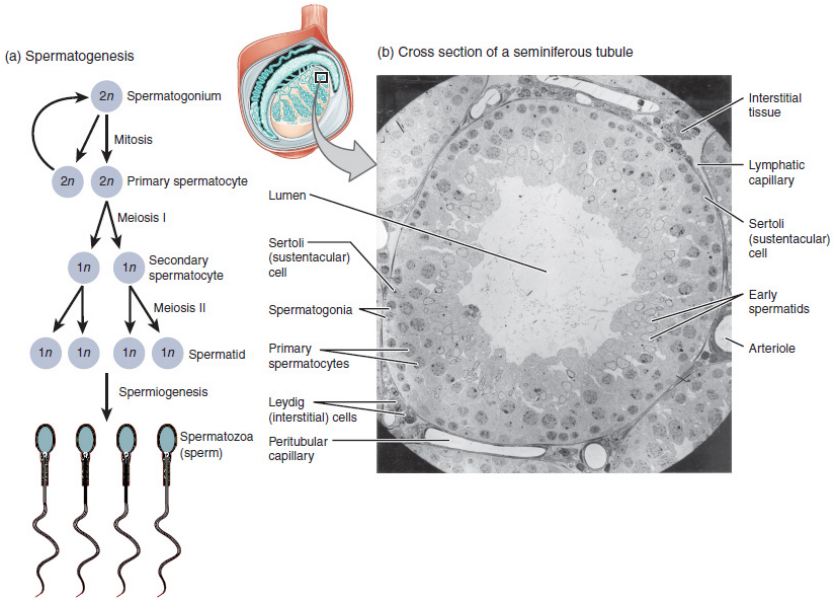


Figure 18.1.4: Spermatogenesis (a) Mitosis of a spermatogonial stem cell involves a single cell division that results in two identical, diploid daughter cells (spermatogonia to primary spermatocyte). Meiosis has two rounds of cell division: primary spermatocyte to secondary spermatocyte, and then secondary spermatocyte to spermatid. This produces four haploid daughter cells (spermatids). (b) In this electron micrograph of a cross-section of a seminiferous tubule from a rat, the lumen is the light-shaded area in the center of the image. The location of the primary spermatocytes is near the basement membrane, and the early spermatids are approaching the lumen (tissue source: rat). EM × 900. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

Two identical diploid cells result from spermatogonia mitosis. One of these cells remains a spermatogonium, and the other becomes a primary spermatocyte, the next stage in the process of spermatogenesis. As in mitosis, DNA is replicated in a primary spermatocyte, before it undergoes a cell division called meiosis I. During meiosis I each of the 23 pairs of chromosomes separates. This results in two cells, called secondary spermatocytes, each with only half the number of chromosomes. Now a second round of cell division (meiosis II) occurs in both of the secondary spermatocytes. During meiosis II each of the 23 replicated chromosomes divides, similar to what happens during mitosis. Thus, meiosis results in separating the chromosome pairs. This second meiotic division results in a total of four cells with only half of the number of chromosomes. Each of these new cells is a spermatid. Although haploid, early spermatids look very similar to cells in the earlier stages of spermatogenesis, with a round shape, central nucleus, and large amount of cytoplasm. A process called spermiogenesis transforms these early spermatids, reducing the cytoplasm, and beginning the formation of the parts of a true sperm. The fifth stage of germ cell formation—spermatozoa, or formed sperm—is the end result of this process, which occurs in the portion of the tubule nearest the lumen. Eventually, the sperm

are released into the lumen and are moved along a series of ducts in the testis toward a structure called the epididymis for the next step of sperm maturation.

Structure of Formed Sperm

Sperm are smaller than most cells in the body; in fact, the volume of a sperm cell is 85,000 times less than that of the female gamete. Approximately 100 to 300 million sperm are produced each day, whereas females typically ovulate only one oocyte per month. As is true for most cells in the body, the structure of sperm cells speaks to their function. Sperm have a distinctive head, mid-piece, and tail region (Figure 18.1.5). The head of the sperm contains the extremely compact haploid nucleus with very little cytoplasm. These qualities contribute to the overall small size of the sperm (the head is only 5 μm long). A structure called the acrosome covers most of the head of the sperm cell as a "cap" that is filled with lysosomal enzymes important for preparing sperm to participate in fertilization. Tightly packed mitochondria fill the mid-piece of the sperm. ATP produced by these mitochondria will power the flagellum, which extends from the neck and the mid-piece through the tail of the sperm, enabling it to move the entire sperm cell. The central strand of the flagellum, the axial filament, is formed from one centriole inside the maturing sperm cell during the final stages of spermatogenesis.

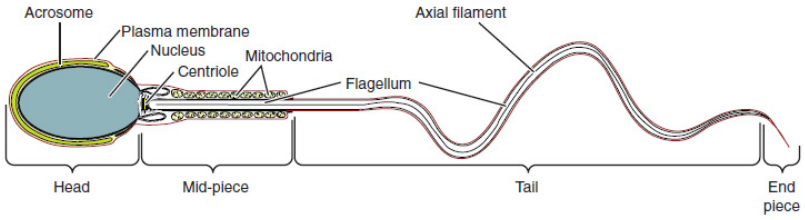


Figure 18.1.5: Structure of Sperm Sperm cells are divided into a head, containing DNA; a mid-piece, containing mitochondria; and a tail, providing motility. The acrosome is oval and somewhat flattened.

Sperm Transport

To fertilize an egg without medical intervention, sperm must be moved from the seminiferous tubules in the testes, through the epididymis, and—later during ejaculation—along the length of the penis and out into the female reproductive tract.

Role of the Epididymis

From the lumen of the seminiferous tubules, the immotile sperm are surrounded by testicular fluid and moved to the epididymis (plural = epididymides), a coiled tube attached to the testis where newly formed sperm continue to mature (see Figure 18.1.3). Though the epididymis does not take up much room in its tightly coiled state, it would be approximately 6 m (20 feet) long if straightened. It takes an average of 12 days for sperm to move through the coils of the epididymis, with the shortest recorded transit time in humans being one day. Sperm enter the head of the epididymis and are moved along predominantly by the contraction of smooth muscles lining the epididymal tubes. As they are moved along the length of the epididymis, the sperm further mature and acquire the ability to move under their own power. Once inside the female reproductive tract, they will use this ability to move independently toward the unfertilized egg. The more mature sperm are then stored in the tail of the epididymis (the final section) until ejaculation occurs.

Duct System

During ejaculation, sperm exit the tail of the epididymis and are pushed by smooth muscle contraction to the ductus deferens (also called the vas deferens). The ductus deferens is a thick, muscular tube that is bundled together inside the scrotum with connective tissue, blood vessels, and nerves into a structure called the spermatic cord (see Figure 18.1.1 and Figure 18.1.2). Because the ductus deferens is physically accessible within the scrotum, surgical sterilization to interrupt sperm delivery can be performed by cutting and sealing a small section of the ductus (vas) deferens. This procedure is called a vasectomy, and it is an effective form of birth control. Although it may be possible to reverse a vasectomy, clinicians consider the procedure permanent, and advise people to undergo it only if they are certain they no longer wish to have children.

Interactive Link

Interactive Link Feature

Watch this video to learn about a vasectomy. As described in this video, a vasectomy is a procedure in which a small section of the ductus (vas) deferens is removed from the scrotum. This interrupts the path taken by sperm through the ductus deferens. If

sperm do not exit through the vas, either because the person has had a vasectomy or has not ejaculated, in what region of the testis do they remain?

From each epididymis, each ductus deferens extends superiorly into the abdominal cavity through the inguinal canal in the abdominal wall. From here, the ductus deferens continues posteriorly to the pelvic cavity, ending posterior to the bladder where it dilates in a region called the ampulla (meaning “flask”).

Sperm make up only 5 percent of the final volume of semen, the thick, milky fluid that is ejaculated. The bulk of semen is produced by three critical accessory glands of the male reproductive system: the seminal vesicles, the prostate, and the bulbourethral glands.

Seminal Vesicles

As sperm pass through the ampulla of the ductus deferens at ejaculation, they mix with fluid from the associated seminal vesicle (see Figure 27.2). The paired seminal vesicles are glands that contribute approximately 60 percent of the semen volume. Seminal vesicle fluid contains large amounts of fructose, which is used by the sperm mitochondria to generate ATP to allow movement through the female reproductive tract.

The fluid, now containing both sperm and seminal vesicle secretions, next moves into the associated ejaculatory duct, a short structure formed from the ampulla of the ductus deferens and the duct of the seminal vesicle. The paired ejaculatory ducts transport the seminal fluid into the next structure, the prostate gland.

Prostate Gland

As shown in Figure 27.2, the centrally located prostate gland sits anterior to the rectum at the base of the bladder surrounding the prostatic urethra (the portion of the urethra that runs within the prostate). About the size of a walnut, the prostate is formed of both muscular and glandular tissues. It excretes an alkaline, milky fluid to the passing seminal fluid—now called semen—that is critical to first coagulate and then decoagulate the semen following ejaculation. The temporary thickening of semen helps retain it within the female reproductive tract, providing time for sperm to utilize the fructose provided by seminal vesicle secretions. When the semen regains its fluid state, sperm can then pass farther into the female reproductive tract.

The prostate normally doubles in size during puberty. At approximately age 25, it gradually begins to enlarge again. This enlargement does not usually cause problems; however, abnormal growth of the prostate, or benign prostatic hyperplasia (BPH), can cause constriction of the urethra as it passes through the middle of the prostate gland, leading to a number of lower urinary tract symptoms, such as a frequent and intense urge to urinate, a weak stream, and a sensation that the bladder has not emptied completely. By age 60, approximately 40 percent of males have some degree of BPH. By age 80, the number of affected individuals has jumped to as many as 80 percent. Treatments for BPH attempt to relieve the pressure on the urethra so that urine can flow more normally. Mild to moderate symptoms are treated with medication, whereas severe enlargement of the prostate is treated by surgery in which a portion of the prostate tissue is removed.

Another common disorder involving the prostate is prostate cancer. According to the Centers for Disease Control and Prevention (CDC), prostate cancer is the second most common cancer in males. However, some forms of prostate cancer grow very slowly and thus may not ever require treatment. Aggressive forms of prostate cancer, in contrast, involve metastasis to vulnerable organs like the lungs and brain. There is no link between BPH and prostate cancer, but the symptoms are similar. Prostate cancer is detected by a medical history, a blood test, and a rectal exam that allows physicians to palpate the prostate and check for unusual masses. If a mass is detected, the cancer diagnosis is confirmed by biopsy of the cells.

Bulbourethral Glands

The final addition to semen is made by two bulbourethral glands (or Cowper’s glands) that release a thick, salty fluid that lubricates the end of the urethra and the vagina, and helps to clean urine residues from the penile urethra. The fluid from these accessory glands is released after the male becomes sexually aroused, and shortly before the release of the semen. It is therefore sometimes called pre-ejaculate. It is important to note that, in addition to the lubricating proteins, it is possible for bulbourethral fluid to pick up sperm already present in the urethra, and therefore it may be able to cause pregnancy.

Interactive Link

Interactive Link Feature

Watch this video to explore the structures of the male reproductive system and the path of sperm, which starts in the testes and ends as the sperm leave the penis through the urethra. Where are sperm deposited after they leave the ejaculatory duct?

The Penis

The penis is the male organ of copulation (sexual intercourse). It is flaccid for non-sexual actions, such as urination, and turgid and rod-like with sexual arousal. When erect, the stiffness of the organ allows it to penetrate into the vagina and deposit semen into the female reproductive tract.

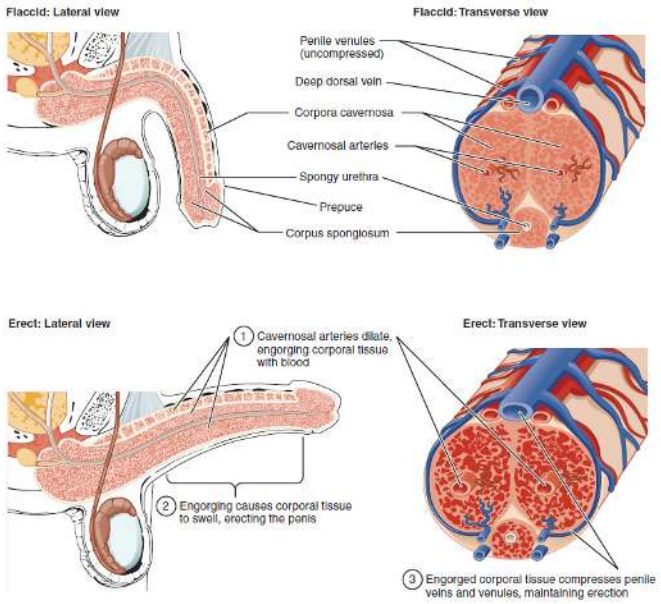


Figure 18.1.6: Cross-Sectional Anatomy of the Penis Three columns of erectile tissue make up most of the volume of the penis.

The shaft of the penis surrounds the urethra (Figure 18.1.6). The shaft is composed of three column-like chambers of erectile tissue that span the length of the shaft. Each of the two larger lateral chambers is called a corpus cavernosum (plural = corpora cavernosa). Together, these make up the bulk of the penis. The corpus spongiosum, which can be felt as a raised ridge on the erect penis, is a smaller chamber that surrounds the spongy, or penile, urethra. The end of the penis, called the glans penis, has a high concentration of nerve endings, resulting in very sensitive skin that influences the likelihood of ejaculation (see Figure 27.2). The skin from the shaft extends down over the glans and forms a collar called the prepuce (or foreskin). The foreskin also contains a dense concentration of nerve endings, and both lubricate and protect the sensitive skin of the glans penis. A surgical procedure called circumcision, often performed for religious or social reasons, removes the prepuce, typically within days of birth.

Both sexual arousal and REM sleep (during which dreaming occurs) can induce an erection. Penile erections are the result of vasocongestion, or engorgement of the tissues because of more arterial blood flowing into the penis than is leaving in the veins. During sexual arousal, nitric oxide (NO) is released from nerve endings near blood vessels within the corpora cavernosa and spongiosum. Release of NO activates a signaling pathway that results in relaxation of the smooth muscles that surround the penile arteries, causing them to dilate. This dilation increases the amount of blood that can enter the penis and induces the endothelial cells in the penile arterial walls to also secrete NO and perpetuate the vasodilation. The rapid increase in blood volume fills the erectile chambers, and the increased pressure of the filled chambers compresses the thin-walled penile venules, preventing venous drainage of the penis. The result of this increased blood flow to the penis and reduced blood return from the penis is erection. Depending on the flaccid dimensions of a penis, it can increase in size slightly or greatly during erection, with the average length of an erect penis measuring approximately 15 cm.

Disorders of the...

Male Reproductive System

Erectile dysfunction (ED) is a condition in which a person has difficulty either initiating or maintaining an erection. The combined prevalence of minimal, moderate, and complete ED is approximately 40 percent in males at age 40, and reaches

nearly 70 percent by 70 years of age. In addition to aging, ED is associated with diabetes, vascular disease, psychiatric disorders, prostate disorders, the use of some drugs such as certain antidepressants, and problems with the testes resulting in low testosterone concentrations. These physical and emotional conditions can lead to interruptions in the vasodilation pathway and result in an inability to achieve an erection.

Recall that the release of NO induces relaxation of the smooth muscles that surround the penile arteries, leading to the vasodilation necessary to achieve an erection. To reverse the process of vasodilation, an enzyme called phosphodiesterase (PDE) degrades a key component of the NO signaling pathway called cGMP. There are several different forms of this enzyme, and PDE type 5 is the type of PDE found in the tissues of the penis. Scientists discovered that inhibiting PDE5 increases blood flow, and allows vasodilation of the penis to occur.

PDEs and the vasodilation signaling pathway are found in the vasculature in other parts of the body. In the 1990s, clinical trials of a PDE5 inhibitor called sildenafil were initiated to treat hypertension and angina pectoris (chest pain caused by poor blood flow through the heart). The trial showed that the drug was not effective at treating heart conditions, but many men experienced erection and priapism (erection lasting longer than 4 hours). Because of this, a clinical trial was started to investigate the ability of sildenafil to promote erections in men suffering from ED. In 1998, the FDA approved the drug, marketed as Viagra®. Since approval of the drug, sildenafil and similar PDE inhibitors now generate over a billion dollars a year in sales, and are reported to be effective in treating approximately 70 to 85 percent of cases of ED. Importantly, men with health problems—especially those with cardiac disease taking nitrates—should avoid Viagra or talk to their physician to find out if they are a candidate for the use of this drug, as deaths have been reported for at-risk users.

Testosterone

Testosterone, an androgen, is a steroid hormone produced by Leydig cells. The alternate term for Leydig cells, interstitial cells, reflects their location between the seminiferous tubules in the testes. In male embryos, testosterone is secreted by Leydig cells by the seventh week of development, with peak concentrations reached in the second trimester. This early release of testosterone results in the anatomical differentiation of the male sexual organs. In childhood, testosterone concentrations are low. They increase during puberty, activating characteristic physical changes and initiating spermatogenesis.

Functions of Testosterone

The continued presence of testosterone is necessary to keep the male reproductive system working properly, and Leydig cells produce approximately 6 to 7 mg of testosterone per day. Testicular steroidogenesis (the manufacture of androgens, including testosterone) results in testosterone concentrations that are 100 times higher in the testes than in the circulation. Maintaining these normal concentrations of testosterone promotes spermatogenesis, whereas low levels of testosterone can lead to infertility. In addition to intratesticular secretion, testosterone is also released into the systemic circulation and plays an important role in muscle development, bone growth, the development of secondary sex characteristics, and maintaining libido (sex drive) in both males and females. In females, the ovaries secrete small amounts of testosterone, although most is converted to estradiol. A small amount of testosterone is also secreted by the adrenal glands in both sexes.

Control of Testosterone

The regulation of testosterone concentrations throughout the body is critical for male reproductive function. The intricate interplay between the endocrine system and the reproductive system is shown in Figure 18.1.7.

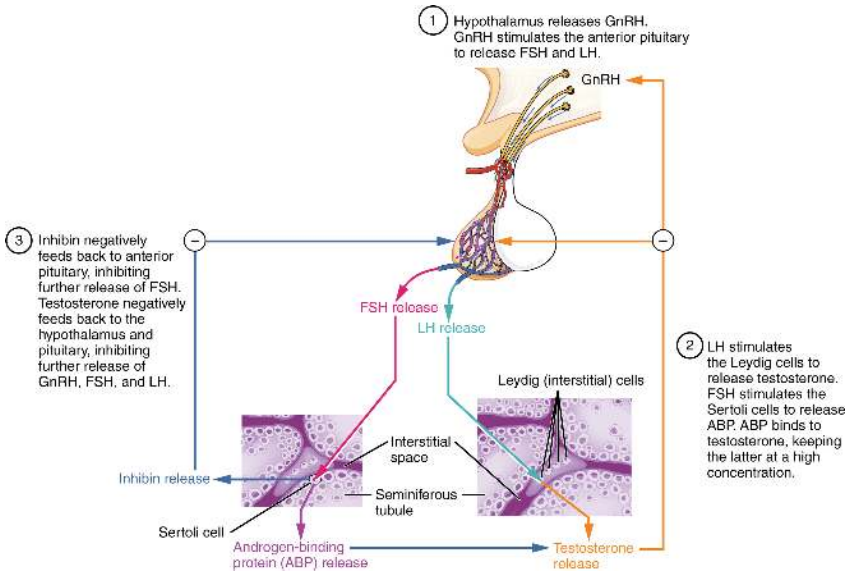


Figure 18.1.7: Regulation of Testosterone Production The hypothalamus and pituitary gland regulate the production of testosterone and the cells that assist in spermatogenesis. GnRH activates the anterior pituitary to produce LH and FSH, which in turn stimulate Leydig cells and Sertoli cells, respectively. The system is a negative feedback loop because the end products of the pathway, testosterone and inhibin, interact with the activity of GnRH to inhibit their own production.

The regulation of Leydig cell production of testosterone begins outside of the testes. The hypothalamus and the pituitary gland in the brain integrate external and internal signals to control testosterone synthesis and secretion. The regulation begins in the hypothalamus. Pulsatile release of a hormone called gonadotropin-releasing hormone (GnRH) from the hypothalamus stimulates the endocrine release of hormones from the pituitary gland. Binding of GnRH to its receptors on the anterior pituitary gland stimulates release of the two gonadotropins: luteinizing hormone (LH) and follicle-stimulating hormone (FSH). These two hormones are critical for reproductive function in all humans. In the testes, FSH binds predominantly to the Sertoli cells within the seminiferous tubules to promote spermatogenesis. FSH also stimulates the Sertoli cells to produce hormones called inhibins, which function to inhibit FSH release from the pituitary, thus reducing testosterone secretion. These polypeptide hormones correlate directly with Sertoli cell function and sperm number; inhibin B can be used as a marker of spermatogenic activity. LH binds to receptors on Leydig cells in the testes and upregulates the production of testosterone.

A negative feedback loop predominantly controls the synthesis and secretion of both FSH and LH. Low blood concentrations of testosterone stimulate the hypothalamic release of GnRH. GnRH then stimulates the anterior pituitary to secrete LH into the bloodstream. In the testis, LH binds to LH receptors on Leydig cells and stimulates the release of testosterone. When concentrations of testosterone in the blood reach a critical threshold, testosterone itself will bind to androgen receptors on both the hypothalamus and the anterior pituitary, inhibiting the synthesis and secretion of GnRH and LH, respectively. When the blood concentrations of testosterone once again decline, testosterone no longer interacts with the receptors to the same degree and GnRH and LH are once again secreted, stimulating more testosterone production. This same process occurs with FSH and inhibin to control spermatogenesis.

Aging and the...

Male Reproductive System

Declines in Leydig cell activity can occur in males beginning at 40 to 50 years of age. The resulting reduction in circulating testosterone concentrations can lead to symptoms of andropause, also known as male menopause. While the reduction in sex steroids is akin to female menopause, there is no clear sign—such as a lack of a menstrual period—to denote the initiation of andropause. Instead, people with this condition report feelings of fatigue, reduced muscle mass, depression, anxiety, irritability, loss of libido, and insomnia. A reduction in spermatogenesis resulting in lowered fertility is also reported, and sexual dysfunction can also be associated with andropausal symptoms.

Whereas some researchers believe that certain aspects of andropause are difficult to tease apart from aging in general, testosterone replacement is sometimes prescribed to alleviate some symptoms. Recent studies have shown a benefit from androgen replacement therapy on the new onset of depression in elderly males; however, other studies caution against testosterone replacement for long-term treatment of andropause symptoms, showing that high doses can sharply increase the risk of both heart disease and prostate cancer.

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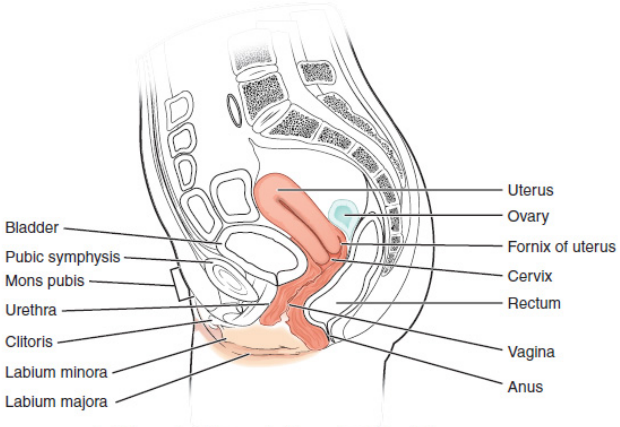
18.2: Anatomy and Physiology of the Female Reproductive System

Learning Objectives

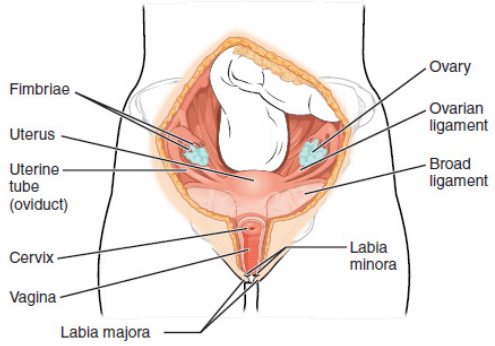
By the end of this section, you will be able to:

- Describe the structure and function of the organs of the ovarian reproductive system
- List the steps of oogenesis
- Describe the hormonal changes that occur during the ovarian and menstrual cycles
- Trace the path of an oocyte from ovary to fertilization

The female, or ovarian, reproductive system functions to produce gametes and reproductive hormones, just like the male reproductive system; however, it also has the additional task of supporting the developing fetus and delivering it to the outside world. Unlike its male counterpart, the female reproductive system is located primarily inside the pelvic cavity (Figure 18.2.1). Recall that the ovaries are the female gonads. The gamete they produce is called an oocyte. We'll discuss the production of oocytes in detail shortly. First, let's look at some of the structures of the female reproductive system.



(a) Human female reproductive system: lateral view



(b) Human female reproductive system: anterior view

Figure 18.2.1: Female Reproductive System The major organs of the female reproductive system are located inside the pelvic cavity.

External Female Genitals

The external female reproductive structures are referred to collectively as the vulva (Figure 18.2.2). The mons pubis is a pad of fat that is located at the anterior, over the pubic bone. After puberty, it becomes covered in pubic hair. The labia majora (labia = "lips"; majora = "larger") are folds of hair-covered skin that begin just posterior to the mons pubis. The thinner and more pigmented labia minora (labia = "lips"; minora = "smaller") extend medial to the labia majora. Although they naturally vary in shape and size from person to person, the labia minora serve to protect the urethra and the entrance to the reproductive tract.

The superior, anterior portions of the labia minora come together to encircle the clitoris (or glans clitoris), an organ that originates from the same cells as the glans penis and has abundant nerves that make it important in sexual sensation and orgasm. The hymen is a thin membrane that sometimes partially covers the entrance to the vagina. An intact hymen cannot be used as an indication of "virginity"; even at birth, this is only a partial membrane, as menstrual fluid and other secretions must be able to exit the body, regardless of penile–vaginal intercourse. The vaginal opening is located between the opening of the urethra and the anus. It is flanked by outlets to the Bartholin's glands (or greater vestibular glands).

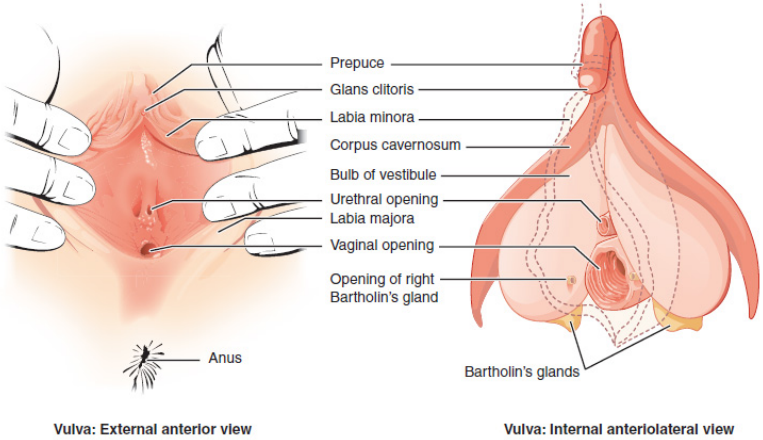


Figure 18.2.2: The Vulva The external female genitalia are referred to collectively as the vulva.

Vagina

The vagina, shown at the bottom of Figure 18.2.1 and Figure 18.2.2, is a muscular canal (approximately 10 cm long) that serves as the entrance to the reproductive tract. It also serves as the exit from the uterus during menses and childbirth. The outer walls of the anterior and posterior vagina are formed into longitudinal columns, or ridges, and the superior portion of the vagina—called the fornix—meets the protruding uterine cervix. The walls of the vagina are lined with an outer, fibrous adventitia; a middle layer of smooth muscle; and an inner mucous membrane with transverse folds called rugae. Together, the middle and inner layers allow the expansion of the vagina to accommodate intercourse and childbirth. The thin, perforated hymen can partially surround the opening to the vaginal orifice. The hymen can be ruptured with strenuous physical exercise, penile–vaginal intercourse, and childbirth. The Bartholin's glands and the lesser vestibular glands (located near the clitoris) secrete mucus, which keeps the vestibular area moist.

The vagina is home to a normal population of microorganisms that help to protect against infection by pathogenic bacteria, yeast, or other organisms that can enter the vagina. In a healthy person, the most predominant type of vaginal bacteria is from the genus *Lactobacillus*. This family of beneficial bacterial flora secretes lactic acid, and thus protects the vagina by maintaining an acidic pH (below 4.5). Potential pathogens are less likely to survive in these acidic conditions. Lactic acid, in combination with other vaginal secretions, makes the vagina a self-cleansing organ. However, douching—or washing out the vagina with fluid—can disrupt the normal balance of healthy microorganisms, and actually increase risk for infections and irritation. Indeed, the American College of Obstetricians and Gynecologists recommend that people do not douche, and that they allow the vagina to maintain its normal healthy population of protective microbial flora.

Ovaries

The ovaries are the female gonads (see Figure 27.9). Paired ovals, they are each about 2 to 3 cm in length, about the size of an almond. The ovaries are located within the pelvic cavity, and are supported by the mesovarium, an extension of the peritoneum that connects the ovaries to the broad ligament. Extending from the mesovarium itself is the suspensory ligament that contains the ovarian blood and lymph vessels. Finally, the ovary itself is attached to the uterus via the ovarian ligament.

The ovary comprises an outer covering of cuboidal epithelium called the ovarian surface epithelium that is superficial to a dense connective tissue covering called the tunica albuginea. Beneath the tunica albuginea is the cortex, or outer portion, of the organ. The cortex is composed of a tissue framework called the ovarian stroma that forms the bulk of the adult ovary. Oocytes develop within the outer layer of this stroma, each surrounded by supporting cells. This grouping of an oocyte and its supporting cells is called a follicle. The growth and development of ovarian follicles will be described shortly. Beneath the cortex lies the inner ovarian medulla, the site of blood vessels, lymph vessels, and the nerves of the ovary. You will learn more about the overall anatomy of the female reproductive system at the end of this section.

The Ovarian Cycle

The ovarian cycle is a set of predictable changes in oocytes and ovarian follicles. During the reproductive years, it is a roughly 28-day cycle that can be correlated with, but is not the same as, the menstrual cycle (discussed shortly). The cycle includes two interrelated processes: oogenesis (the production of gametes) and folliculogenesis (the growth and development of ovarian follicles).

Oogenesis

Gametogenesis in females is called oogenesis. The process begins with the ovarian stem cells, or oogonia (Figure 18.2.3). Oogonia are formed during fetal development, and divide via mitosis, much like spermatogonia in the testis. Unlike spermatogonia, however, oogonia form primary oocytes in the fetal ovary prior to birth. These primary oocytes are then arrested in this stage of meiosis I, only to resume it years later, beginning at puberty and continuing until the person is near menopause (the cessation of a female's reproductive functions). The number of primary oocytes present in the ovaries declines from one to two million in an infant, to approximately 400,000 at puberty, to zero by the end of menopause.

The initiation of ovulation—the release of an oocyte from the ovary—marks the transition from puberty into reproductive maturity. From then on, throughout a the reproductive years, ovulation occurs approximately once every 28 days. Just prior to ovulation, a surge of luteinizing hormone triggers the resumption of meiosis in a primary oocyte. This initiates the transition from primary to secondary oocyte. However, as you can see in Figure 18.2.3, this cell division does not result in two identical cells. Instead, the cytoplasm is divided unequally, and one daughter cell is much larger than the other. This larger cell, the secondary oocyte, eventually leaves the ovary during ovulation. The smaller cell, called the first polar body, may or may not complete meiosis and produce second polar bodies; in either case, it eventually disintegrates. Therefore, even though oogenesis produces up to four cells, only one survives.

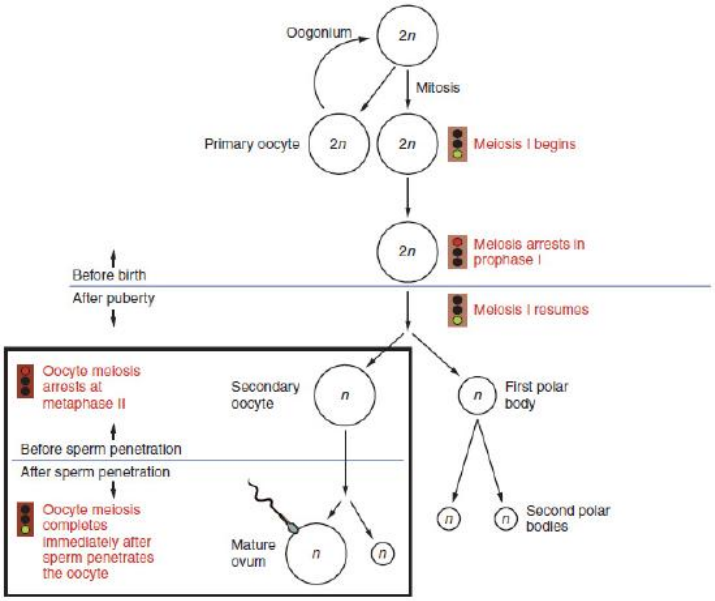


Figure 18.2.3: Oogenesis The unequal cell division of oogenesis produces one to three polar bodies that later degrade, as well as a single haploid ovum, which is produced only if there is penetration of the secondary oocyte by a sperm cell.

How does the diploid secondary oocyte become an ovum—the haploid female gamete? Meiosis of a secondary oocyte is completed only if a sperm succeeds in penetrating its barriers. Meiosis II then resumes, producing one haploid ovum that, at the instant of fertilization by a (haploid) sperm, becomes the first diploid cell of the new offspring (a zygote). Thus, the ovum can be thought of as a brief, transitional, haploid stage between the diploid oocyte and diploid zygote.

The larger amount of cytoplasm contained in the female gamete is used to supply the developing zygote with nutrients during the period between fertilization and implantation into the uterus. Interestingly, sperm contribute only DNA at fertilization —not cytoplasm. Therefore, the cytoplasm and all of the cytoplasmic organelles in the developing embryo are of egg-derived origin. This includes mitochondria, which contain their own DNA. Scientific research in the 1980s determined that mitochondrial DNA was maternally inherited, meaning that you can trace your mitochondrial DNA directly to your biological mother, her mother, and so on back through your female ancestors.

Everyday Connection

Mapping Human History with Mitochondrial DNA

When we talk about human DNA, we're usually referring to nuclear DNA; that is, the DNA coiled into chromosomal bundles in the nucleus of our cells. We inherit half of our nuclear DNA from one parent, and half from the other parent. However, mitochondrial DNA (mtDNA) comes only from the mitochondria in the cytoplasm of the fat ovum we inherit from our mother. Our mother received mtDNA from their mother, who got it from their mother, and so on. Each of our cells contains approximately 1700 mitochondria, with each mitochondrion packed with mtDNA containing approximately 37 genes.

Mutations (changes) in mtDNA occur spontaneously in a somewhat organized pattern at regular intervals in human history. By analyzing these mutational relationships, researchers have been able to determine that we can all trace our ancestry back to one female who lived in Africa about 200,000 years ago. More precisely, that human is our most recent common ancestor through matrilineal descent.

This doesn't mean that everyone's mtDNA today looks exactly like that of our common ancestor. Because of the spontaneous mutations in mtDNA that have occurred over the centuries, researchers can map different "branches" off of the "main trunk" of our mtDNA family tree. Your mtDNA might have a pattern of mutations that aligns more closely with one branch, and your neighbor's may align with another branch. Still, all branches eventually lead back to the common ancestor.

But what happened to the mtDNA of all of the other *Homo sapiens* females who were living 200,000 years ago? Researchers explain that, over the centuries, their female descendants died childless or with only male children, and thus, their maternal line —and its mtDNA—ended.

Folliculogenesis

Again, ovarian follicles are oocytes and their supporting cells. They grow and develop in a process called folliculogenesis, which typically leads to ovulation of one follicle approximately every 28 days, along with death to multiple other follicles. The death of ovarian follicles is called atresia, and can occur at any point during follicular development. Recall that, a female infant at birth will have one to two million oocytes within the ovarian follicles, and that this number declines throughout life until menopause, when no follicles remain. As you'll see next, follicles progress from primordial, to primary, to secondary and tertiary stages prior to ovulation—with the oocyte inside the follicle remaining as a primary oocyte until right before ovulation.

Folliculogenesis begins with follicles in a resting state. These small primordial follicles are present in newborn females and are the prevailing follicle type in the adult ovary (Figure 18.2.4). Primordial follicles have only a single flat layer of support cells, called granulosa cells, that surround the oocyte, and they can stay in this resting state for years—some until right before menopause.

After puberty, a few primordial follicles will respond to a recruitment signal each day, and will join a pool of immature growing follicles called primary follicles. Primary follicles start with a single layer of granulosa cells, but the granulosa cells then become active and transition from a flat or squamous shape to a rounded, cuboidal shape as they increase in size and proliferate. As the granulosa cells divide, the follicles—now called secondary follicles (see Figure 18.2.4)—increase in diameter, adding a new outer layer of connective tissue, blood vessels, and theca cells—cells that work with the granulosa cells to produce estrogens.

Within the growing secondary follicle, the primary oocyte now secretes a thin acellular membrane called the zona pellucida that will play a critical role in fertilization. A thick fluid, called follicular fluid, that has formed between the granulosa cells also begins to collect into one large pool, or antrum. Follicles in which the antrum has become large and fully formed are considered tertiary follicles (or antral follicles). Several follicles reach the tertiary stage at the same time, and most of these will undergo atresia. The one that does not die will continue to grow and develop until ovulation, when it will expel its secondary oocyte surrounded by several layers of granulosa cells from the ovary. Keep in mind that most follicles don't make it to this point. In fact, roughly 99 percent of the follicles in the ovary will undergo atresia, which can occur at any stage of folliculogenesis.

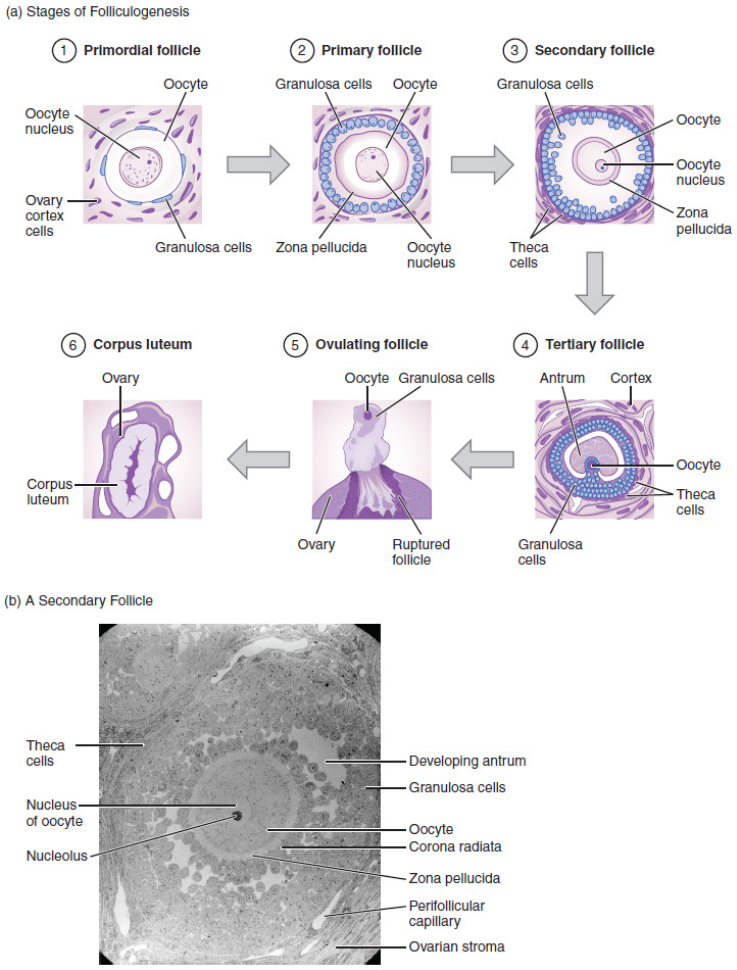


Figure 18.2.4: Folliculogenesis (a) The maturation of a follicle is shown in a clockwise direction proceeding from the primordial follicles. FSH stimulates the growth of a tertiary follicle, and LH stimulates the production of estrogen by granulosa and theca cells. Once the follicle is mature, it ruptures and releases the oocyte. Cells remaining in the follicle then develop into the corpus luteum. (b) In this electron micrograph of a secondary follicle, the oocyte, theca cells (thecae folliculi), and developing antrum are clearly visible. EM × 1100. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

Hormonal Control of the Ovarian Cycle

The process of development that we have just described, from primordial follicle to early tertiary follicle, takes approximately two months in humans. The final stages of development of a small cohort of tertiary follicles, ending with ovulation of a secondary oocyte, occur over a course of approximately 28 days. These changes are regulated by many of the same hormones that regulate the male reproductive system, including GnRH, LH, and FSH.

As in males, the hypothalamus produces GnRH, a hormone that signals the anterior pituitary gland to produce the gonadotropins FSH and LH (Figure 18.2.5). These gonadotropins leave the pituitary and travel through the bloodstream to the ovaries, where they bind to receptors on the granulosa and theca cells of the follicles. FSH stimulates the follicles to grow (hence its name of follicle-stimulating hormone), and the five or six tertiary follicles expand in diameter. The release of LH also stimulates the granulosa and

theca cells of the follicles to produce the sex steroid hormone estradiol, a type of estrogen. This phase of the ovarian cycle, when the tertiary follicles are growing and secreting estrogen, is known as the follicular phase.

The more granulosa and theca cells a follicle has (that is, the larger and more developed it is), the more estrogen it will produce in response to LH stimulation. As a result of these large follicles producing large amounts of estrogen, systemic plasma estrogen concentrations increase. Following a classic negative feedback loop, the high concentrations of estrogen will stimulate the hypothalamus and pituitary to reduce the production of GnRH, LH, and FSH. Because the large tertiary follicles require FSH to grow and survive at this point, this decline in FSH caused by negative feedback leads most of them to die (atresia). Typically only one follicle, now called the dominant follicle, will survive this reduction in FSH, and this follicle will be the one that releases an oocyte. Scientists have studied many factors that lead to a particular follicle becoming dominant: size, the number of granulosa cells, and the number of FSH receptors on those granulosa cells all contribute to a follicle becoming the one surviving dominant follicle.

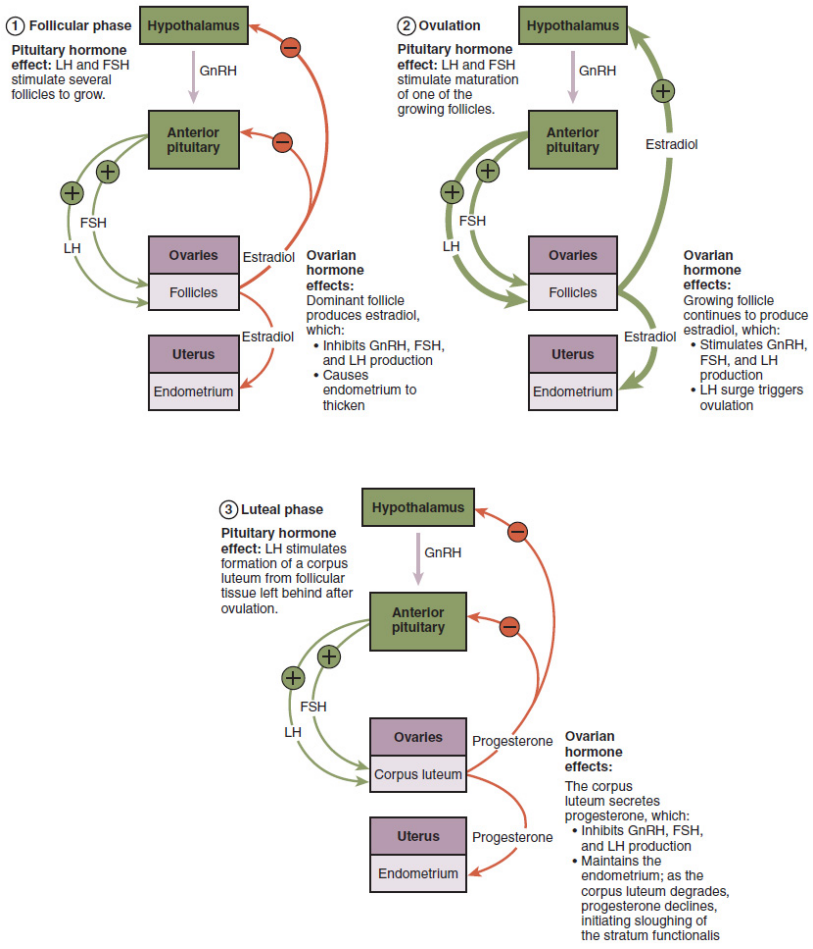


Figure 18.2.5: Hormonal Regulation of Ovulation The hypothalamus and pituitary gland regulate the ovarian cycle and ovulation. GnRH activates the anterior pituitary to produce LH and FSH, which stimulate the production of estrogen and progesterone by the ovaries.

When only the one dominant follicle remains in the ovary, it again begins to secrete estrogen. It produces more estrogen than all of the developing follicles did together before the negative feedback occurred. It produces so much estrogen that the normal negative feedback doesn't occur. Instead, these extremely high concentrations of systemic plasma estrogen trigger a regulatory switch in the anterior pituitary that responds by secreting large amounts of LH and FSH into the bloodstream (see Figure 27.13). The positive feedback loop by which more estrogen triggers release of more LH and FSH only occurs at this point in the cycle.

It is this large burst of LH (called the LH surge) that leads to ovulation of the dominant follicle. The LH surge induces many changes in the dominant follicle, including stimulating the resumption of meiosis of the primary oocyte to a secondary oocyte. As noted earlier, the polar body that results from unequal cell division simply degrades. The LH surge also triggers proteases (enzymes that cleave proteins) to break down structural proteins in the ovary wall on the surface of the bulging dominant follicle. This

degradation of the wall, combined with pressure from the large, fluid-filled antrum, results in the expulsion of the oocyte surrounded by granulosa cells into the peritoneal cavity. This release is ovulation.

In the next section, you will follow the ovulated oocyte as it travels toward the uterus, but there is one more important event that occurs in the ovarian cycle. The surge of LH also stimulates a change in the granulosa and theca cells that remain in the follicle after the oocyte has been ovulated. This change is called luteinization (recall that the full name of LH is luteinizing hormone), and it transforms the collapsed follicle into a new endocrine structure called the corpus luteum, a term meaning “yellowish body” (see Figure 27.12). Instead of estrogen, the luteinized granulosa and theca cells of the corpus luteum begin to produce large amounts of the sex steroid hormone progesterone, a hormone that is critical for the establishment and maintenance of pregnancy. Progesterone triggers negative feedback at the hypothalamus and pituitary, which keeps GnRH, LH, and FSH secretions low, so no new dominant follicles develop at this time.

The post-ovulatory phase of progesterone secretion is known as the luteal phase of the ovarian cycle. If pregnancy does not occur within 10 to 12 days, the corpus luteum will stop secreting progesterone and degrade into the corpus albicans, a nonfunctional “whitish body” that will disintegrate in the ovary over a period of several months. During this time of reduced progesterone secretion, FSH and LH are once again stimulated, and the follicular phase begins again with a new cohort of early tertiary follicles beginning to grow and secrete estrogen.

The Uterine Tubes

The uterine tubes (also called fallopian tubes or oviducts) serve as the conduit of the oocyte from the ovary to the uterus (Figure 18.2.6). Each of the two uterine tubes is close to, but not directly connected to, the ovary and divided into sections. The isthmus is the narrow medial end of each uterine tube that is connected to the uterus. The wide distal infundibulum flares out with slender, finger-like projections called fimbriae. The middle region of the tube, called the ampulla, is where fertilization often occurs. The uterine tubes also have three layers: an outer serosa, a middle smooth muscle layer, and an inner mucosal layer. In addition to its mucus-secreting cells, the inner mucosa contains ciliated cells that beat in the direction of the uterus, producing a current that will be critical to move the oocyte.

Following ovulation, the secondary oocyte surrounded by a few granulosa cells is released into the peritoneal cavity. The nearby uterine tube, either left or right, receives the oocyte. Unlike sperm, oocytes lack flagella, and therefore cannot move on their own. So how do they travel into the uterine tube and toward the uterus? High concentrations of estrogen that occur around the time of ovulation induce contractions of the smooth muscle along the length of the uterine tube. These contractions occur every 4 to 8 seconds, and the result is a coordinated movement that sweeps the surface of the ovary and the pelvic cavity. Current flowing toward the uterus is generated by coordinated beating of the cilia that line the outside and lumen of the length of the uterine tube. These cilia beat more strongly in response to the high estrogen concentrations that occur around the time of ovulation. As a result of these mechanisms, the oocyte–granulosa cell complex is pulled into the interior of the tube. Once inside, the muscular contractions and beating cilia move the oocyte slowly toward the uterus. When fertilization does occur, sperm typically meet the egg while it is still moving through the ampulla.

Interactive Link

Interactive Link

Watch this video to observe ovulation and its initiation in response to the release of FSH and LH from the pituitary gland. What specialized structures help guide the oocyte from the ovary into the uterine tube?

If the oocyte is successfully fertilized, the resulting zygote will begin to divide into two cells, then four, and so on, as it makes its way through the uterine tube and into the uterus. There, it will implant and continue to grow. If the egg is not fertilized, it will simply degrade—either in the uterine tube or in the uterus, where it may be shed with the next menstrual period.

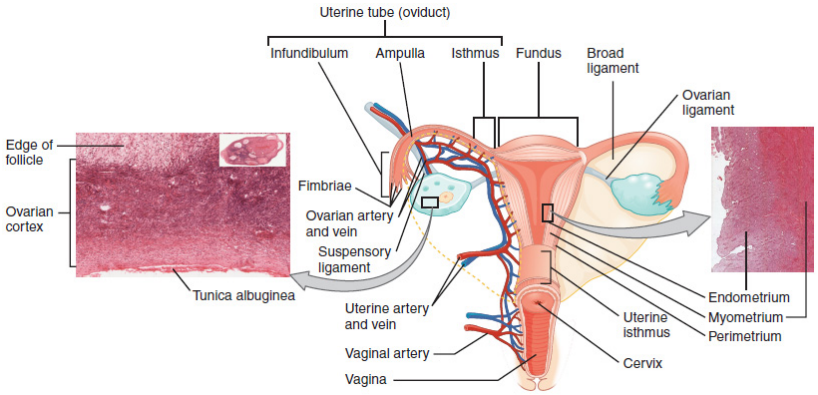
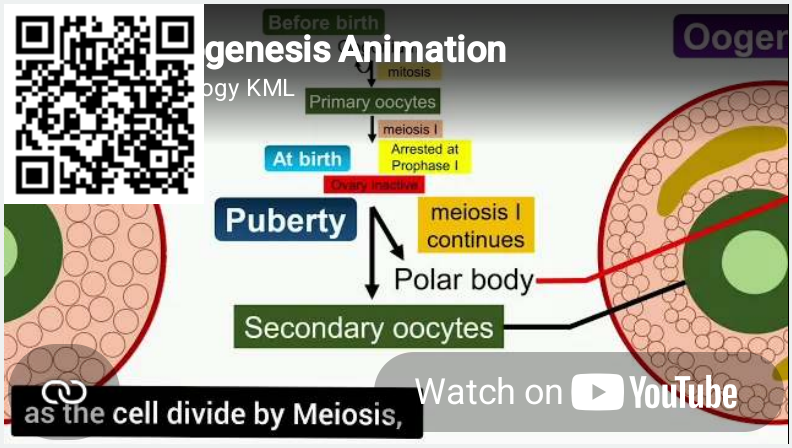


Figure 18.2.6: Ovaries, Uterine Tubes, and Uterus This anterior view shows the relationship of the ovaries, uterine tubes (oviducts), and uterus. Sperm enter through the vagina, and fertilization of an ovulated oocyte usually occurs in the distal uterine tube. From left to right, LM × 400, LM × 20. (Micrographs provided by the Regents of University of Michigan Medical School © 2012)

The open-ended structure of the uterine tubes can have significant health consequences if bacteria or other contagions enter through the vagina and move through the uterus, into the tubes, and then into the pelvic cavity. If this is left unchecked, a bacterial infection (sepsis) could quickly become life-threatening. The spread of an infection in this manner is of special concern when unskilled practitioners perform abortions in non-sterile conditions. Sepsis is also associated with sexually transmitted bacterial infections, especially gonorrhea and chlamydia. These increase a person's risk for pelvic inflammatory disease (PID), infection of the uterine tubes or other reproductive organs. Even when resolved, PID can leave scar tissue in the tubes, leading to infertility.

Interactive Link



Interactive Link

Watch this series of videos to look at the movement of the oocyte through the ovary. The cilia in the uterine tube promote movement of the oocyte. What would likely occur if the cilia were paralyzed at the time of ovulation?

The Uterus and Cervix

The uterus is the muscular organ that nourishes and supports the growing embryo (see Figure 18.2.6). Its average size is approximately 5 cm wide by 7 cm long (approximately 2 in by 3 in) when a female is not pregnant. It has three sections. The

portion of the uterus superior to the opening of the uterine tubes is called the fundus. The middle section of the uterus is called the body of uterus (or corpus). The cervix is the narrow inferior portion of the uterus that projects into the vagina. The cervix produces mucus secretions that become thin and stringy under the influence of high systemic plasma estrogen concentrations, and these secretions can facilitate sperm movement through the reproductive tract.

Several ligaments maintain the position of the uterus within the abdominopelvic cavity. The broad ligament is a fold of peritoneum that serves as a primary support for the uterus, extending laterally from both sides of the uterus and attaching it to the pelvic wall. The round ligament attaches to the uterus near the uterine tubes, and extends to the labia majora. Finally, the uterosacral ligament stabilizes the uterus posteriorly by its connection from the cervix to the pelvic wall.

The wall of the uterus is made up of three layers. The most superficial layer is the serous membrane, or perimetrium, which consists of epithelial tissue that covers the exterior portion of the uterus. The middle layer, or myometrium, is a thick layer of smooth muscle responsible for uterine contractions. Most of the uterus is myometrial tissue, and the muscle fibers run horizontally, vertically, and diagonally, allowing the powerful contractions that occur during labor and the less powerful contractions (or cramps) that help to expel menstrual blood during a woman's period. Anteriorly directed myometrial contractions also occur near the time of ovulation, and are thought to possibly facilitate the transport of sperm through the female reproductive tract.

The innermost layer of the uterus is called the endometrium. The endometrium contains a connective tissue lining, the lamina propria, which is covered by epithelial tissue that lines the lumen. Structurally, the endometrium consists of two layers: the stratum basalis and the stratum functionalis (the basal and functional layers). The stratum basalis layer is part of the lamina propria and is adjacent to the myometrium; this layer does not shed during menses. In contrast, the thicker stratum functionalis layer contains the glandular portion of the lamina propria and the endothelial tissue that lines the uterine lumen. It is the stratum functionalis that grows and thickens in response to increased levels of estrogen and progesterone. In the luteal phase of the menstrual cycle, special branches off of the uterine artery called spiral arteries supply the thickened stratum functionalis. This inner functional layer provides the proper site of implantation for the fertilized egg, and—should fertilization not occur—it is only the stratum functionalis layer of the endometrium that sheds during menstruation.

Recall that during the follicular phase of the ovarian cycle, the tertiary follicles are growing and secreting estrogen. At the same time, the stratum functionalis of the endometrium is thickening to prepare for a potential implantation. The post-ovulatory increase in progesterone, which characterizes the luteal phase, is key for maintaining a thick stratum functionalis. As long as a functional corpus luteum is present in the ovary, the endometrial lining is prepared for implantation. Indeed, if an embryo implants, signals are sent to the corpus luteum to continue secreting progesterone to maintain the endometrium, and thus maintain the pregnancy. If an embryo does not implant, no signal is sent to the corpus luteum and it degrades, ceasing progesterone production and ending the luteal phase. Without progesterone, the endometrium thins and, under the influence of prostaglandins, the spiral arteries of the endometrium constrict and rupture, preventing oxygenated blood from reaching the endometrial tissue. As a result, endometrial tissue dies and blood, pieces of the endometrial tissue, and white blood cells are shed through the vagina during menstruation, or the menses. The first menses after puberty, called menarche, can occur either before or after the first ovulation.

The Menstrual Cycle

Now that we have discussed the maturation of the cohort of tertiary follicles in the ovary, the build-up and then shedding of the endometrial lining in the uterus, and the function of the uterine tubes and vagina, we can put everything together to talk about the three phases of the menstrual cycle—the series of changes in which the uterine lining is shed, rebuilds, and prepares for implantation.

The timing of the menstrual cycle starts with the first day of menses, referred to as day one of a period. Cycle length is determined by counting the days between the onset of bleeding in two subsequent cycles. Because the average length of a menstrual cycle is 28 days, this is the time period used to identify the timing of events in the cycle. However, the length of the menstrual cycle varies, and even in the same person from one cycle to the next, typically from 21 to 32 days.

Just as the hormones produced by the granulosa and theca cells of the ovary "drive" the follicular and luteal phases of the ovarian cycle, they also control the three distinct phases of the menstrual cycle. These are the menses phase, the proliferative phase, and the secretory phase.

Menses Phase

The menses phase of the menstrual cycle is the phase during which the lining is shed; that is, the days that the person menstruates. Although it averages approximately five days, the menses phase can last from 2 to 7 days, or longer. As shown in Figure 18.2.7, the

menses phase occurs during the early days of the follicular phase of the ovarian cycle, when progesterone, FSH, and LH levels are low. Recall that progesterone concentrations decline as a result of the degradation of the corpus luteum, marking the end of the luteal phase. This decline in progesterone triggers the shedding of the stratum functionalis of the endometrium.

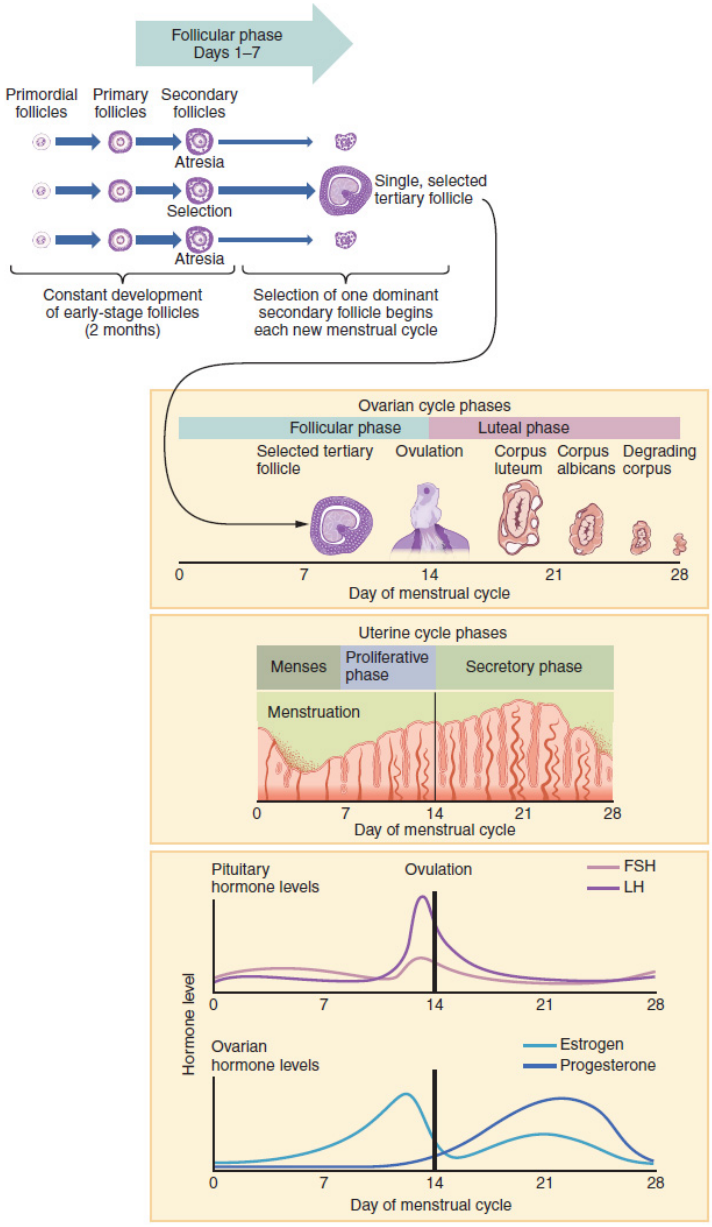


Figure 18.2.7: Hormone Levels in Ovarian and Menstrual Cycles The correlation of the hormone levels and their effects on the female reproductive system is shown in this timeline of the ovarian and menstrual cycles. The menstrual cycle begins at day one with the start of menses. Ovulation occurs around day 14 of a 28-day cycle, triggered by the LH surge.

Proliferative Phase

Once menstrual flow ceases, the endometrium begins to proliferate again, marking the beginning of the proliferative phase of the menstrual cycle (see Figure 27.15). It occurs when the granulosa and theca cells of the tertiary follicles begin to produce increased amounts of estrogen. These rising estrogen concentrations stimulate the endometrial lining to rebuild.

Recall that the high estrogen concentrations will eventually lead to a decrease in FSH as a result of negative feedback, resulting in atresia of all but one of the developing tertiary follicles. The switch to positive feedback—which occurs with the elevated estrogen production from the dominant follicle—then stimulates the LH surge that will trigger ovulation. In a typical 28-day menstrual cycle, ovulation occurs on day 14. Ovulation marks the end of the proliferative phase as well as the end of the follicular phase.

Secretory Phase

In addition to prompting the LH surge, high estrogen levels increase the uterine tube contractions that facilitate the pick-up and transfer of the ovulated oocyte. High estrogen levels also slightly decrease the acidity of the vagina, making it more hospitable to sperm. In the ovary, the luteinization of the granulosa cells of the collapsed follicle forms the progesterone-producing corpus luteum, marking the beginning of the luteal phase of the ovarian cycle. In the uterus, progesterone from the corpus luteum begins the secretory phase of the menstrual cycle, in which the endometrial lining prepares for implantation (see Figure 27.15). Over the next 10 to 12 days, the endometrial glands secrete a fluid rich in glycogen. If fertilization has occurred, this fluid will nourish the ball of cells now developing from the zygote. At the same time, the spiral arteries develop to provide blood to the thickened stratum functionalis.

If no pregnancy occurs within approximately 10 to 12 days, the corpus luteum will degrade into the corpus albicans. Levels of both estrogen and progesterone will fall, and the endometrium will grow thinner. Prostaglandins will be secreted that cause constriction of the spiral arteries, reducing oxygen supply. The endometrial tissue will die, resulting in menses—or the first day of the next cycle.

Disorders of the...

Female Reproductive System

Research over many years has confirmed that cervical cancer is most often caused by a sexually transmitted infection with human papillomavirus (HPV). There are over 100 related viruses in the HPV family, and the characteristics of each strain determine the outcome of the infection. In all cases, the virus enters body cells and uses its own genetic material to take over the host cell's metabolic machinery and produce more virus particles.

HPV infections are common in all people. Indeed, a recent study determined that 42.5 percent of females had HPV at the time of testing. These people ranged in age from 14 to 59 years and differed in race, ethnicity, and number of sexual partners. Of note, the prevalence of HPV infection was 53.8 percent among females aged 20 to 24 years, the age group with the highest infection rate.

HPV strains are classified as high or low risk according to their potential to cause cancer. Though most HPV infections do not cause disease, the disruption of normal cellular functions in the low-risk forms of HPV can cause the human host to develop genital warts. Often, the body is able to clear an HPV infection by normal immune responses within 2 years. However, the more serious, high-risk infection by certain types of HPV can result in cancer of the cervix (Figure 18.2.8). Infection with either of the cancer-causing variants HPV 16 or HPV 18 has been linked to more than 70 percent of all cervical cancer diagnoses. Although even these high-risk HPV strains can be cleared from the body over time, infections persist in some individuals. If this happens, the HPV infection can influence the cells of the cervix to develop precancerous changes.

Risk factors for cervical cancer include having unprotected sex; having multiple sexual partners; a first sexual experience at a younger age, when the cells of the cervix are not fully mature; failure to receive the HPV vaccine; a compromised immune system; and smoking. The risk of developing cervical cancer is doubled with cigarette smoking.

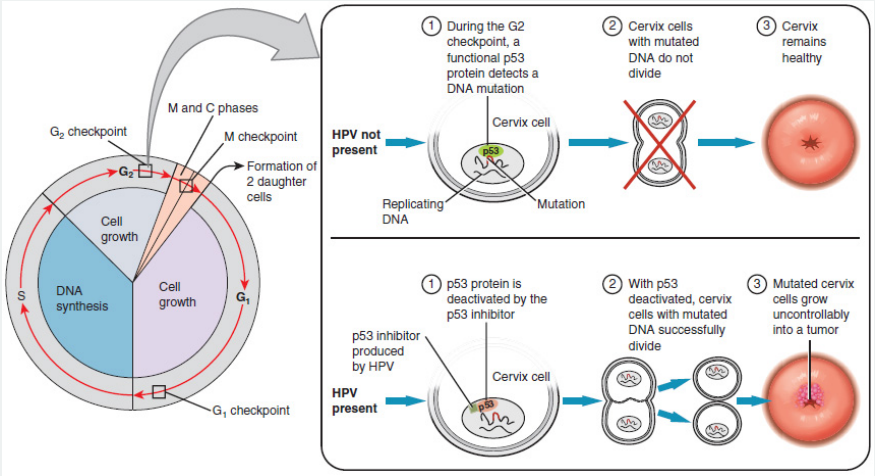


Figure 18.2.8: Development of Cervical Cancer In most cases, cells infected with the HPV virus heal on their own. In some cases, however, the virus continues to spread and becomes an invasive cancer.

When the high-risk types of HPV enter a cell, two viral proteins are used to neutralize proteins that the host cells use as checkpoints in the cell cycle. The best studied of these proteins is p53. In a normal cell, p53 detects DNA damage in the cell's genome and either halts the progression of the cell cycle—allowing time for DNA repair to occur—or initiates apoptosis. Both of these processes prevent the accumulation of mutations in a cell's genome. High-risk HPV can neutralize p53, keeping the cell in a state in which fast growth is possible and impairing apoptosis, allowing mutations to accumulate in the cellular DNA.

The prevalence of cervical cancer in the United States is very low because of regular screening exams called pap smears. Pap smears sample cells of the cervix, allowing the detection of abnormal cells. If pre-cancerous cells are detected, there are several highly effective techniques that are currently in use to remove them before they pose a danger. However, people in lower-income countries often do not have access to regular pap smears. As a result, these females in lower-income countries account for as many as 80 percent of the cases of cervical cancer worldwide.

In 2006, the first vaccine against the high-risk types of HPV was approved. There are now two HPV vaccines available: Gardasil® and Cervarix®. Whereas these vaccines were initially only targeted for females, because HPV is sexually transmitted, all people require vaccination for this approach to achieve its maximum efficacy. A recent study suggests that the HPV vaccine has cut the rates of HPV infection by the four targeted strains at least in half. Unfortunately, the high cost of manufacturing the vaccine is currently limiting access to many people worldwide.

The Breasts

Whereas the breasts are located far from the other female reproductive organs, they are considered accessory organs of the female reproductive system. The function of the breasts is to supply milk to an infant in a process called lactation. The external features of the breast include a nipple surrounded by a pigmented areola (Figure 18.2.9), whose coloration may deepen during pregnancy. The areola is typically circular and can vary in size from 25 to 100 mm in diameter. The areolar region is characterized by small, raised areolar glands that secrete lubricating fluid during lactation to protect the nipple from chafing. When a baby nurses, or draws milk from the breast, the entire areolar region is taken into the mouth.

Breast milk is produced by the mammary glands, which are modified sweat glands. The milk itself exits the breast through the nipple via 15 to 20 lactiferous ducts that open on the surface of the nipple. These lactiferous ducts each extend to a lactiferous sinus that connects to a glandular lobe within the breast itself that contains groups of milk-secreting cells in clusters called alveoli (see Figure 18.2.9). The clusters can change in size depending on the amount of milk in the alveolar lumen. Once milk is made in the alveoli, stimulated myoepithelial cells that surround the alveoli contract to push the milk to the lactiferous sinuses. From here, the baby can draw milk through the lactiferous ducts by suckling. The lobes themselves are surrounded by fat tissue, which determines the size of the breast; breast size differs between individuals and does not affect the amount of milk produced. Supporting the breasts are multiple bands of connective tissue called suspensory ligaments that connect the breast tissue to the dermis of the overlying skin.

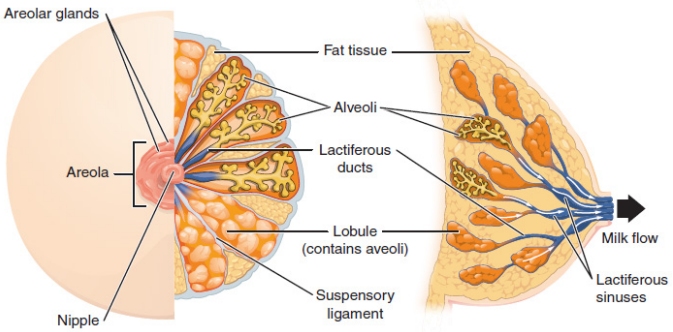


Figure 18.2.9: Anatomy of the Breast During lactation, milk moves from the alveoli through the lactiferous ducts to the nipple.

During the normal hormonal fluctuations in the menstrual cycle, breast tissue responds to changing levels of estrogen and progesterone, which can lead to swelling and breast tenderness in some individuals, especially during the secretory phase. If pregnancy occurs, the increase in hormones leads to further development of the mammary tissue and enlargement of the breasts.

Hormonal Birth Control

Birth control pills take advantage of the negative feedback system that regulates the ovarian and menstrual cycles to stop ovulation and prevent pregnancy. Typically they work by providing a constant level of both estrogen and progesterone, which negatively feeds back onto the hypothalamus and pituitary, thus preventing the release of FSH and LH. Without FSH, the follicles do not mature, and without the LH surge, ovulation does not occur. Although the estrogen in birth control pills does stimulate some thickening of the endometrial wall, it is reduced compared with a normal cycle and is less likely to support implantation.

Some birth control pills contain 21 active pills containing hormones, and 7 inactive pills (placebos). The decline in hormones during the week that the person takes the placebo pills triggers menses, although it is typically lighter than a normal menstrual flow because of the reduced endometrial thickening. Newer types of birth control pills have been developed that deliver low-dose estrogens and progesterone for the entire cycle (these are meant to be taken 365 days a year), and menses never occurs. While some people prefer to have the proof of a lack of pregnancy that a monthly period provides, menstruation every 28 days is not required for health reasons, and there are no reported adverse effects of not having a menstrual period in an otherwise healthy individual.

Because birth control pills function by providing constant estrogen and progesterone levels and disrupting negative feedback, skipping even just one or two pills at certain points of the cycle (or even being several hours late taking the pill) can lead to an increase in FSH and LH and result in ovulation. It is important, therefore, to follow the directions on the birth control pill package to successfully prevent pregnancy.

Aging and the...

Female Reproductive System

Female fertility (the ability to conceive) peaks when people are in their twenties, and is slowly reduced until 35 years of age. After that time, fertility declines more rapidly, until it ends completely at the end of menopause. Menopause is the cessation of the menstrual cycle that occurs as a result of the loss of ovarian follicles and the hormones that they produce. Menopause is considered complete if an individual has not menstruated in a full year. After that point, they are considered postmenopausal. The average age for this change is consistent worldwide at between 50 and 52 years of age, but it can normally occur at any time in a person's forties or fifties. Poor health, including smoking, can lead to earlier loss of fertility and earlier menopause.

As the age of menopause approaches, depletion of the number of viable follicles in the ovaries due to atresia affects the hormonal regulation of the menstrual cycle. During the years leading up to menopause, there is a decrease in the levels of the hormone inhibin, which normally participates in a negative feedback loop to the pituitary to control the production of FSH. The menopausal decrease in inhibin leads to an increase in FSH. The presence of FSH stimulates more follicles to grow and secrete estrogen. Because small, secondary follicles also respond to increases in FSH levels, larger numbers of follicles are stimulated to grow; however, most undergo atresia and die. Eventually, this process leads to the depletion of all follicles in the ovaries, and the production of estrogen falls off dramatically. It is primarily the lack of estrogens that leads to the symptoms of menopause.

The earliest changes occur during the menopausal transition, often referred to as peri-menopause, when a mestrual cycle becomes irregular but does not stop entirely. Although the levels of estrogen are still nearly the same as before the transition, the level of progesterone produced by the corpus luteum is reduced. This decline in progesterone can lead to abnormal growth, or hyperplasia, of the endometrium. This condition is a concern because it increases the risk of developing endometrial cancer. Two harmless conditions that can develop during the transition are uterine fibroids, which are benign masses of cells, and irregular bleeding. As estrogen levels change, other symptoms that occur are hot flashes and night sweats, trouble sleeping, vaginal dryness, mood swings, difficulty focusing, and thinning of hair on the head along with the growth of more hair on the face. Depending on the individual, these symptoms can be entirely absent, moderate, or severe.

After menopause, lower amounts of estrogens can lead to other changes. Cardiovascular disease becomes as prevalent in females as in males, possibly because estrogens reduce the amount of cholesterol in the blood vessels. When estrogen is lacking, many people find that they suddenly have problems with high cholesterol and the cardiovascular issues that accompany it. Osteoporosis is another problem because bone density decreases rapidly in the first years after menopause. The reduction in bone density leads to a higher incidence of fractures.

Hormone therapy (HT), which employs medication (synthetic estrogens and progestins) to increase estrogen and progestin levels, can alleviate some of the symptoms of menopause. In 2002, the Women’s Health Initiative began a study to observe for the long-term outcomes of hormone replacement therapy over 8.5 years. However, the study was prematurely terminated after

5.2 years because of evidence of a higher than normal risk of breast cancer in patients taking estrogen-only HT. The potential positive effects on cardiovascular disease were also not realized in the estrogen-only patients. The results of other hormone replacement studies over the last 50 years, including a 2012 study that followed over 1,000 menopausal women for 10 years, have shown cardiovascular benefits from estrogen and no increased risk for cancer. Some researchers believe that the age group tested in the 2002 trial may have been too old to benefit from the therapy, thus skewing the results. In the meantime, intense debate and study of the benefits and risks of replacement therapy is ongoing. Current guidelines approve HT for the reduction of hot flashes or flushes, but this treatment is generally only considered when people first start showing signs of menopausal changes, is used in the lowest dose possible for the shortest time possible (5 years or less), and it is suggested that people on HT have regular pelvic and breast exams.

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CHAPTER OVERVIEW

19: Optional Reading

19.1: Accessory Structures of the Skin
19.2: Functions of the Integumentary System
19.3: Bone Formation and Development
19.4: Divisions of the Skeletal System
19.4.1: The Skull
19.4.2: The Vertebral Column
19.4.3: The Thoracic Cage
19.4.4: The Pectoral Girdle
19.4.5: Bones of the Upper Limb
19.4.6: The Pelvic Girdle and Pelvis
19.4.7: Bones of the Lower Limb
19.5: Introduction to the Muscular System
19.5.1: Axial Muscles of the Head, Neck, and Back
19.5.2: Axial Muscles of the Abdominal Wall and Thorax
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
19.6: Special Senses - Others
19.7: Coronary Circulation
19.8: Mean Arterial Pressure and Pulse Pressure

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19.1: Accessory Structures of the Skin

Learning Objectives

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

- 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 19.1.1).

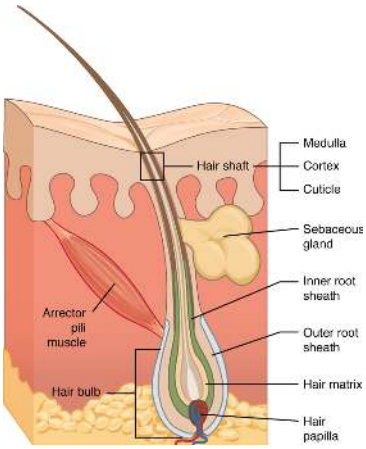


Figure 19.1.1: Hair Hair follicles originate in the epidermis and have many different parts.

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 19.1.2), 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.

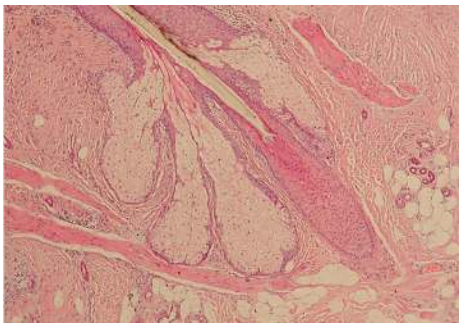


Figure 19.1.2: Hair Follicle The slide shows a cross-section of a hair follicle. Basal cells of the hair matrix in the center differentiate into cells of the inner root sheath. Basal cells at the base of the hair root form the outer root sheath. LM × 4. (credit: modification of work by “kilbad”/Wikimedia 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.

Interactive Link

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.

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 19.1.3). 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.

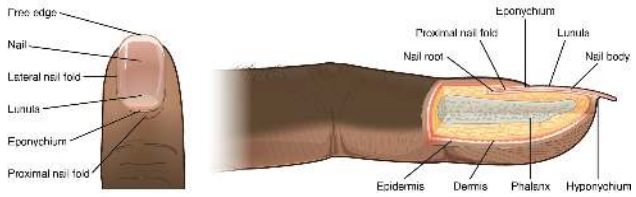


Figure 19.1.3: Nails The nail is an accessory structure of the integumentary system

Interactive Link

Nails are accessory structures of the integumentary system. Visit this link to learn more about the origin and growth of fingernails.

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 19.1.4). 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.

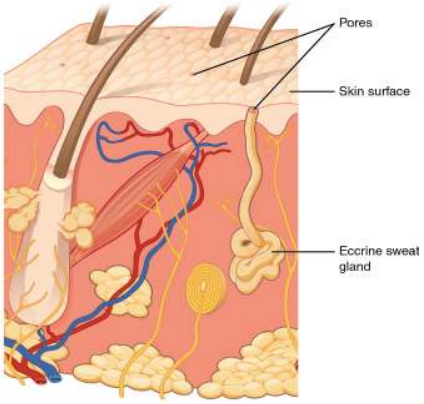


Figure 19.1.4: Eccrine Gland Eccrine glands are coiled glands in the dermis that release sweat that is mostly water.

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.

Interactive Link

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.

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19.2: Functions of the Integumentary System

Learning Objectives

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

- 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.

Interactive Link

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. Watch this video 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 19.2.1), 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.

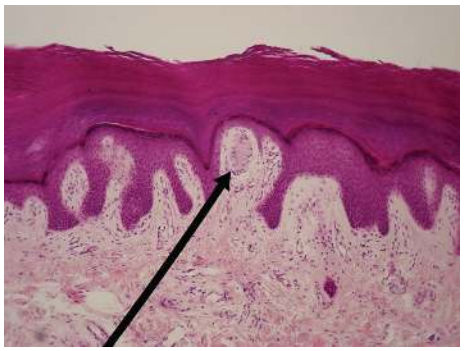


Figure 19.2.1: Light Micrograph of a Meissner Corpuscle In this micrograph of a skin cross-section, you can see a Meissner corpuscle (arrow), a type of touch receptor located in a dermal papilla adjacent to the basement membrane and stratum basale of the overlying epidermis. LM × 100. (credit: “Wbensmith”/Wikimedia 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 (19.2.2**ac**), 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 19.2.2**b**). This accounts for the skin redness that many people experience when exercising.

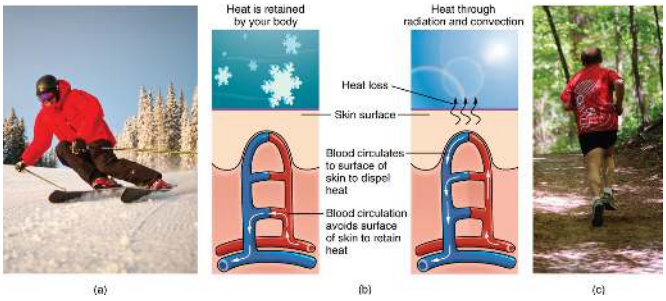


Figure 19.2.2: Thermoregulation During strenuous physical activities, such as skiing (a) or running (c), the dermal blood vessels dilate and sweat secretion increases (b). These mechanisms prevent the body from overheating. In contrast, the dermal blood vessels constrict to minimize heat loss in response 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 19.2.3). 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 19.2.3: Aging 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.

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19.3: Bone Formation and Development

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

- 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, which are surrounded by a lacuna. Unlike most connective tissues, cartilage is avascular, meaning that it has no blood vessels supplying nutrients and removing metabolic wastes. 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 19.3.1.*a*). Some of these cells differentiate and form the tissues of 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 19.3.1.*b*). 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. At the surfaces of the forming osseus tissue mesenchymal cells differentiate into fibroblasts which surround the forming structure with fibrous periosteum while osteoblasts, osteoclasts and osteogenic cells form the cellular (osteogenic) layer. (Figure 19.3.1.*c*). 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 19.3.1.*d*).

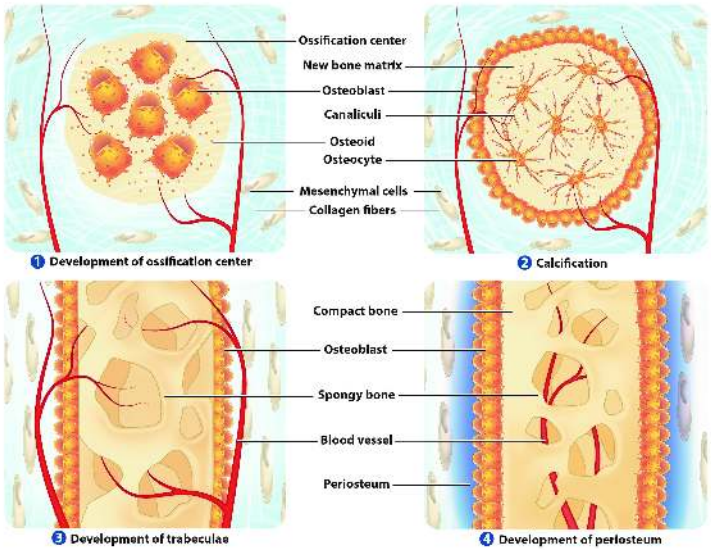


Figure 19.3.1: Intramembranous Ossification. Intramembranous ossification follows four steps. (1) Cells group into clusters and ossification centers form. (2) Secreted osteoid traps osteoblasts, which then become osteocytes. (3) Trabeculae of cancellous (spongy) form. (d) Compact bone develops superficial to the cancellous bone, and periosteum forms. *(Image credit: "Intramembraneous Ossification" by BlueLink is licensed under CC BY-NC 4.0 with notification of the original authors.)*

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 are examples of bones that 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 19.3.2.1). Soon after, cellular differentiation produces cells that form the **perichondrium**, a membrane that covers the cartilage.

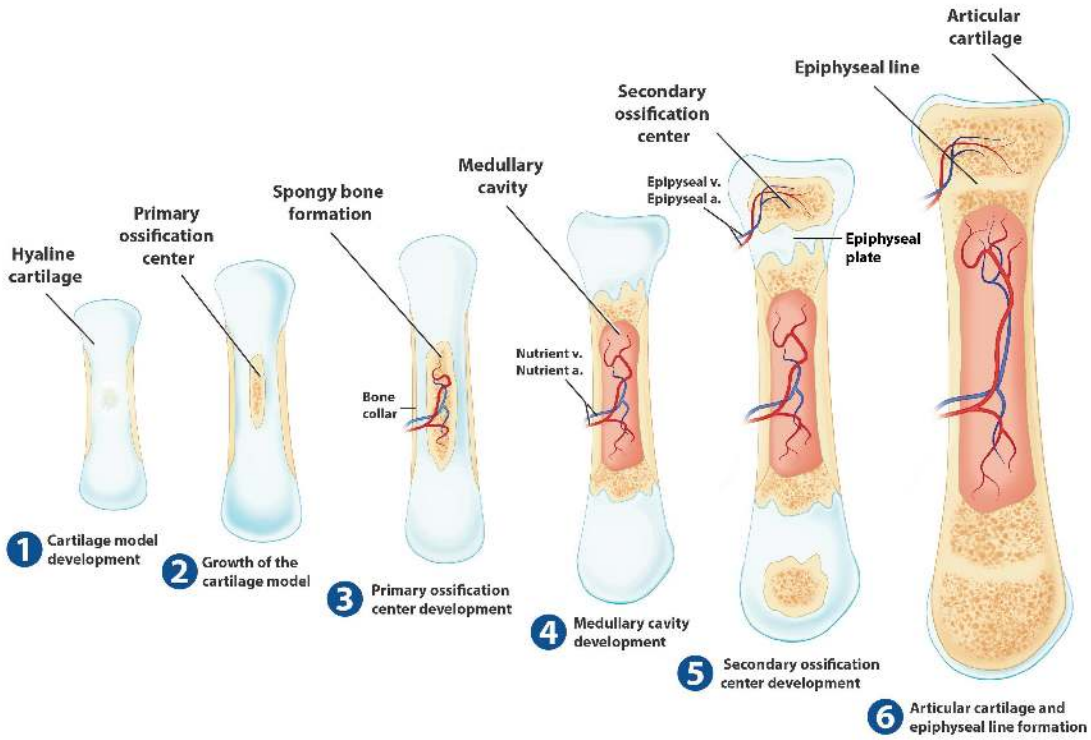


Figure 19.3.2: Endochondral Ossification. Endochondral ossification follows five steps. (1) Mesenchymal cells differentiate into chondrocytes and form the cartilage model. (2) The cartilage model of the future bony skeleton and the perichondrium grows. (3) Capillaries penetrate cartilage. Periosteal bone collar develops and primary ossification center develops. (4) Cartilage and chondrocytes continue to grow at ends of the bone; the medullary cavity forms. (5) Secondary ossification centers develop in the epiphyses; cartilage remains at epiphyseal (growth) plate. (6) Epiphyseal plate ossifies and becomes epiphyseal line; cartilage remains only at joint surface as articular cartilage. *(Image credit: "Endochondral Ossification" by BlueLink is licensed under CC BY-NC 4.0 with notification of the original authors.)*

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.

This invasion of blood vessels 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 19.3.2.3).

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 19.3.2.5).

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 19.3.3). 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.

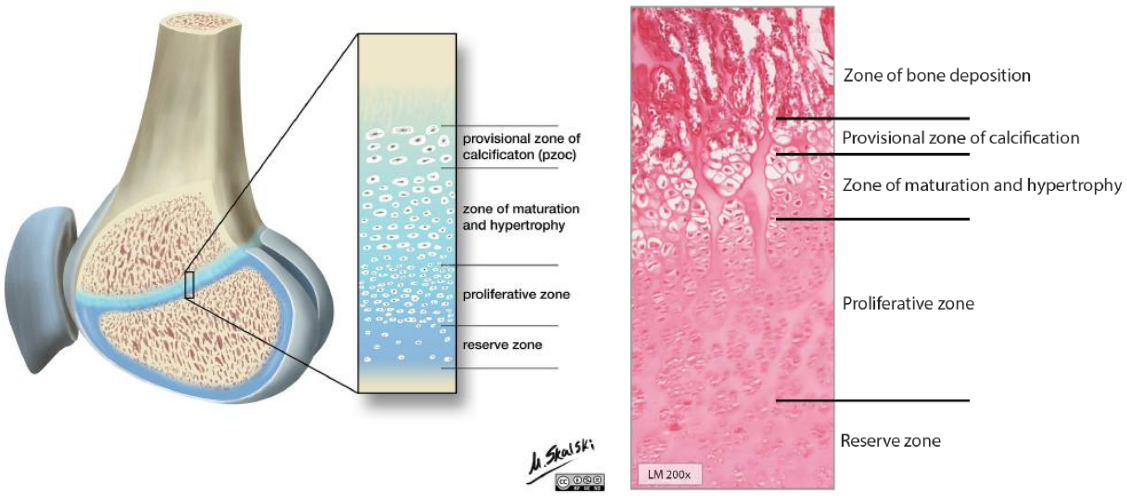


Figure 19.3.3: Longitudinal Bone Growth. The epiphyseal plate is responsible for longitudinal bone growth, displaying five distinct zones of cartilage growth and ossification. *(Image credit - illustration: "Physeal Anatomy" courtesy of Dr. Matt Skalski, Radiopaedia.org, from the case rID: 27354, is licensed under CC BY-NC-ND 4.0). Micrograph: "Longitudinal Bone Growth" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, image provided by the Regents of the University of Michigan Medical School under CC-BY-NC-SA 4.0 © 2022)*

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.

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 19.3.4).

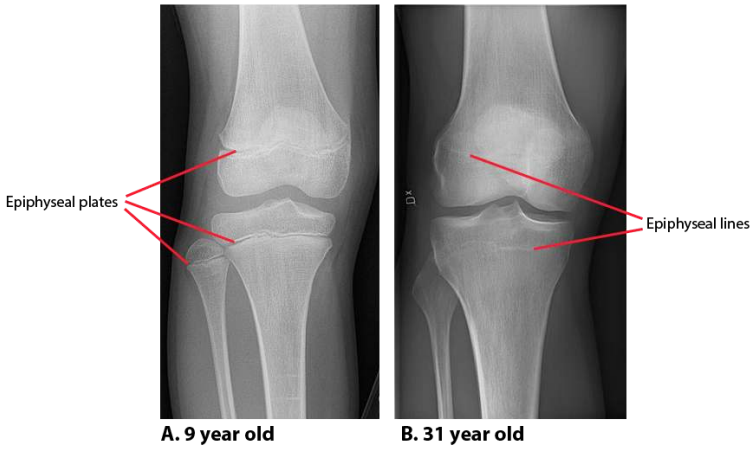


Figure 19.3.4: Epiphyseal Plate to Epiphyseal Line. As a bone matures the epiphyseal plate progresses to an epiphyseal line. (A) Epiphyseal plates are visible in the growing bones of a 9 year old. (B) Epiphyseal lines are the remnants of epiphyseal plates in a mature bone. (Image credit: "Epiphyseal Plate to Epiphyseal Line" by Jennifer Lange is licensed under CC BY-NC-SA 4.0; X-ray A: Staff at the Department of Radiology, UC San Diego Health., Public domain, via Wikimedia Commons; X-ray B: Mikael Häggström, M.D., Public Domain, via Wikimedia Commons)

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 (Figure 19.3.5). Osteoclasts resorb old bone that lines the medullary cavity, while osteoblasts 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**.

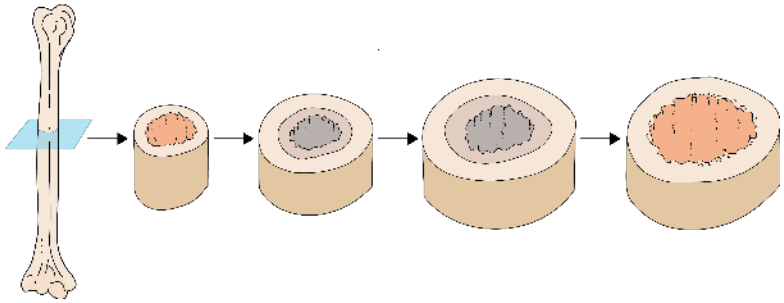


Figure 19.3.5: Appositional Growth. Growth in the diameter of a bone is known as appositional growth. Both osteoblasts and osteoclasts are active during the process of remodeling. ("Appositional Growth" by Daniel Donnelly is licensed under CC BY 4.0)

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 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 (red arrows) 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.

Concept Review

All bone formation is a replacement process. Embryos develop a cartilaginous skeleton and various membranes. During development, these are replaced by bone during the ossification process. In intramembranous ossification, bone develops directly from sheets of mesenchymal connective tissue. In endochondral ossification, bone develops by replacing hyaline cartilage. Activity in the epiphyseal plate enables bones to grow in length. Modeling allows bones to grow in diameter. Remodeling occurs as bone is resorbed and replaced by new bone. Osteogenesis imperfecta is a genetic disease in which collagen production is altered, resulting in fragile, brittle bones.

Review Questions

Critical Thinking Questions

Glossary

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19.4: Divisions of the Skeletal System

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

- Distinguish between the axial skeleton and appendicular skeleton
- Discuss the functions of 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. See Table 19.4.1 for a full list of the bones as well as how many of each are found in the body.

The Axial Skeleton

The **axial skeleton** forms the vertical, central axis of the body and includes all bones of the head, neck, chest, and back (Figure 19.4.1). 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 has two main divisions, the cranial portion and the facial portion, and 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.

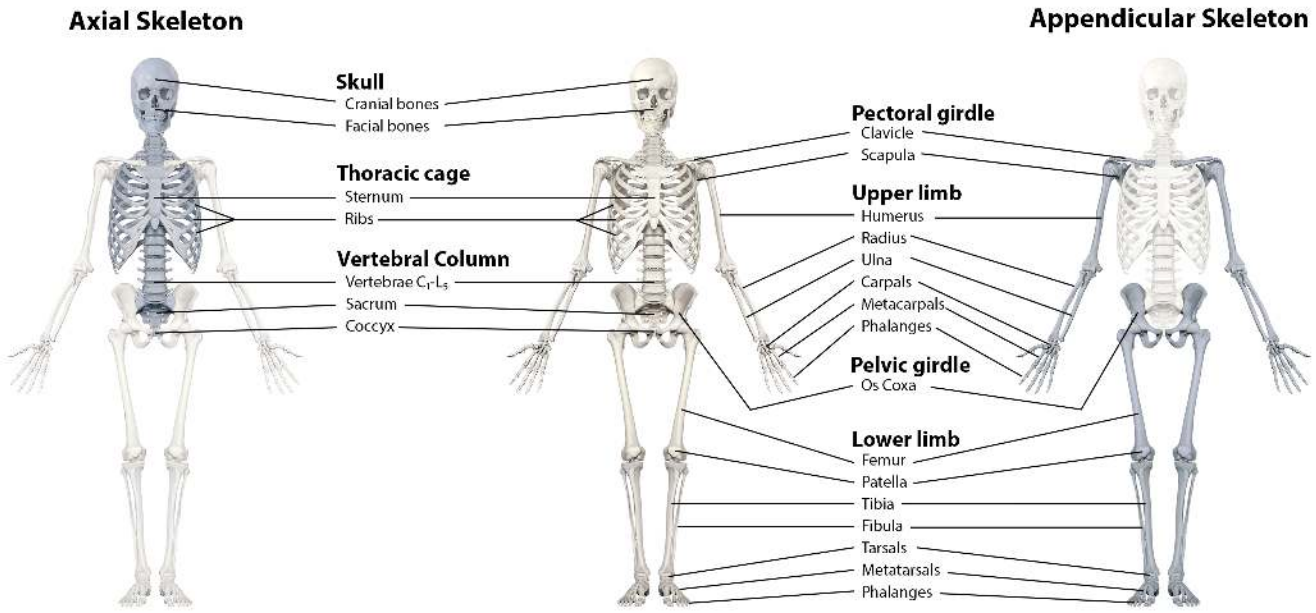


Figure 19.4.1: Axial and Appendicular Skeleton. The axial skeleton supports the head, neck, back, and chest and thus forms the vertical axis of the body. It consists of the skull, vertebral column (including the sacrum and coccyx), and the thoracic cage, formed by the ribs and sternum. The appendicular skeleton is made up of all bones of the upper and lower limbs. *(Image credit: "Axial and Appendicular Skeleton" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of images from Anatomy Standard under CC BY-NC 4.0.)*

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 that attach the upper limbs to the axial skeleton, include the clavicle and scapula, and are collectively known as the pectoral (shoulder) girdle. Bones of the upper limb include the humerus, ulna, radius, carpals, metacarpals and phalanges. The pelvic girdle, which attaches the lower limbs to the axial skeleton, is made up of the hip bones (coxae; singular coxa). Bones of the lower limb include the femur, patella, tibia, fibula, tarsals, metatarsals, and phalanges. The bones of the appendicular skeleton serve as attachment sites for muscles that move the appendages. The bones of the lower limb are structured to bear the weight of the body as well.

Table 19.4.1: Bones of the Skeleton. A table lists the bones in each region.

Axial Skeleton

Skull	**Cranial Bones (8)** • Ethmoid bone (1) • Frontal bone (1) • Occipital bone (1) • Parietal bones (2) • Sphenoid bone (1) • Temporal bones (2) **Facial Bones (14)** • Inferior nasal conchae (2) • Lacrimal bones (2) • Mandible (1) • Maxilla (1) • Nasal bones (2) • Palatine bone (1) • Vomer (1) • Zygomatic bones (2) **Associated Bones (7)** • Auditory ossicles [malleus (2), incus (2), stapes (2)] • Hyoid bone (1)
Vertebral Column	**Vertebrae (24)** • Cervical vertebrae (7) • Thoracic vertebrae (12) • Lumbar vertebrae (5) **Sacrum (1)** **Coccyx (1)**
Thoracic Cage	**Sternum (1)** **Ribs (24)**
Appendicular Skeleton	
Pectoral Girdle	**Clavicle (2)** **Scapula (2)**
Upper Limb	**Humerus (2)** **Radius (2)** **Ulna (2)** **Carpals (16)** • Scaphoid (2) • Lunate (2) • Triquetrum (2) • Pisiform (2) • Trapezius (2) • Trapezoid (2) • Capitate (2) • Hamate (2) **Metacarpals (10)** **Phalanges (28)** • Proximal (10) • Middle (8) • Distal (10)
Pelvic Girdle	**Os Coxa (2)**

Lower Limb	**Femur (2)** **Patella (2)** **Tibia (2)** **Fibula (2)** **Tarsals (16)** • Medial cuneiform (2) • Intermediate cuneiform (2) • Lateral cuneiform (2) • Cuboid (2) • Navicular (2) • Talus (2) • Calcaneus (2) **Metatarsals (10)** **Phalanges (28)** • Proximal (10) • Middle (8) • Distal (10)

Concept Review

The skeletal system includes all of the bones, cartilages, and ligaments of the body. It serves to support the body, protect the brain and other internal organs, and provides a rigid structure upon which muscles can pull to generate body movements. It also stores fat and the tissue responsible for the production of blood cells. The skeleton is subdivided into two parts. The axial skeleton forms a vertical axis that includes the head, neck, back, and chest. It has 80 bones and consists of the skull, vertebral column, and thoracic cage. The adult vertebral column consists of 24 vertebrae plus the sacrum and coccyx. The thoracic cage is formed by 12 pairs of ribs and the sternum. The appendicular skeleton consists of 126 bones in the adult and includes all of the bones of the upper and lower limbs plus the bones that anchor each limb to the axial skeleton.

Review Questions

Critical Thinking Question

Glossary

Contributors and Attributions

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19.4.1: The Skull

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

- 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
- 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 **skull** is the skeletal structure of the head that supports the face and protects the brain. It is subdivided into the **facial bones** (also called **viscerocranium**) and the **cranium** (also called **neurocranium**) (Figure 19.4.1.1). 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.

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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.

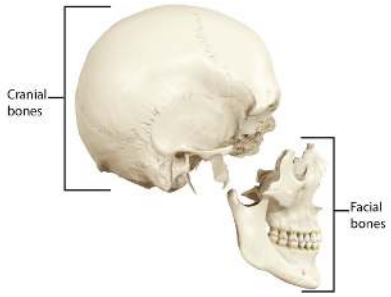


Figure 19.4.1.1: Parts of the Skull. The skull consists of the rounded cranial bones that protect the brain and the facial bones that form the upper and lower jaws, nose, orbits, and other facial structures.
(Image credit: "Bones of the Skull - Lateral View" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.))

The bones that make up the adult skull can either be paired, one on the right side and one on the left side, or singular. Singular bones cross the midline and often are formed by the fusion of the right and left bones present in the fetus. (Figure 19.4.1.2)

The paired bones of the cranium (there is a right and a left) are:

- Parietal bones
- Temporal bones

The singular bones of the cranium are:

- Ethmoid bone
- Frontal bone
- Occipital bone
- Sphenoid bone

The paired bones of the face (there is a right and a left) are:

- Inferior nasal conchae
- Lacrimal bones
- Nasal bones
- Zygomatic bones

The singular bones of the face are:

- Mandible
- Maxilla
- Palatine bone
- Vomer

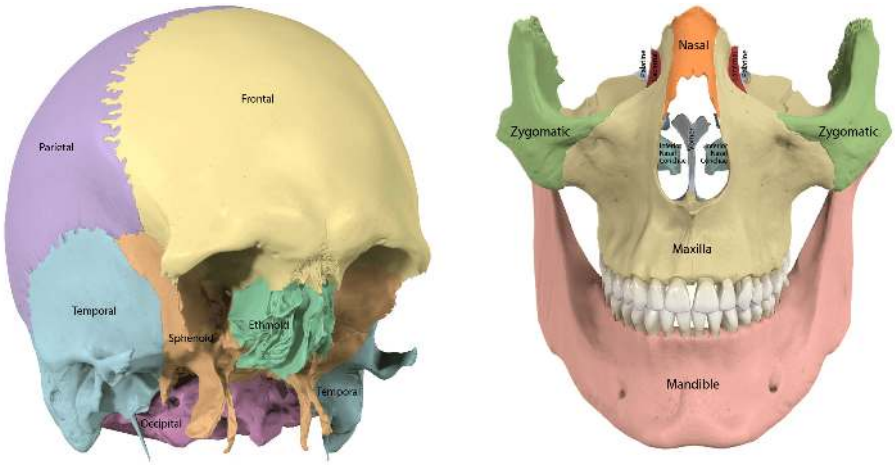


Figure 19.4.1.2: Skull Bones. The adult skull is comprised of 22 individual bones. *(Image credits: "Cranial Bones" and "Facial Bones" by Mark Schaeffer are licensed under CC BY-NC-SA 4.0, modification of images from Anatomy Standard under CC BY-NC 4.0.)*

Bones of the Skull

The bones of the skull have complex shapes and they fit together like the pieces of a very intricate jigsaw puzzle. We will first examine the skull as a whole, from multiple viewpoints, and then we will look at specific features of each bone or group of bones. These specific features, called landmarks, are the ridges where muscles attach, the concave and convex surfaces of a joint, or the holes that allow for the passage of blood vessels or nerves.

Anterior View

The anterior view of the skull (Figure 19.4.1.3 is dominated by the forehead, formed mainly by the **frontal bone**, and the openings of the orbits and the nasal cavity. Also seen are the upper and lower jaws, with their respective teeth.

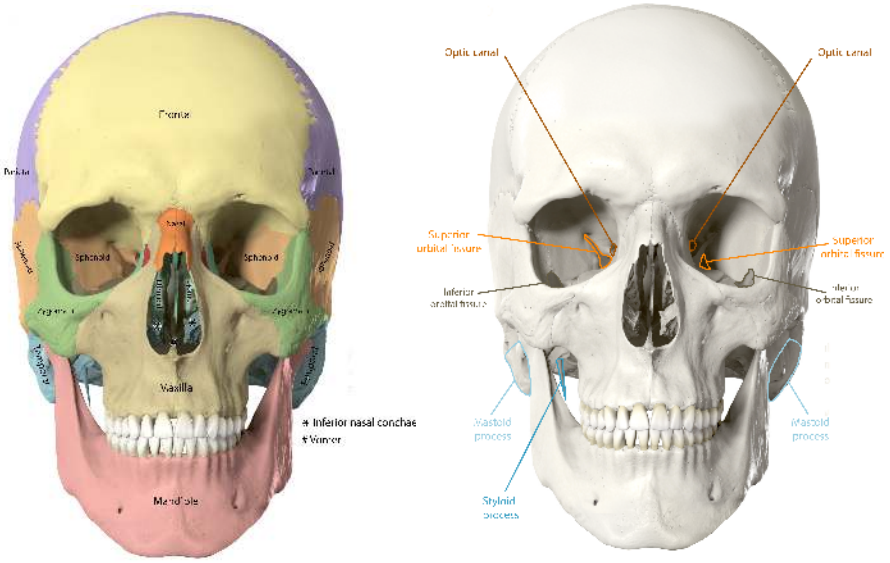


Figure 19.4.1.3: Anterior Views of the Skull. Anterior views of the skull shows the bones that form the forehead, orbits (eye sockets), nasal cavity, nasal septum, and upper and lower jaws. *(Image credits: "Skull Bones Anterior View" by Mark Schaeffer are licensed under CC BY-NC-SA 4.0, modification of images from Anatomy Standard under CC BY-NC 4.0.)*

The **orbit** is the bony socket that houses the eyeball and muscles that move the eyeball or open the upper eyelid. The walls of the orbit are formed by multiple bones. The majority of the socket consists of parts of the **frontal bone, maxilla, sphenoid bone,** and **zygomatic bone**. Small parts of the **ethmoid bone, lacrimal bone**, and **palatine bone** also contribute to the medial wall. (Figure 19.4.1.4) Within the orbit are three openings that allow for blood vessels and nerves to pass:

- **Inferior orbital fissure** - This opening is found on the floor of the orbit between the sphenoid, maxillary, and zygomatic bones. Traveling through this fissure are nerves that provide sensory information to the skin that covers the temporal and zygomatic bones and that regulate blood flow to the nasal mucosa, allowing for the warming/cooling of air in the nasal cavity. This fissure also allows for the passage of blood vessels.
- **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.
- **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.

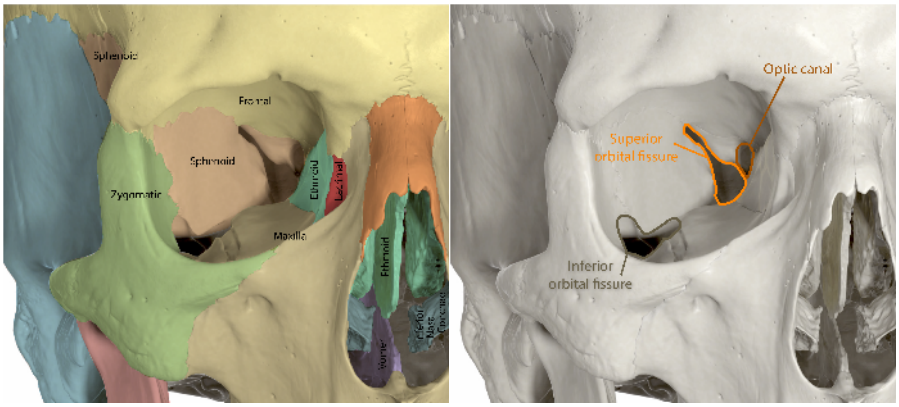


Figure 19.4.1.4: Bones of the Orbit. Several bones comprise the walls of the orbit. *(Image credit: "Bones of the Orbit Close-up" by Mark Schaeffer is licensed under CC BY-NC-SA 4.0, modification of images from Anatomy Standard under CC BY-NC 4.0.)*

Inside the nasal area of the skull (Figure 19.4.1.5), 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 formed by 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. Two additional ridges located just above the inferior concha in the upper nasal cavity, the **middle nasal concha** and **superior nasal concha**, are parts of the ethmoid bone and are not visible here.

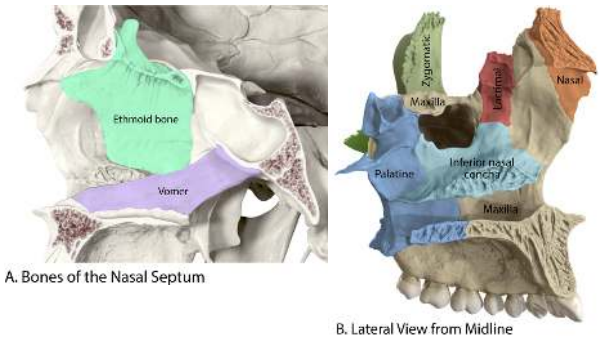


Figure 19.4.1.5: Bones of the Nasal Complex. The nasal septum has two major bones - the ethmoid bone and the vomer - that divide the nasal cavity into left and right components. The lateral walls of the nasal cavity contain the inferior nasal conchae, that serve to spin inhaled air. *(Image credit: "Bones of the Nasal Complex" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of images from Anatomy Standard.)*

Lateral View of Skull

A view of the lateral skull is dominated by the large, rounded brain case, zygomatic (cheek) bones, and the maxilla and mandible with their teeth (Figure 19.4.1.6). Connecting these areas is a bridge of bone called the **zygomatic arch**. All of the cranial bones can be seen from the lateral view: frontal, parietal, occipital, sphenoid (starting with the forehead and tracing a "C" the order of the bones follow the pneumonic "FPOTS") and the ethmoid is in the "eye".

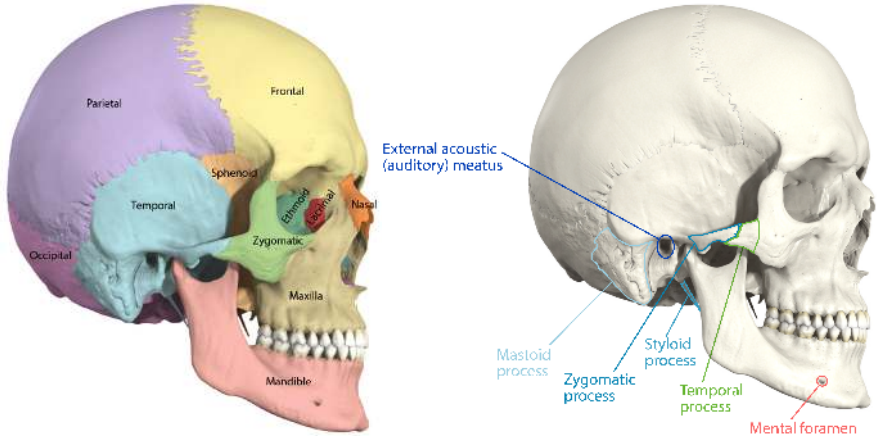


Figure 19.4.1.6: Lateral View of Skull. The lateral skull shows the large rounded brain case, zygomatic arch, and the upper and lower jaws. The zygomatic arch is formed jointly by the temporal bone and the zygomatic bone. *(Image credit: "Lateral View of the Skull" by Mark Schaeffer is licensed under CC BY-NC-SA 4.0, modification of images from Anatomy Standard under CC BY-NC 4.0.)*

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.

Superior View

Viewed from above, only four skull bones are visible: frontal, right parietal, left parietal, and occipital. These four bones make up the **calvaria**, or the skull roof. In your anatomy lab you will most likely be able to remove the calvaria from the skull models so you can view the interior structures. (Figure 19.4.1.7).

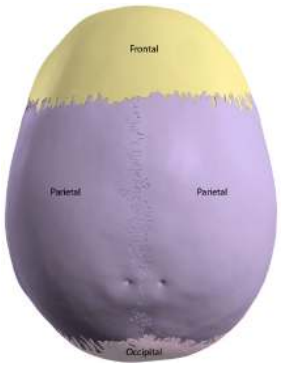


Figure \(\PageIndex{7}\): Superior View of Skull. The superior skull shows the large rounded brain case. In this view both the right and left parietal bones are visible, as well as the singular occipital and frontal bones. *(Image credit: "Superior View of the Skull" by Mark Schaeffer is licensed under CC BY-NC-SA 4.0, modification of images from Anatomy Standard under CC BY-NC 4.0.)*

Inferior View

The inferior aspect of the skull is complex in shape as it is the location of multiple foraminae for the passage of multiple blood vessels, nerves, and the spinal cord. Tracing the anterior border of the sphenoid bone gives you the junction between the bones of the face and cranium (Figure 19.4.1.8).

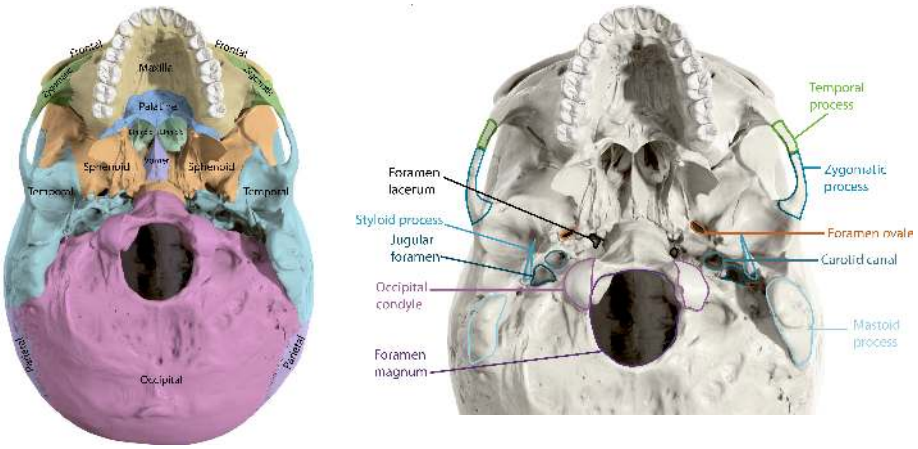


Figure 19.4.1.8: Inferior View of the Skull. Viewed from the inferior, the full width of the sphenoid bone can easily be seen. The landmarks allowing passage of nerves, blood vessels, and the spinal cord as well as several muscle attachment points are shown; each is outlined in a color of its respective bone. *(Image credit: "Inferior View of the Skull" by Mark Schaeffer is licensed under CC BY-NC-SA 4.0, modification of images from Anatomy Standard under CC BY-NC 4.0.)*

Foramina visible include:

- **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.
- **Foramen ovale** - is an oval shaped opening in the sphenoid bone that allows for passage of blood vessels and nerves, the largest of which is the mandibular branch of cranial nerve V.
- **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.
- **Jugular foramen** - In this external view the jugular foramen is located slightly posterior and lateral to the carotid canal, as the internal jugular vein runs adjacent to the internal carotid artery. Because veins lack blood pressure, their walls tend to partially collapse instead of maintaining a round shape (as arteries do). Thus, the jugular foramen is not a uniformly round hole.
- **Foramen magnum** - Being "magnum" this is the largest foramen in the skull. The foramen magnum serves as the dividing line between the brain and the spinal cord, even though they are continuous with each other on a structural level.

Bones of the Neurocranium

The cranial bones (the neurocranium) contain and protect the brain. The interior space that is almost completely occupied by the brain is called the **cranial cavity**. The floor of the neurocranium is referred to as the base of the skull. The neurocranium consists of eight bones: the paired parietal and temporal bones, plus the unpaired frontal, occipital, sphenoid, and ethmoid bones.

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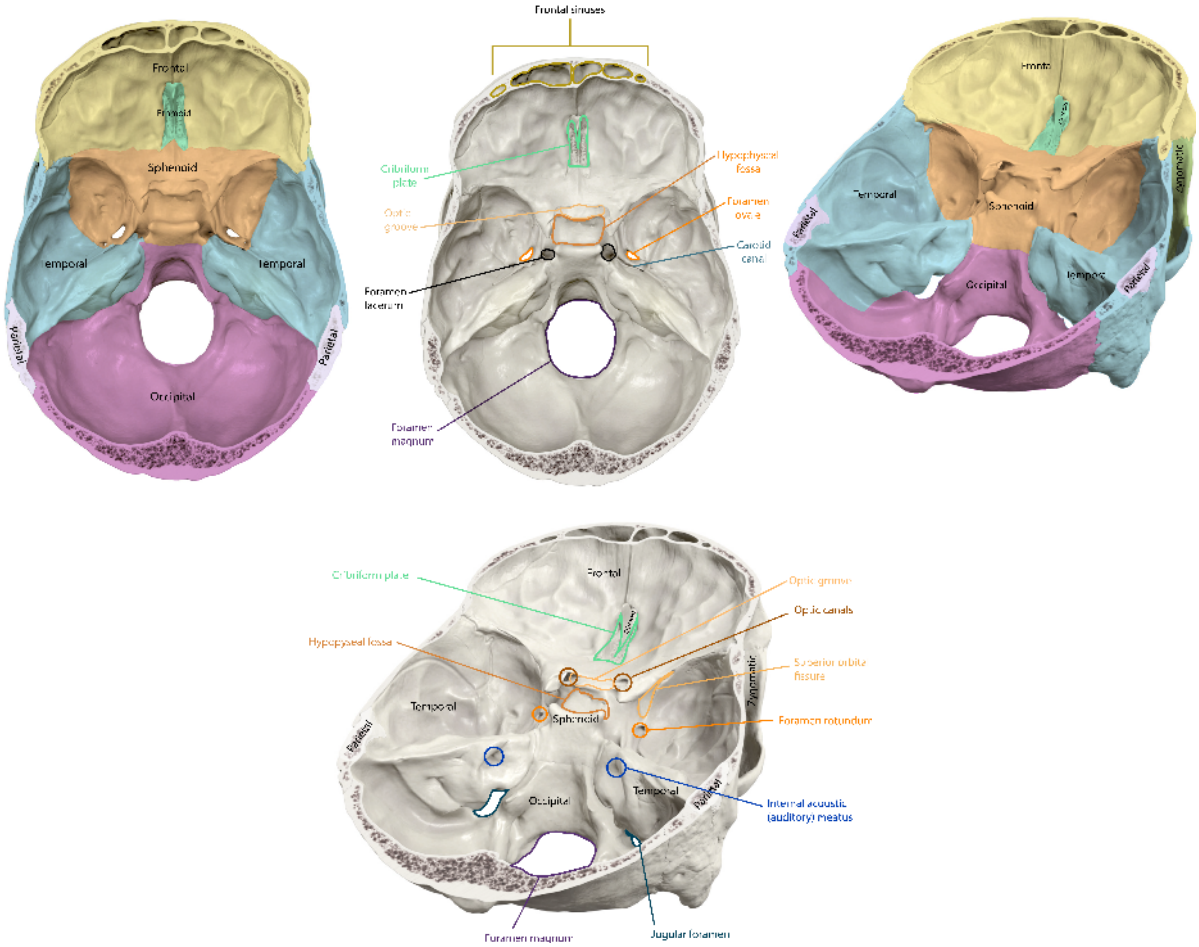


Figure 19.4.1.9: Interior Views of the Skull. Viewed from the inferior, the full width of the sphenoid bone can easily be seen. The landmarks allowing passage of nerves, blood vessels, and the spinal cord as well as several muscle attachment points are shown; each is outlined in a color of its respective bone. *(Image credit: "Inferior View of the Skull" by Mark Schaeffer is licensed under CC BY-NC-SA 4.0, modification of images from Anatomy Standard under CC BY-NC 4.0.)*

Parietal Bones

The **parietal bone** forms most of the upper lateral side wall of the skull (parietal = "wall") (Figure 19.4.1.10). These are paired bones, with the right and left parietal bones joining together at the top of the skull. Each parietal bone is also bordered anteriorly by the frontal bone, inferiorly by the temporal bone, and posteriorly by the occipital bone.



Parietal Bone Ex Situ **Parietal Bone In Situ**

Figure 19.4.1.10: Parietal Bone. The right parietal bone in situ and ex situ. *(Image credits: "Parietal Bone In Situ" and "Parietal Bone Ex Situ" by Sofia Elizondo is licensed under CC BY-NC-SA 4.0, modification of images from Anatomy Standard under CC BY-NC 4.0.)*

Temporal Bones

The **temporal bone** forms the lower lateral side of the skull (Figure 19.4.1.6). 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 has three processes for muscle attachment (Figure 19.4.1.11):

- the **zygomatic process** of the temporal bone projects anteriorly to meet the zygomatic bone and it forms the posterior portion of the zygomatic arch,
- the **mastoid process** projects inferiorly and can easily be felt on the side of the head just behind your earlobe,
- the s**tyloid process** is an elongated, downward bony projection posterior to the mandibular fossa on the external base of the skull; so named because of its resemblance to a stylus (a pen or writing tool).

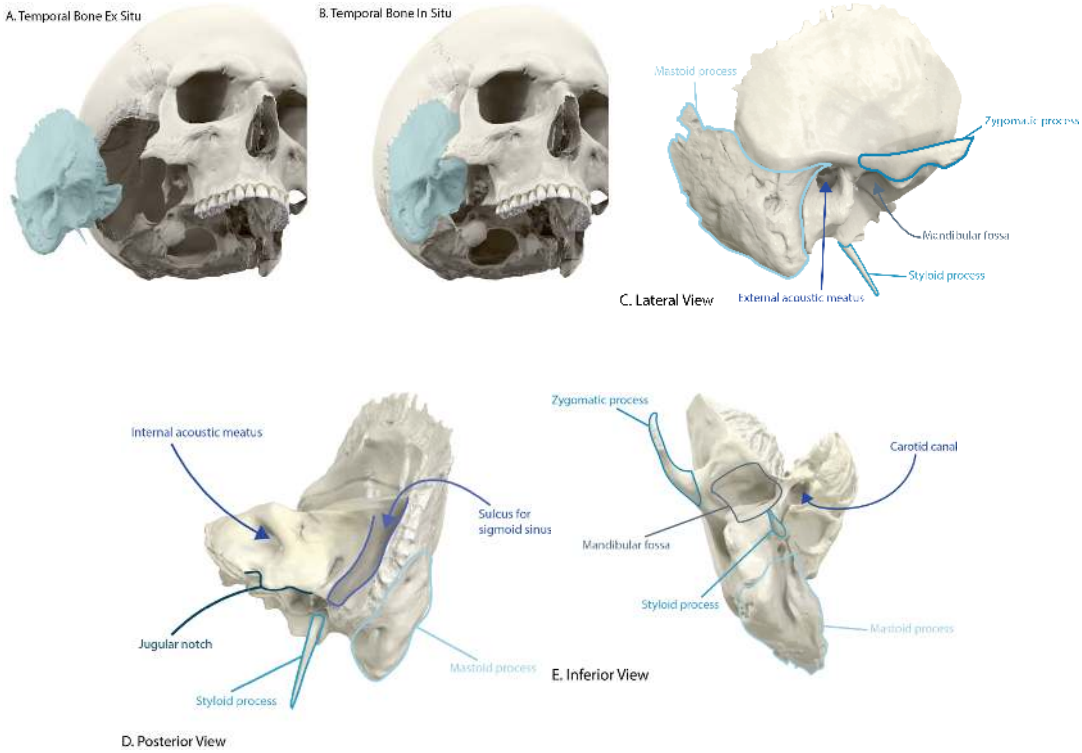


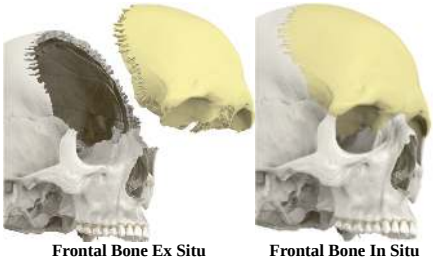
Figure 19.4.1.11: Temporal Bone and Landmarks. Shown in isolation in (C) lateral, (D) posterior, and (E) inferior views, the temporal bone surrounds the structures of the ear, your temple, and the posterior part of your cheek bone line. The temporal bone has an opening for the passage of the largest artery serving the brain - the carotid canal - and a notch that forms one wall of the jugular foramen. On the external surface, sound waves enter the external acoustic meatus and the nerve carrying auditory information exits through the internal acoustic meatus. *(Image credit: "Temporal Bone and Landmarks" by Sofia Elizondo is licensed under CC BY-NC-SA 4.0, modification of images from Anatomy Standard under CC BY-NC 4.0.)*

Important landmarks of the temporal bone, as seen in Figures 19.4.1.11 and 19.4.1.9, 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.
- Immediately inferior to the internal acoustic meatus is the large, irregularly shaped **jugular foramen**. 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.
- **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.

Frontal Bone

The **frontal bone** is the single bone that forms the forehead. It has two main parts, the squamous part, which forms the large, flat, superior portion of the bone, and the orbit part. 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 part of the floor of the cranial cavity above (Figure 19.4.1.12).

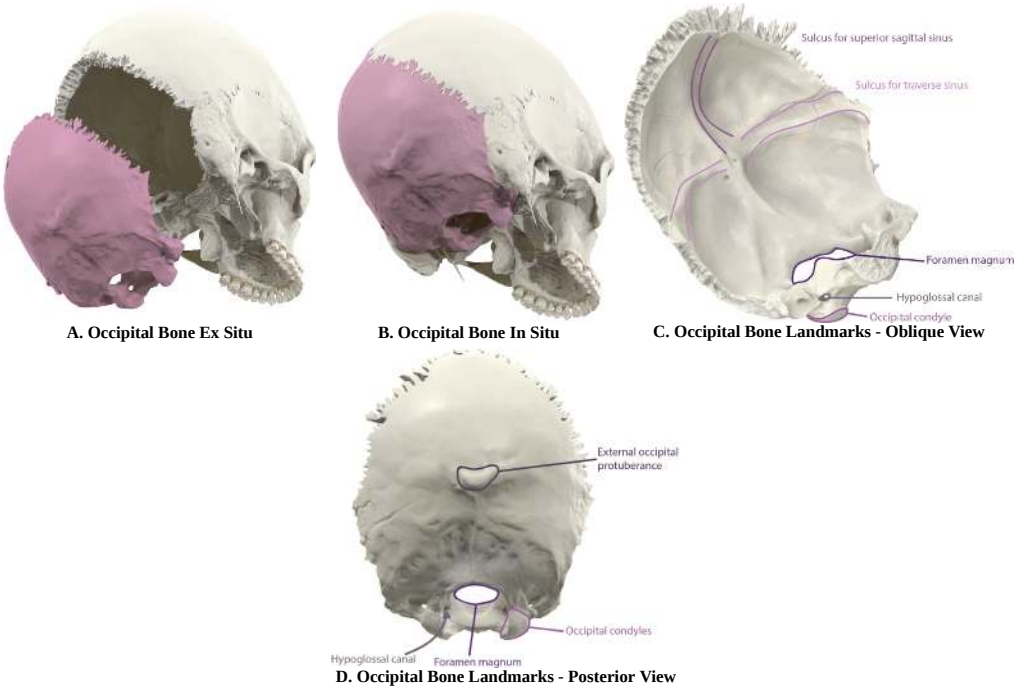


Frontal Bone Ex Situ **Frontal Bone In Situ**

Figure 19.4.1.12: The Frontal Bone Ex Situ and In Situ. The frontal bone forms the anterior wall of the cranial cavity and the superior wall of the orbit. *(Image credit: "Frontal Bone Ex Situ and In Situ" by Sofia Elizondo are licensed under CC BY-NC-SA 4.0, modification of images from Anatomy Standard under CC BY-NC 4.0.)*

Occipital Bone

The **occipital bone** is the single bone that forms the posterior skull and posterior base of the cranial cavity (Figure 19.4.1.6; see also Figure 19.4.1.13). 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. Superficially, 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.



A. Occipital Bone Ex Situ **B. Occipital Bone In Situ** **C. Occipital Bone Landmarks - Oblique View**

D. Occipital Bone Landmarks - Posterior View

Figure 19.4.1.13: Occipital Bone and Landmarks. The occipital bone forms the posterior and inferior portion of the cranium. It serves as the connection point between the skull and the vertebral column, with the articular surfaces of the occipital condyles. The foramen magnum is the large hole the spinal cord passes through. *(Image credit: "Occipital Bone and Landmarks" by Sofia Elizondo are licensed under CC BY-NC-SA 4.0, modification of images from Anatomy Standard under CC BY-NC 4.0.)*

Sphenoid Bone

The **sphenoid bone** is a single, complex bone of the central skull (Figure 19.4.1.8). 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 and also extends laterally to contribute to the sides of the skull. Inside the cranial cavity, the right and left lesser wings of the sphenoid bone resemble the wings of a flying bird or a moth (Figure 19.4.1.9). The **sella turcica** ("Turkish saddle") is located at the midline, on the body of the sphenoid bone (Figure 19.4.1.14). The rounded depression in the floor of the sella turcica is the **hypophyseal (pituitary) fossa**, which houses the pea-sized pituitary (hypophyseal) gland and the posterior wall is the **dorsum sellae.** 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 temporal bone.

The sphenoid bone has several openings for the passage of blood vessels and cranial nerves, which include (Figure 19.4.1.14):

- **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** — 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.
- **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 19.4.1.6.*a*). 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.

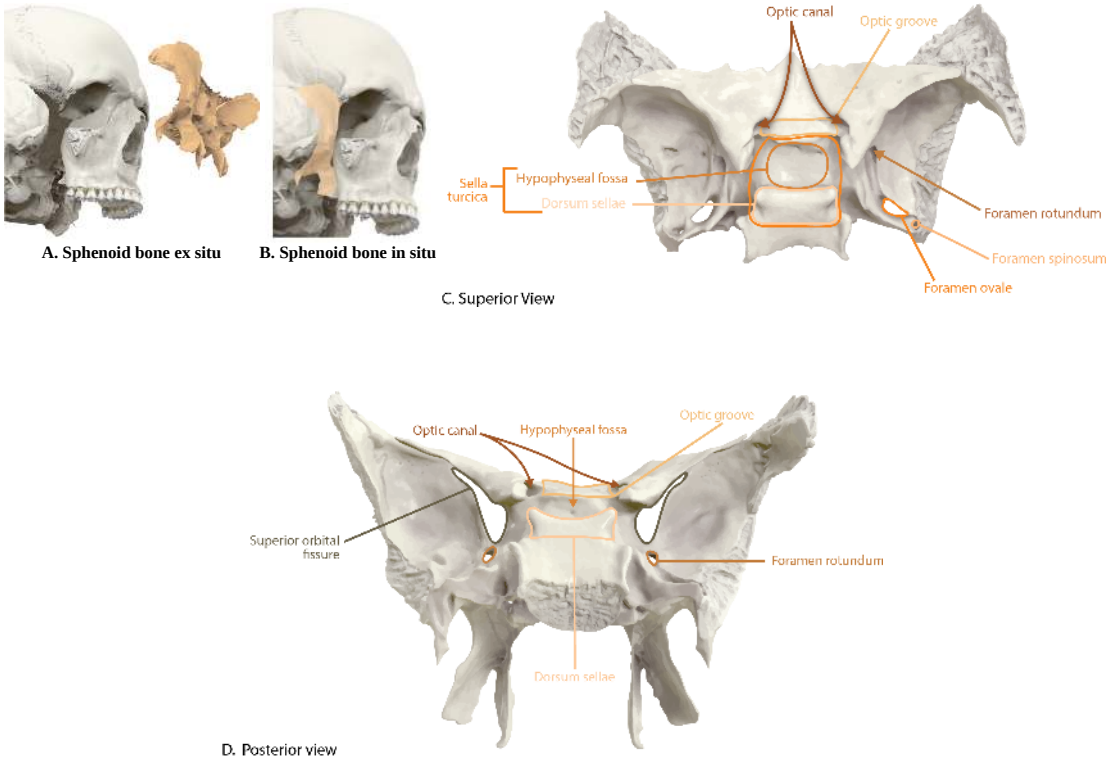


Figure 19.4.1.14: Sphenoid Bone and Landmarks. Shown in isolation in (C) superior and (D) posterior views, the sphenoid bone is a single midline bone that forms the anterior walls and floor of the middle cranial fossa. The hypophyseal fossa and the dorsum sellae are within the sella turcica and serve as the surrounds for the pituitary gland. 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. *(Image credit: "Sphenoid Bone and Landmarks" by Sofia Elizondo is licensed under CC BY-NC-SA 4.0, modification of images from Anatomy Standard under CC BY-NC 4.0.)*

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 19.4.1.4. On the interior of the skull, the ethmoid also forms a portion of the floor of the anterior cranial cavity (see Figure 19.4.1.5).

Within the nasal cavity, the **perpendicular plate** of the ethmoid bone forms the upper portion of the nasal septum (Figure 19.4.1.5. 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 to increase the surface area of the nasal passages and to cause the incoming air to spin (see Respiratory System chapter).

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 (Figure 19.4.1.15). 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 connective tissue 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 (smell) areas of the nasal cavity pass through these openings to enter the brain.

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. The **ethmoid air cells**, spaces creating a honeycomb-like structure in the lateral portions of the bone, form the ethmoidal sinuses (Figure 19.4.1.15), one of the four pairs of paranasal sinus. The paranasal sinuses also play a role in the respiratory system.

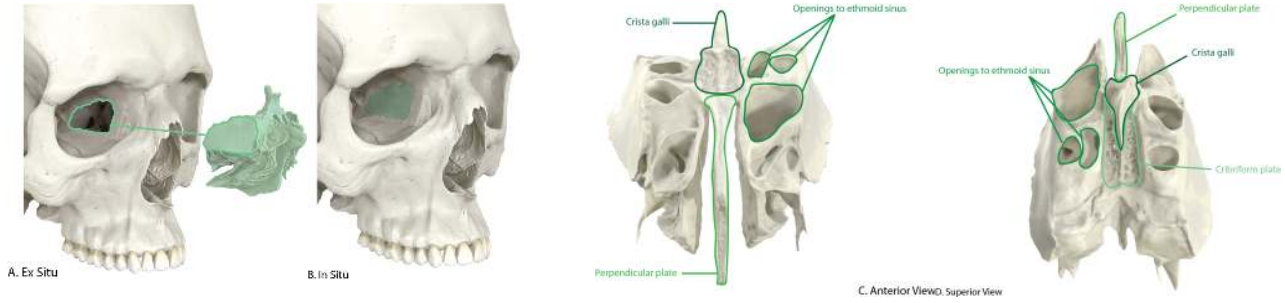


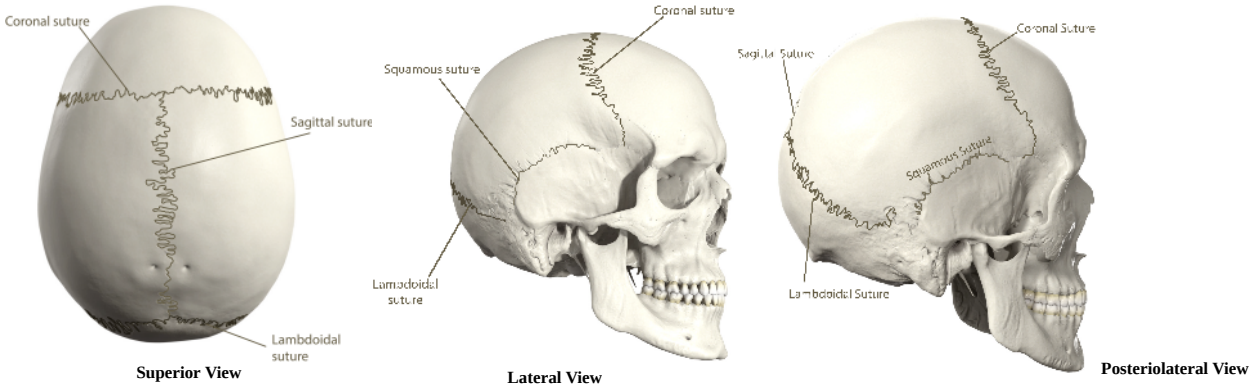
Figure 19.4.1.15: Ethmoid Bone. The unpaired ethmoid bone is located at the midline within the central skull. It has an upward projection, the crista galli, and a downward projection, the perpendicular plate, which forms the upper nasal septum. The cribriform plates form both the roof of the nasal cavity 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. *(Image credit: "Ethmoid Bone" by Sofia Elizondo is licensed under CC BY-NC-SA 4.0, modification of images from Anatomy Standard under CC BY-NC 4.0.)*

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 irregular 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.

Figure 19.4.1.16 shows the major sutures of the skull. 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. 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. 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. 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.



Superior View **Lateral View** **Posteriolateral View**

Figure 19.4.1.16: Sutures of the Skull. Sutures represent the immovable joints found between skull bones. In the superior view the coronal, sagittal and lambdoid sutures are visible. A lateral view of the skull shows the coronal, squamous, and lambdoid sutures. A posterior view shows the sagittal, lambdoid, and squamous sutures. *("Sutures of the Skull" by Mark Schaeffer is licensed under CC BY-NC-SA 4.0, modification of images from Anatomy Standard under CC BY-NC 4.0.)*

DISORDERS OF THE...

Skeletal System: Cranial Fractures

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 (Figure 19.4.1.20). 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.

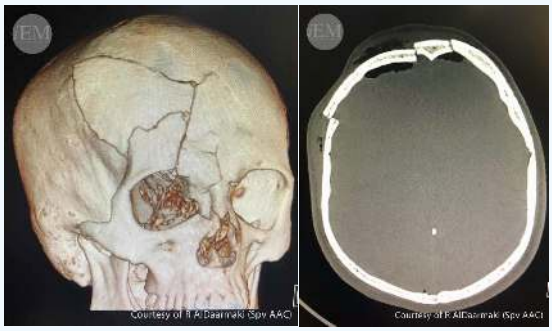


Figure 19.4.1.17: Skull Fracture. A 31-year-old male presented to the Emergency Room after falling from a 3-meter wall and landing on his face. (Skull Fracture and Skull Fracture Scan by iEM is licensed under CC BY-NC-S 2.0)

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. 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 (Figure 19.4.1.18). 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.

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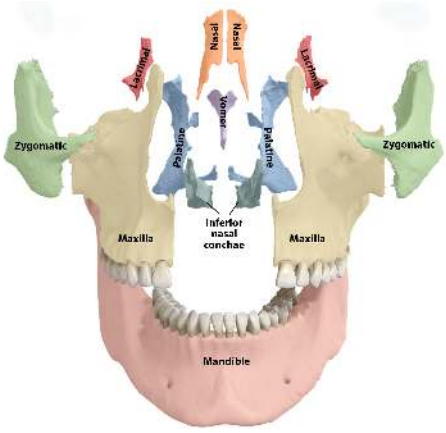


Figure 19.4.1.18: Facial Bones Separated. The facial bones contain six pairs and two singular bones. *(Image credit: "Facial Bones Separated" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of images from Anatomy Standard under CC BY-NC 4.0.)*

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 19.4.1.2). The curved, inferior margin of the maxillary bone that forms the upper jaw and contains the upper teeth (Figure 19.4.1.19). Each tooth is anchored into a deep socket. 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 maxillary bone can be seen forming the anterior three-quarters of the hard palate (see Figure 19.4.1.8). 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. On the lateral side of each maxillary bone is where the maxilla articulates (connects) with the zygomatic bone.

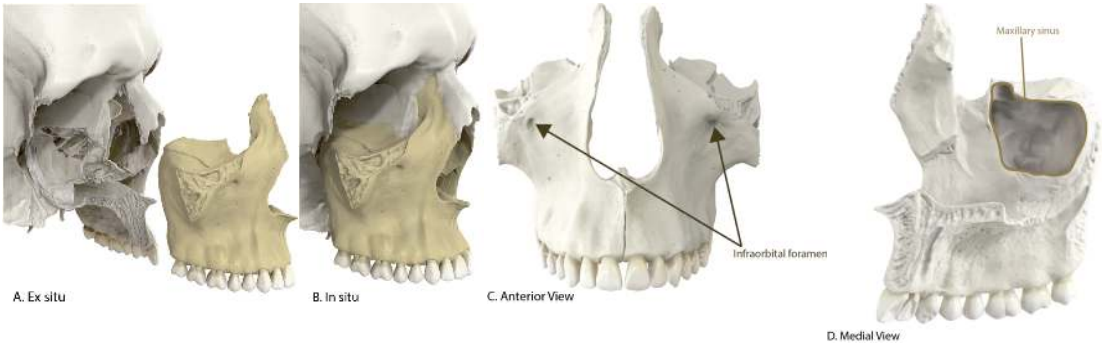
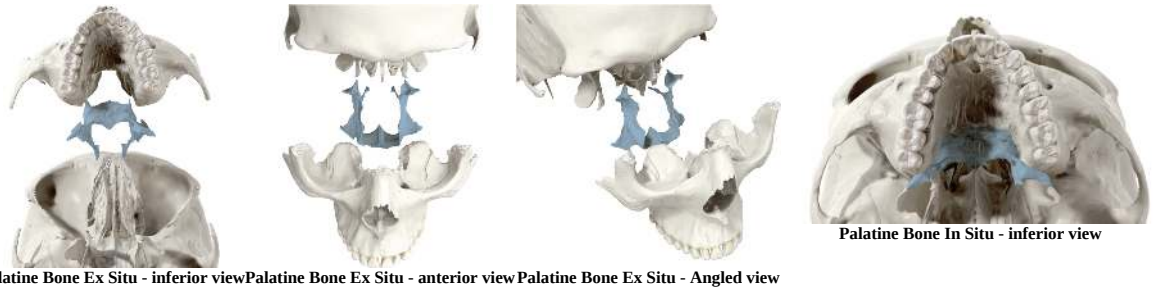


Figure 19.4.1.19: Maxillary Bone. The maxillary bone forms the upper jaw and supports the upper teeth. Each maxilla also forms the lateral floor of each orbit and the majority of the hard palate. *(Image credit: "Maxillary Bone" by Sofia Elizondo is licensed under CC BY-NC-SA 4.0, modification of images from Anatomy Standard under CC BY-NC 4.0.)*

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 that forms the posterior aspect of the roof of your mouth. 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 19.4.1.20 and Figure 19.4.1.8). Thus, the palatine bones are best seen in an inferior view of the skull and hard palate.



Palatine Bone Ex Situ - inferior view **Palatine Bone Ex Situ - anterior view** **Palatine Bone Ex Situ - Angled view** **Palatine Bone In Situ - inferior view**

Figure 19.4.1.20: Palatine Bone - Ex Situ and In Situ. The palatine bone has a "U" shape and form the posterior aspect of the hard palate (posterior to the maxilla).

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).

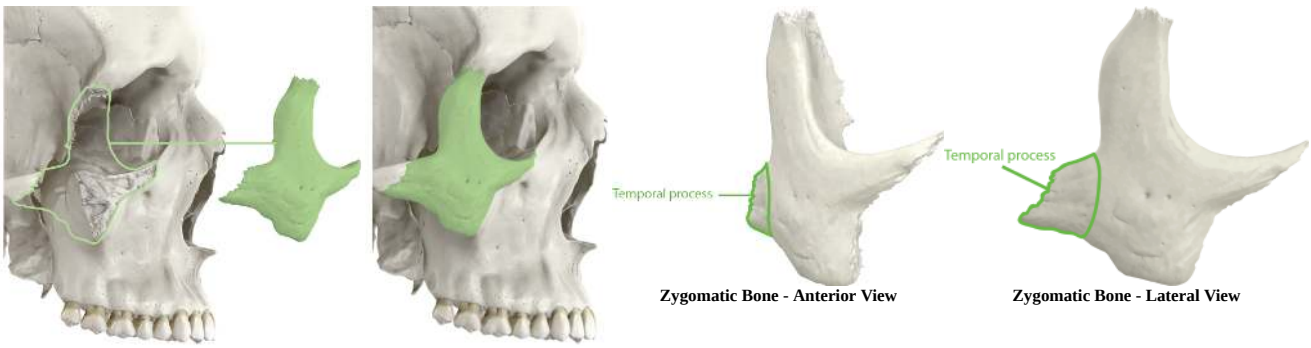


Figure 19.4.1.21: Illustrations and photographs of cleft palate and cleft lip. *(Image credits: "Infant with Cleft Palate Illustration" and "Infant with a Cleft Lip" by Centers for Disease Control and Prevention is in the public domain, via Wikimedia Commons; photograph of cleft palate by the Trinity Care Foundation is licensed under CC BY-NC-ND 2.0; "Infant with a Cleft Lip" by Perryrosen1 is licensed under CC BY-SA 4.0, via Wikimedia Commons.)*

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 (Figure 19.4.1.2). The short **temporal process of the zygomatic bone** projects posteriorly (Figure 19.4.1.22, where it forms the anterior portion of the **zygomatic arch** (Figure 19.4.1.3).

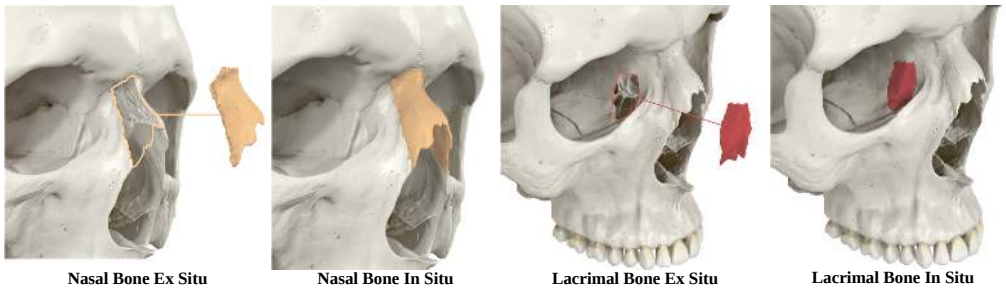


Zygomatic Bone Ex Situ **Zygomatic Bone In Situ** **Zygomatic Bone - Anterior View** **Zygomatic Bone - Lateral View**

Figure 19.4.1.22: The zygomatic bone is the lateral facial bone. Its temporal process articulates with the temporal bone to form the zygomatic arch. *(Image credits: "Zygomatic Bone Ex Situ and In Situ" and "Zygomatic Bone Anterior and Lateral View" by Sofia Elizondo are licensed under CC BY-NC-SA 4.0, modification of images from Anatomy Standard under CC BY-NC 4.0.)*

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 (Figure 19.4.1.23 and Figure 19.4.1.3). These are the bones that are damaged when the nose is broken.



Nasal Bone Ex Situ **Nasal Bone In Situ** **Lacrimal Bone Ex Situ** **Lacrimal Bone In Situ**

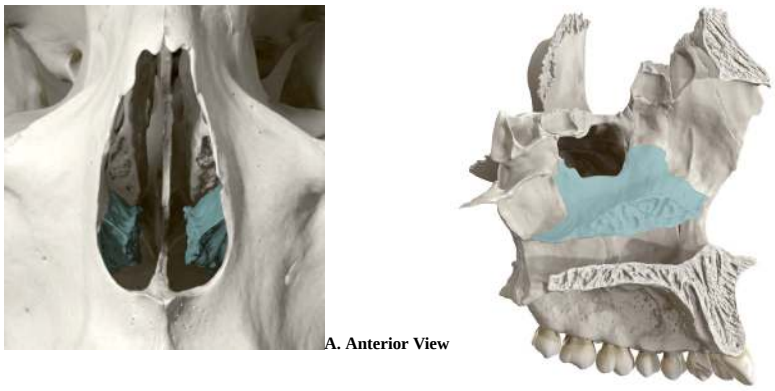
Figure 19.4.1.23: Nasal Bone and Lacrimal Bone Ex Situ and In Situ. The nasal bones form the superior, hard portion of the bridge of your nose. The lacrimal bones are within the orbit, forming part of the medial wall. *(Image credits: "Nasal Bone Ex Situ and In Situ" and "Lacrimal Bone Ex Situ and In Situ" by Sofia Elizondo are licensed under CC BY-NC-SA 4.0, modification of images from Anatomy Standard under CC BY-NC 4.0.)*

Lacrimal Bone

Each **lacrimal bone** is a small, rectangular bone that forms the anterior, medial wall of the orbit (Figure 19.4.1.23 and Figure 19.4.1.4). The anterior portion of the lacrimal bone forms a shallow depression 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 (Figure 19.4.1.24 and Figure 19.4.1.5). 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.

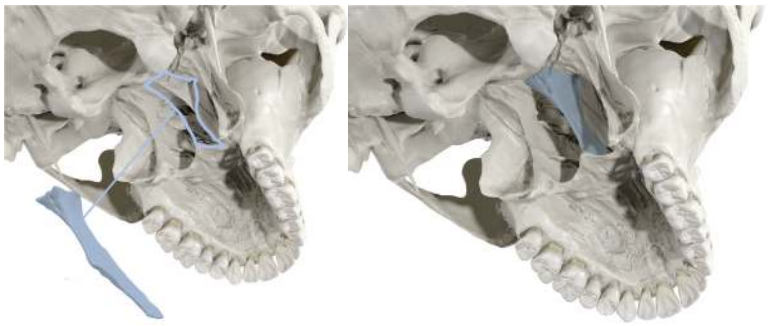


A. Anterior View **B. Lateral View from Midline**

Figure 19.4.1.24: Inferior Nasal Conchae. These bones form ridges on the lateral walls of the nasal cavities. *(Image credits: "Inferior Nasal Conchae" by Jennifer Lange are licensed under CC BY-NC-SA 4.0, modification of images from Anatomy Standard.)*

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 19.4.1.25). The vomer is best seen when looking from behind into the posterior openings of the nasal cavity (see Figure 19.4.1.8). 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.



Vomer Ex Situ **Vomer In Situ**

Figure 19.4.1.25: Vomer. The vomer is a small bone that makes up the inferior portion of the nasal septum. *(Image credits: "Vomer Ex Situ and In Situ" by Sofia Elizondo are licensed under CC BY-NC-SA 4.0, modification of images from Anatomy Standard under CC BY-NC 4.0.)*

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 (Figure 19.4.1.26).

The each side of the mandible has two upward-going bony projections. 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 19.4.1.6).

Important landmarks of the mandible, as seen in Figure 19.4.1.26, include the 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.

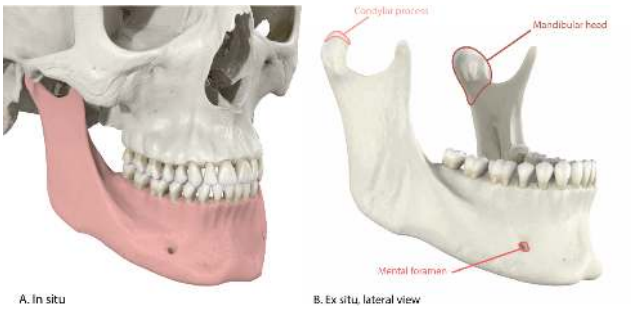


Figure 19.4.1.26: Mandible. The mandible is the only moveable bone of the skull. The condylar process on the mandibular head articulates with the mandibular fossa of the temporal bone. *(Image credits: "Mandible" by Sofia Elizondo are licensed under CC BY-NC-SA 4.0, modification of images from Anatomy Standard under CC BY-NC 4.0.)*

Paranasal Sinuses

The **paranasal sinuses** are hollow, air-filled spaces located within certain bones of the skull (Figure 19.4.1.27). 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 (Figure 19.4.1.9). 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** (Figure 19.4.1.19). 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 (Figure 19.4.1.15). 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.

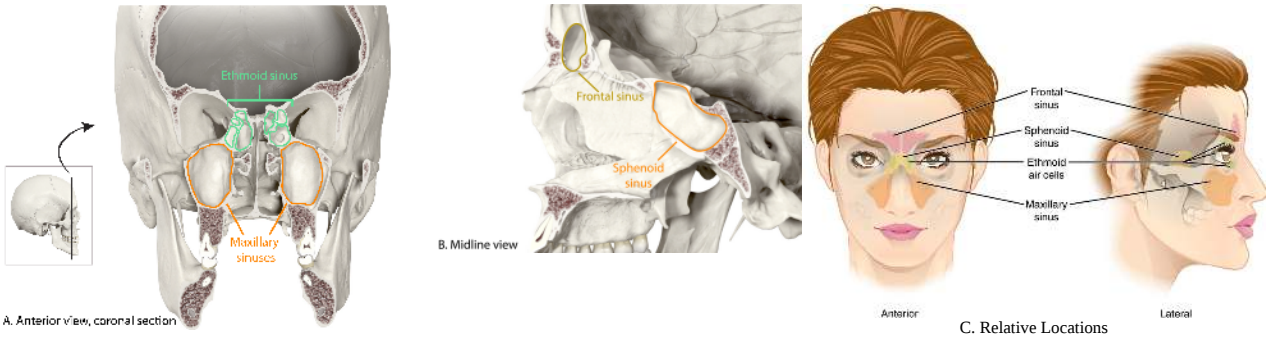


Figure 19.4.1.27: Paranasal Sinuses. The paranasal sinuses are hollow, air-filled spaces named for the skull bone that each occupies. The most anterior is the frontal sinus, located in the frontal bone above the eyebrows. The largest are the maxillary sinuses, located in the right and left maxillary 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. *(Images A and B credit: "Paranasal Sinuses" by Mark Schaeffer are licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0. Image C credit: "Paranasal Sinuses" by OpenStax is licensed under CC BY 3.0)*

Hyoid Bone

The **hyoid bone** is an independent bone that does not articulate (form a joint) any other bone and thus is not part of the skull. In fact, it is the only bone in the human body that does not articulate with another bone, making it unique. 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 (Figure 19.4.1.28). 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 19.4.1.28: 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. *(Image credits: "Hyoid Bone Position" by Sofia Elizondo is licensed under CC BY-NC-SA 4.0, modification of images from Anatomy Standard under CC BY-NC 4.0. "Hyoid Bone Anterior and Anterolateral Views" by Anatomy Standard are licensed under CC BY-NC 4.0.)*

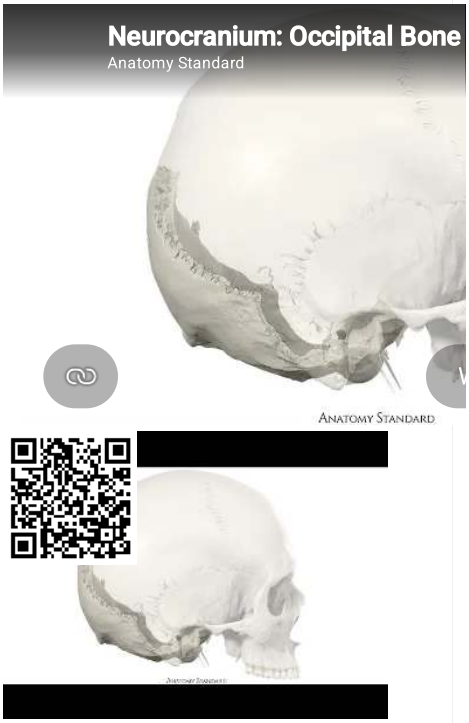
Concept Review

The skull consists of the cranial bones and the facial bones. The cranial bones surround and protect the brain, which occupies the cranial cavity inside the skull. The brain case is formed by eight bones, the paired parietal and temporal bones plus the unpaired frontal, occipital, sphenoid, and ethmoid bones. The narrow gap between the bones is filled with dense, fibrous connective tissue that unites the bones to form sutures. The sagittal suture joins the right and left parietal bones. The coronal suture joins the parietal bones to the frontal bone, the lambdoid suture joins them to the occipital bone, and the squamous suture joins them to the temporal bone.

The facial bones support the facial structures and form the upper and lower jaws. These consist of 14 bones, with the paired maxillary, palatine, zygomatic, nasal, lacrimal, and inferior conchae bones and the unpaired vomer and mandible bones. The ethmoid bone also contributes to the formation of facial structures. The maxilla forms the upper jaw and the mandible forms the lower jaw. The maxilla also forms the larger anterior portion of the hard palate, which is completed by the smaller palatine bones that form the posterior portion of the hard palate.

Summary Table: Cranial Bones

Bone	Major Landmarks	Animation
Frontal	• frontal sinus	403
Parietal (right and left)		403

Bone	Major Landmarks	Animation
Occipital	• external occipital protuberance • foramen magnum • hypoglossal canal • occipital condyles • sulci for the transverse sinus and the superior sagittal sinus	
Temporal (right and left)	• carotid canal • external acoustic meatus • internal acoustic meatus • jugular foramen • mastoid process • styloid process • zygomatic process (part of zygomatic arch)	

Bone	Major Landmarks	Animation
Sphenoid	• foramen ovale • foramen rotundum • foramen spinosum • inferior orbital fissure • optic canal • optic groove • sella turcica with hypophyseal fossa and dorsum sellae • sphenoid sinus • superior orbital fissure	
Ethmoid	• cribriform plate • crista galli • ethmoid air cells • middle nasal conchae • perpendicular plate • superior nasal conchae	

Summary Table: Facial Bones

Bone	Major Landmarks	Animation
Inferior nasal conchae		
Lacrimal		
Mandible	• condylar process • mandibular head • mental foramen	

Bone	Major Landmarks	Animation
Maxilla	• infraorbital foramen • maxillary sinus	
Nasal		
Palatine		
Vomer		
Zygomatic	• temporal process (part of zygomatic arch)	

The hyoid bone is located in the upper neck and does not join with any other bone. It is held in position by muscles and serves to support the tongue above, the larynx below, and the pharynx posteriorly.

Review Questions

Critical Thinking Questions

References

Centers for Disease Control and Prevention (US). Injury prevention and control: traumatic brain injury [Internet]. Atlanta, GA; [cited 2013 Mar 18]. Available from: http://www.cdc.gov/traumaticbraininjury/statistics.html.

Glossary

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19.4.2: The Vertebral Column

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

- 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 19.4.2.1). It consists of a sequence of vertebrae (singular = vertebra), each of which is separated and united by an **intervertebral disc,** composed of a pad of fibrocartilage. 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.

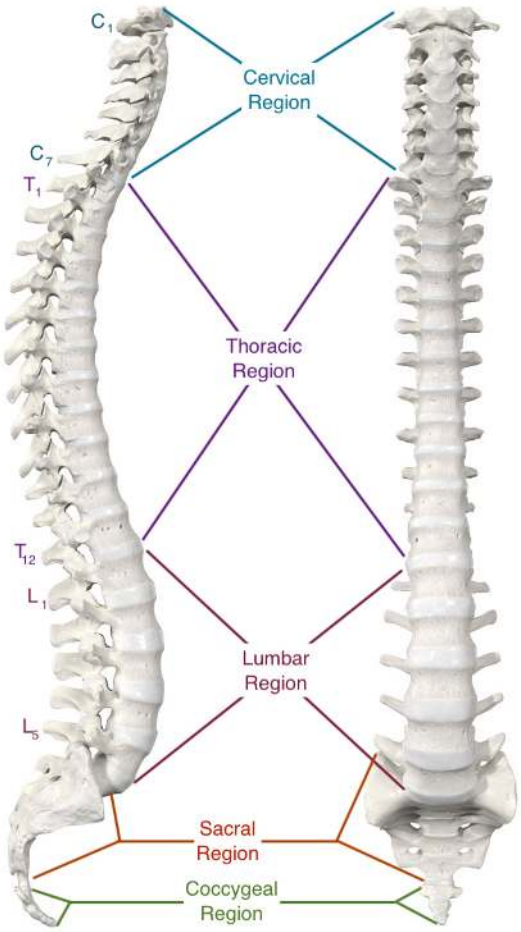


Figure 19.4.2.1: Vertebral Column. The adult vertebral column consists of 24 vertebrae, plus the sacrum and coccyx. The vertebrae are divided into three regions: cervical C1–C7 vertebrae, thoracic T1–T12 vertebrae, and lumbar L1–L5 vertebrae. *(Image credit: "Vertebral Column Regions" by Jennifer Lange is licensed under CC BY-NC-SA 4.0>, modification of image from Anatomy Standard under CC BY-NC 4.0.*

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 occipital bone of the skull.

Inferiorly, C1 articulates with the superior portion of the C2 vertebra. The inferior portion of C2 then articulates with the superior portion of the C3 vertebra, and so on. Below the cervical vertebrae 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 usually completed around age 30.

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 19.4.2.2). 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.

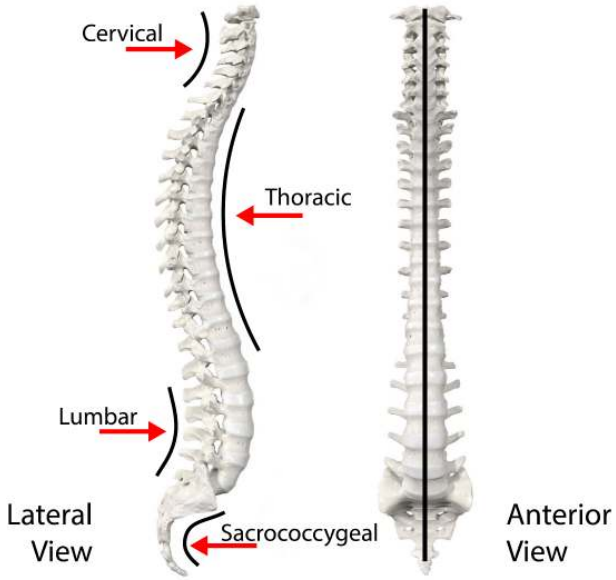


Figure 19.4.2.2: When viewed laterally, the vertebral column has four curves: the thoracic and sacrococcygeal regions are concave on the anterior side while the cervical and lumbar regions are concave on the posterior side. When viewed anteriorly (or posteriorly) the vertebral column is straight. *(Image credit: "Vertebral Column Curvatures" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.)*

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, which helps to reduce back pressure during pregnancy.

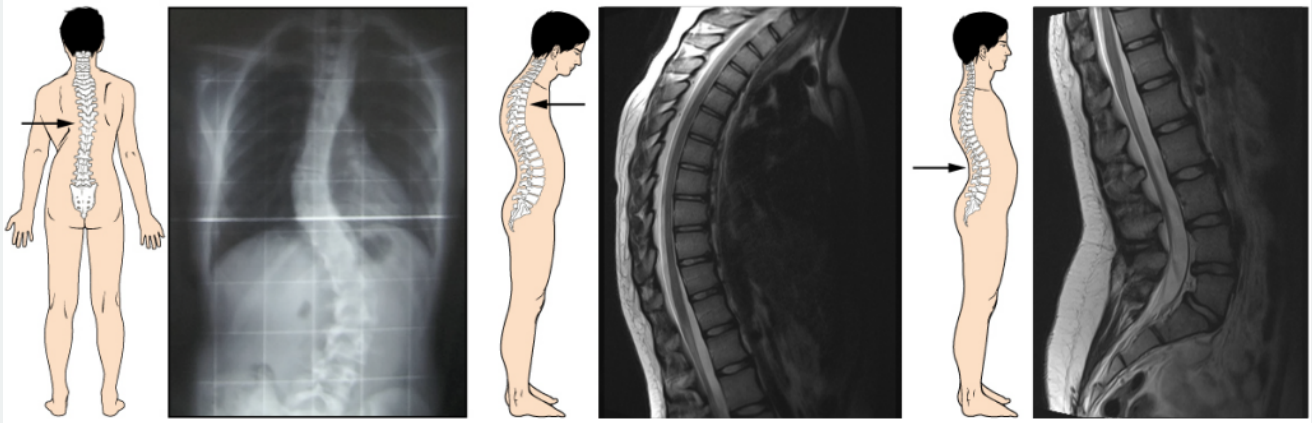
DISORDERS OF THE...

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 19.4.2.3). **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. **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.

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.



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.

Figure 19.4.2.3: 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. (*Image credit: "Abnormal Curves of Vertebral Column" by Jennifer Lange is licensed under CC BY-NC-SA 4.0. Modification of original by OpenStax. "Kyphosis" and "Lordosis" MRI images from Radiopedia. Case courtesy of Mostafa El-Feky.)*

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 19.4.2.4). 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.

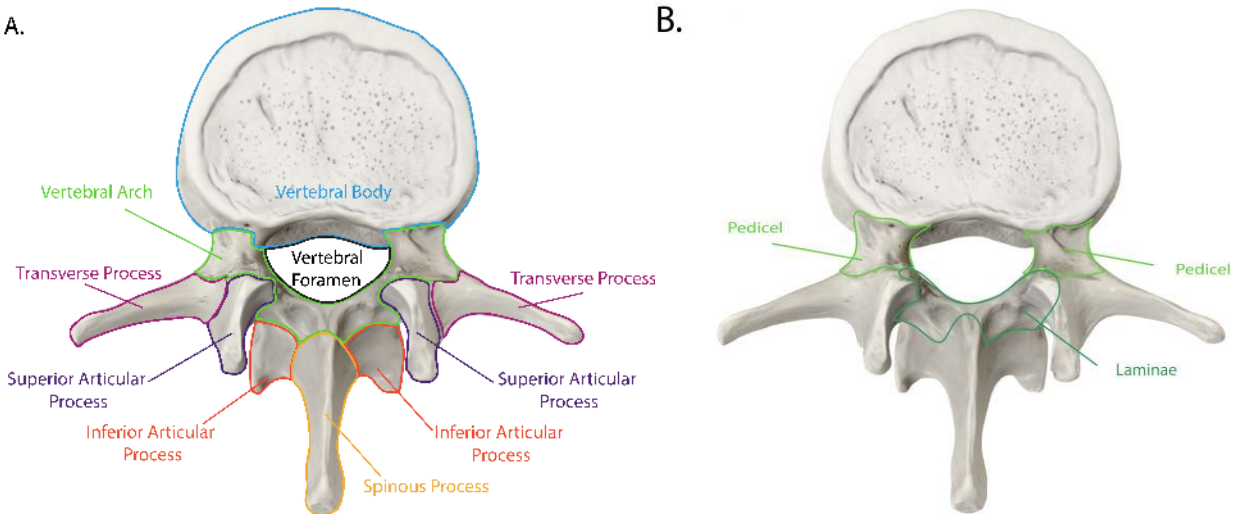


Figure 19.4.2.4: Parts of a Typical Vertebra. A typical vertebra consists of a body and a vertebral arch. The arch is formed by the paired pedicles and paired laminae (B). Arising from the vertebral arch are the transverse, spinous, superior articular, and inferior articular processes. *(Image credit: "Typical Vertebral Structure" by Gabrielle Spurlock is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.)*

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 (Figure 19.4.2.5). 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.

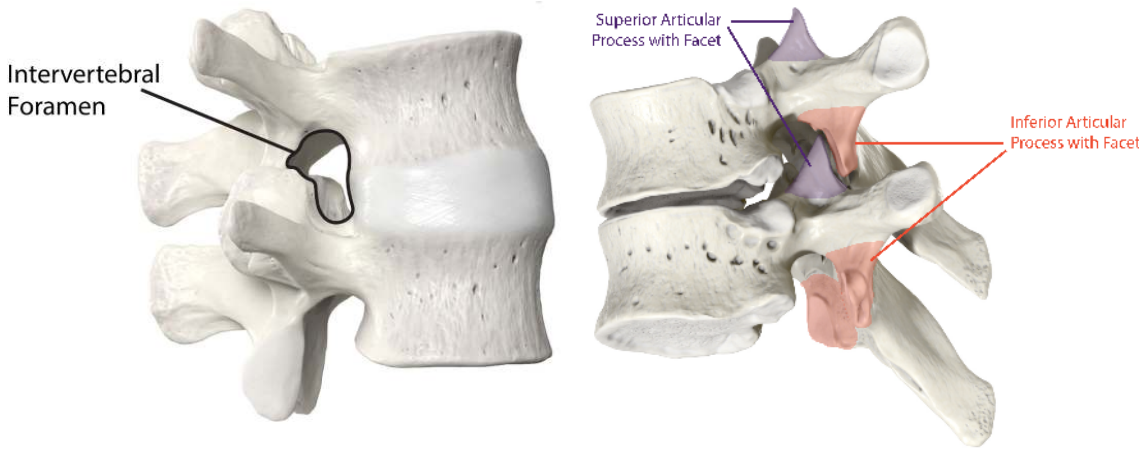


Figure 19.4.2.5: Intervertebral Features. The intervertebral foramen is the space through which spinal nerves pass that is located between the pedicels of adjacent vertebrae. The vertebral facet joints occur between adjacent superior and inferior articular processes, with the specific contact points being their facets. *(Image credit: "Intervertebral Foramen" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.)*

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. Each process has a **facet**, or flat surface, to accommodate this joining of the vertebrae. 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.

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. For example, cervical vertebrae are smaller than lumbar vertebrae due to differences in the proportion of body weight that each supports. Only 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 C3 through C7, have several characteristic features that differentiate them from thoracic or lumbar vertebrae (Figure 19.4.2.6). 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. Because of this feature, the C7 vertebra is also known as the **vertebra prominens**. 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.

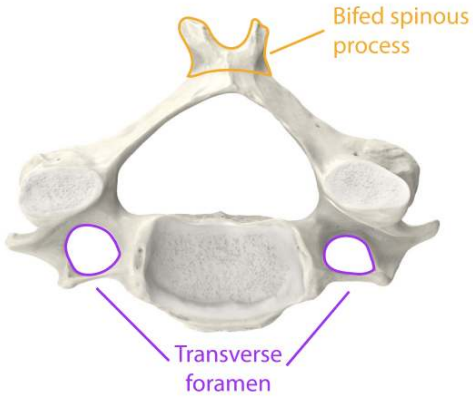


Figure 19.4.2.6: Cervical Vertebrae. A typical cervical vertebra has a small body, a bifid spinous process, transverse processes that have a transverse foramen that allow for passage of arteries to the brain. The atlas (C1 vertebra) does not have a body or spinous process. It consists of an anterior 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. *(Image credit: "Typical Vertebra Structure" by Gabrielle Spurlock is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.)*

The first and second cervical vertebrae are further modified, giving each a distinctive appearance (Figure 19.4.2.7). 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.

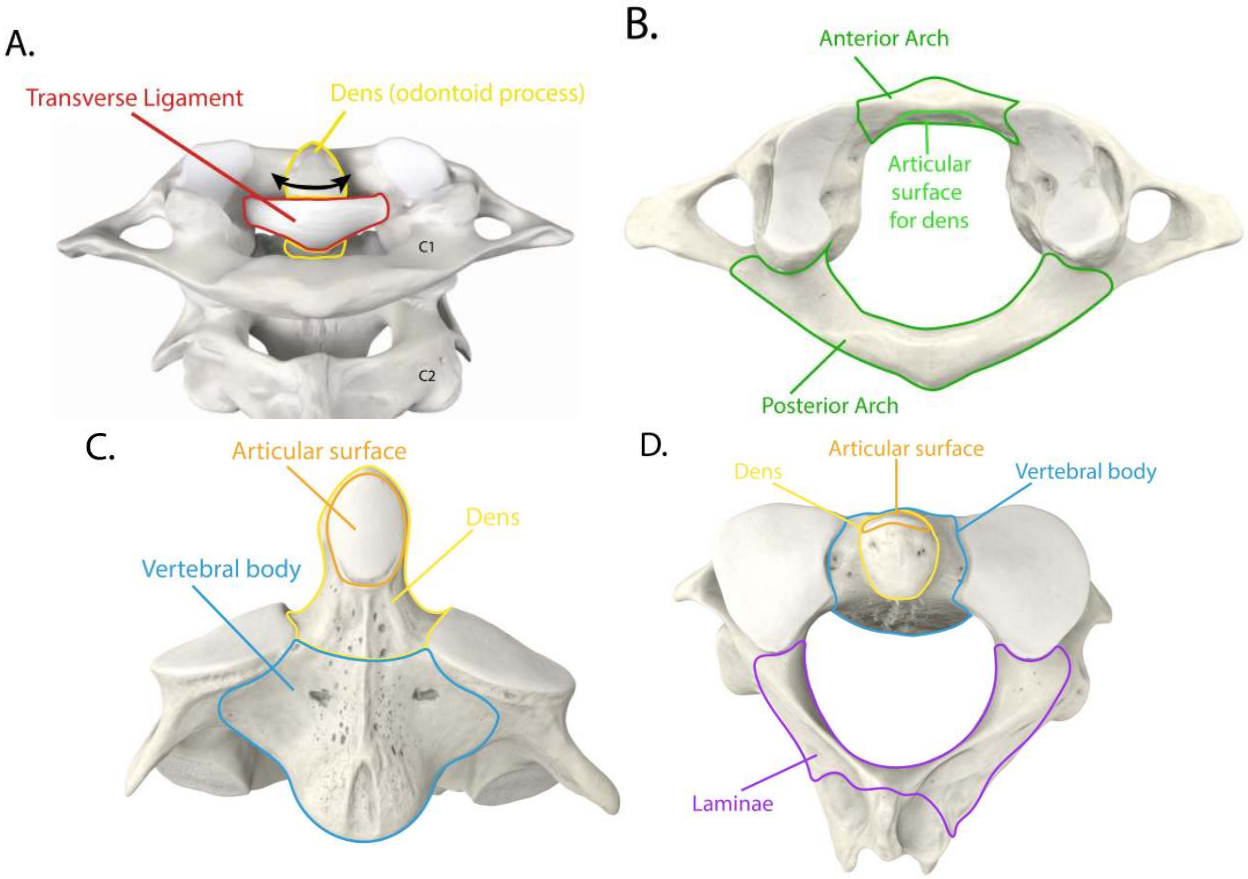


Figure 19.4.2.7: B. The atlas (C1 vertebra) does not have a body or spinous process. It consists of an anterior and a posterior arch and elongated transverse processes. C & D. The axis (C2 vertebra) has the upward projecting dens, which articulates with the anterior arch of the atlas. *(Image credit: "C1 and C2 Vertebrae Structure" by Gabrielle Spurlock is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.)*

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 the **transverse ligament**.

Thoracic Vertebrae

The bodies of the **thoracic vertebrae** are larger than those of cervical vertebrae (Figure 19.4.2.8). 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.

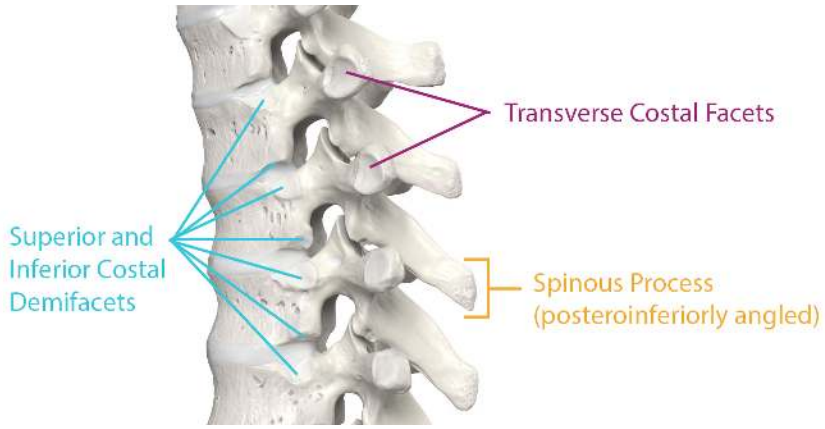


Figure 19.4.2.8: Thoracic Vertebrae. A typical thoracic vertebra is distinguished by the spinous process, which is long and projects downward to overlap the next inferior vertebra. It also has articulation sites (facets) on the vertebral body and the transverse process for rib attachment. *(Image credit: "Thoracic Vertebral Column Features" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.)*

Thoracic vertebrae are the only ones with several additional articulation sites, each of which is called a **facet**, where a rib is attached (Figure 19.4.2.9). Most thoracic vertebrae have a superior and inferior facet located on the lateral sides of the body, each of which is called a **costal demifacet** (costal = "rib"). These are for articulation with the head (end) of a rib. An additional facet, the **transverse costal facet**, is located on the transverse process for articulation with the tubercle of a rib.

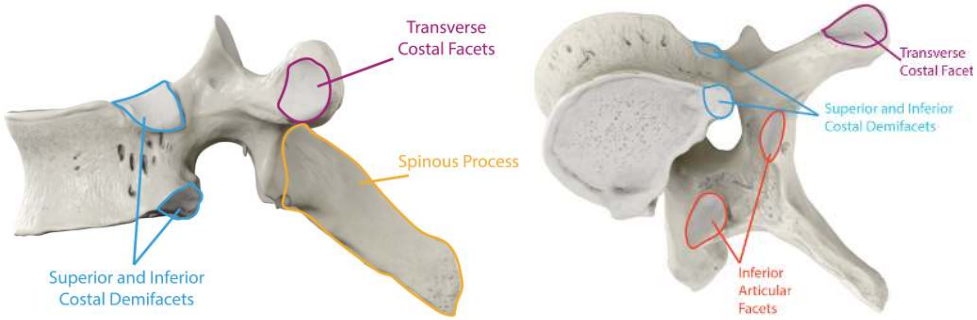


Figure 19.4.2.9: Unique features of a thoracic vertebra are the facets for articulating with the ribs and the spinous process that is long, slender, and angled in an inferior direction. *(Image credit: "Thoracic Vertebrae Features" by Gabrielle Spurlock is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.)*

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 19.4.2.10). 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.

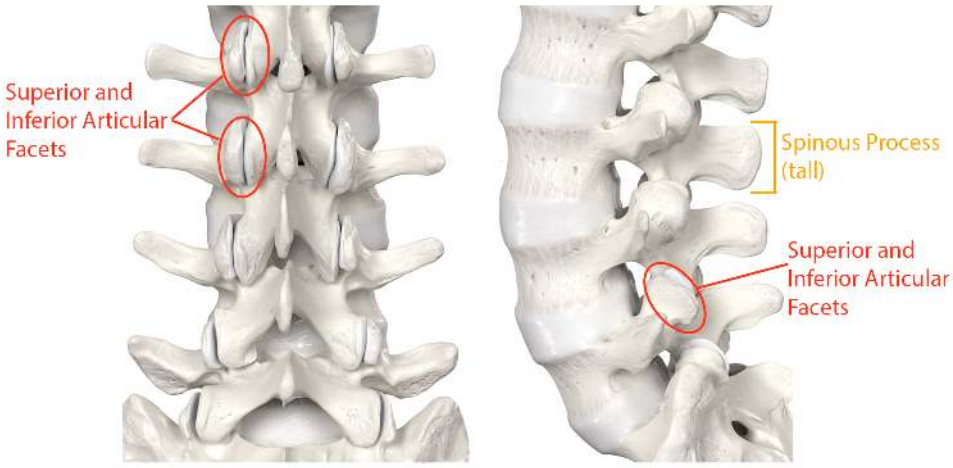


Figure 19.4.2.10: Lumbar vertebrae are characterized by having a large, thick body and a tall, robust spinous process. The articular processes are angled close to the sagittal plane, so the facets face medially and laterally. *(Image credit: "Lumbar Vertebral Column Features" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.)*

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 19.4.2.11). It is formed by the fusion of five sacral vertebrae, a process that does not begin until after the age of 20 and continues until around age 30. 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. 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** through which the spinal nerves pass. The anterior and posterior surfaces of the sacrum have a series of paired openings, called foramina, that connect to the sacral canal. 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 body of the sacrum articulates with the body of vertebra L5.

The **coccyx**, or tailbone, is derived from the fusion of four very small coccygeal vertebrae (see Figure 19.4.2.11). 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.

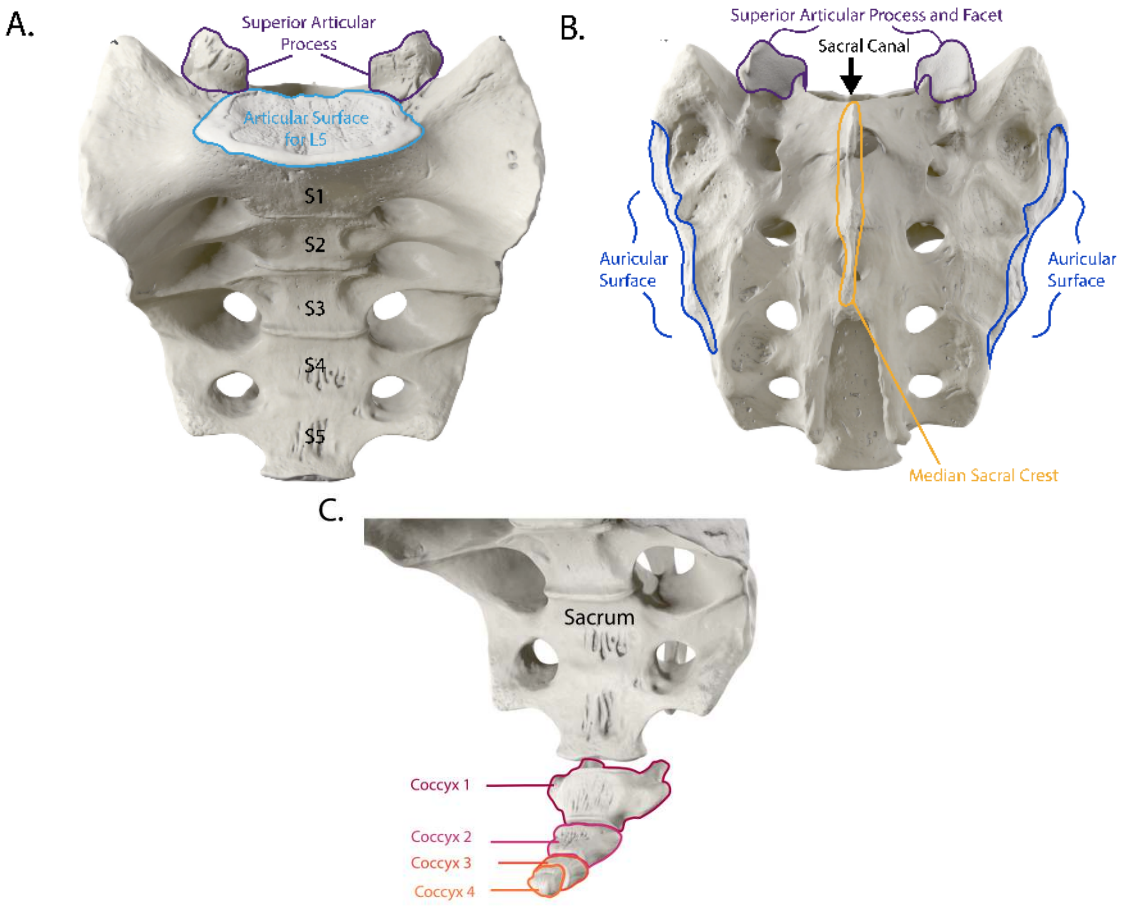


Figure 19.4.2.11: Sacrum and Coccyx. A) Anterior view: the sacrum is formed from the fusion of five sacral vertebrae. The superior aspect retains the articular surfaces for the lumbosacral joints. B) Posterior view: the fused spinous processes form the median sacral crest. Laterally, the auricular surface serves as the point of connection to the ileum. C) The coccyx is formed by the fusion of four small coccygeal vertebrae. *(Image credit: "Sacrum and Coccyx" by Gabrielle Spurlock is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.)*

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 when they bear weight, 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 (Figure 19.4.2.12). Each disc is anchored to the bodies of its adjacent vertebrae, thus strongly uniting the set. 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.

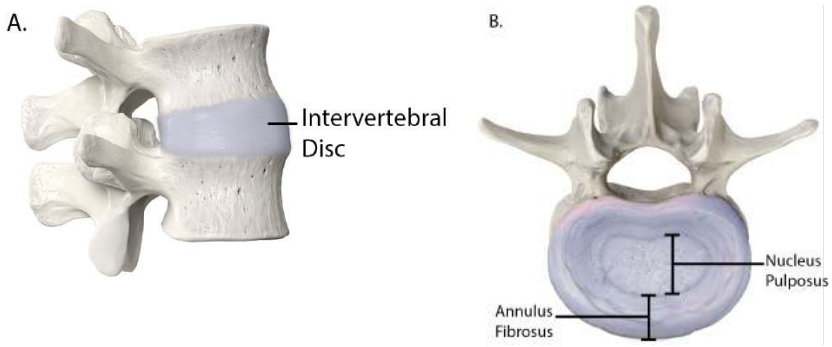


Figure 19.4.2.12: The bodies of adjacent vertebrae are separated and united by an intervertebral disc, which provides padding and allows for movements between adjacent vertebrae. The disc consists of a fibrous outer layer called the anulus fibrosus and a gel-like center called the nucleus pulposus. *(Image credit: "Intervertebral Discs" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of images from Anatomy Standard under CC BY-NC 4.0. and BruceBlaus, CC BY-SA 4.0, via Wikimedia Commons.)*

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 19.4.2.13). 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.

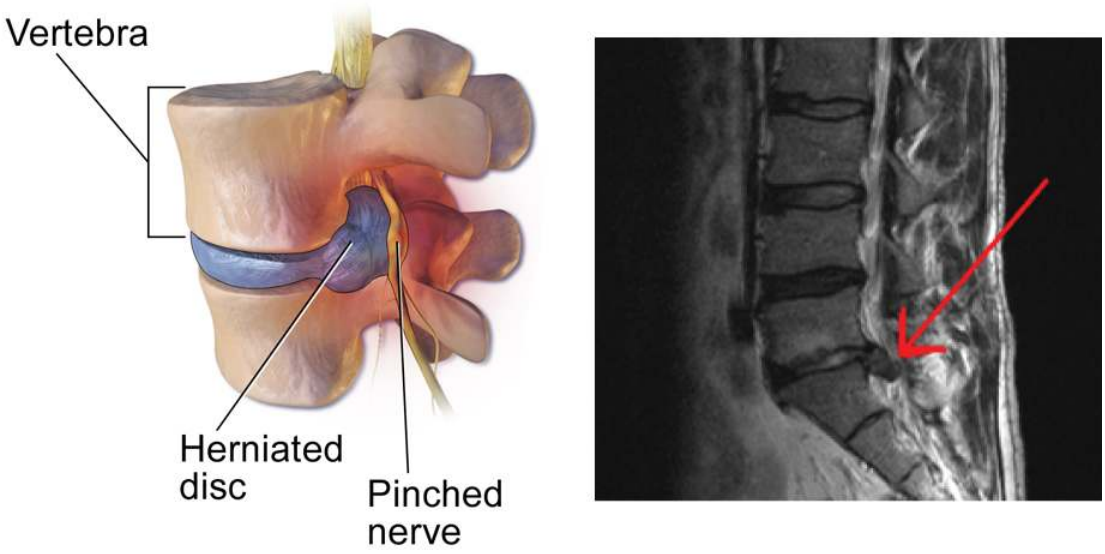


Figure 19.4.2.13: Herniated Intervertebral Disc. Weakening of the anulus fibrosus can result in herniation (protrusion) of the nucleus pulposus and compression of a spinal nerve, resulting in pain and/or muscle weakness in the body regions supplied by that nerve. *(Image credit: "Herniated Disc" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of images from BruceBlaus and from OpenStax via Wikimedia Commons.)*

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 19.4.2.14). These serve to resist excess forward or backward bending movements of the vertebral column, respectively.

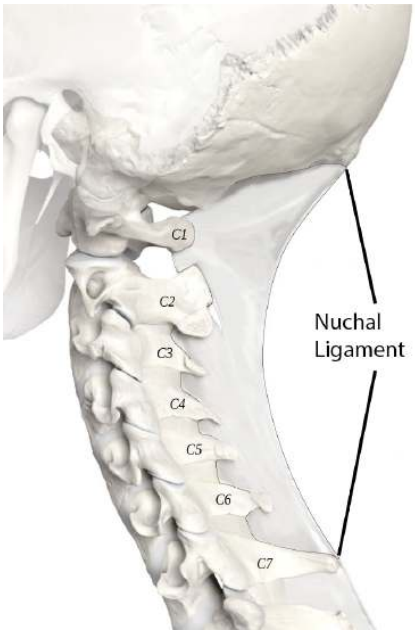


Figure 19.4.2.14: Nuchal Ligament. In the posterior neck, the nuchal ligament attaches to the cervical spinous processes and to the base of the skull. *(Image credit: "Nuchal Ligament" by Gabrielle Spurlock is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.)*

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.

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.

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.



Spring Aragon, a chiropractor at Branch Health Clinic Bangor, examines a patient's neck during a consultation. Chiropractic care emphasizes the recuperative power of the body to heal itself without the use of drugs or surgery. (U.S. Navy photo by Mass Communication Specialist 2nd Class Zulema Sotelo, public domain.)

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.

Concept Review

The vertebral column forms the neck and back. The vertebral column originally develops as 33 vertebrae, but is eventually reduced to 24 vertebrae, plus the sacrum and coccyx. The vertebrae are divided into the cervical region (C1–C7 vertebrae), the thoracic region (T1–T12 vertebrae), and the lumbar region (L1–L5 vertebrae). The sacrum arises from the fusion of five sacral vertebrae and the coccyx from the fusion of four small coccygeal vertebrae. The vertebral column has four curvatures, the cervical, thoracic, lumbar, and sacrococcygeal curves. The thoracic and sacrococcygeal curves are primary curves retained from the original fetal curvature. The cervical and lumbar curves develop after birth and thus are secondary curves. The cervical curve develops as the infant begins to hold up the head, and the lumbar curve appears with standing and walking.

A typical vertebra consists of an enlarged anterior portion called the body, which provides weight-bearing support. Attached posteriorly to the body is a vertebral arch, which surrounds and defines the vertebral foramen for passage of the spinal cord. The vertebral arch consists of the pedicles, which attach to the vertebral body, and the laminae, which come together to form the roof of the arch. Arising from the vertebral arch are the laterally projecting transverse processes and the posteriorly oriented spinous process. The superior articular processes project upward, where they articulate with the downward projecting inferior articular processes of the next higher vertebrae.

A typical cervical vertebra has a small body, a bifid (Y-shaped) spinous process, and U-shaped transverse processes with a transverse foramen. In addition to these characteristics, the axis (C2 vertebra) also has the dens projecting upward from the vertebral body. The atlas (C1 vertebra) differs from the other cervical vertebrae in that it does not have a body, but instead consists of bony ring formed by the anterior and posterior arches. The atlas articulates with the dens from the axis. A typical thoracic vertebra is distinguished by its long, downward projecting spinous process. Thoracic vertebrae also have articulation facets on the body and transverse processes for attachment of the ribs. Lumbar vertebrae support the greatest amount of body weight and thus have a large, thick body. They also have a short, blunt spinous process. The sacrum is triangular in shape. The median sacral crest is formed by the fused vertebral spinous processes and the lateral sacral crest is derived from the fused transverse processes. Anterior (ventral) and posterior (dorsal) sacral foramina allow branches of the sacral spinal nerves to exit the sacrum. The auricular

surfaces are articulation sites on the lateral sacrum that anchor the sacrum to the hipbones to form the pelvis. The coccyx is small and derived from the fusion of four small vertebrae.

The intervertebral discs fill in the gaps between the bodies of adjacent vertebrae. They provide strong attachments and padding between the vertebrae. The outer, fibrous layer of a disc is called the anulus fibrosus. The gel-like interior is called the nucleus pulposus. The disc can change shape to allow for movement between vertebrae. If the anulus fibrosus is weakened or damaged, the nucleus pulposus can protrude outward, resulting in a herniated disc.

The anterior longitudinal ligament runs along the full length of the anterior vertebral column, uniting the vertebral bodies. The supraspinous ligament is located posteriorly and interconnects the spinous processes of the thoracic and lumbar vertebrae. In the neck, this ligament expands to become the nuchal ligament. The nuchal ligament is attached to the cervical spinous processes and superiorly to the base of the skull, out to the external occipital protuberance. The posterior longitudinal ligament runs within the vertebral canal and unites the posterior sides of the vertebral bodies. The ligamentum flavum unites the lamina of adjacent vertebrae.

Review Questions

Critical Thinking Questions

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19.4.3: The Thoracic Cage

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

- 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 19.4.3.1). The ribs are anchored posteriorly to the 12 thoracic vertebrae (T1–T12). The thoracic cage protects the heart and lungs.

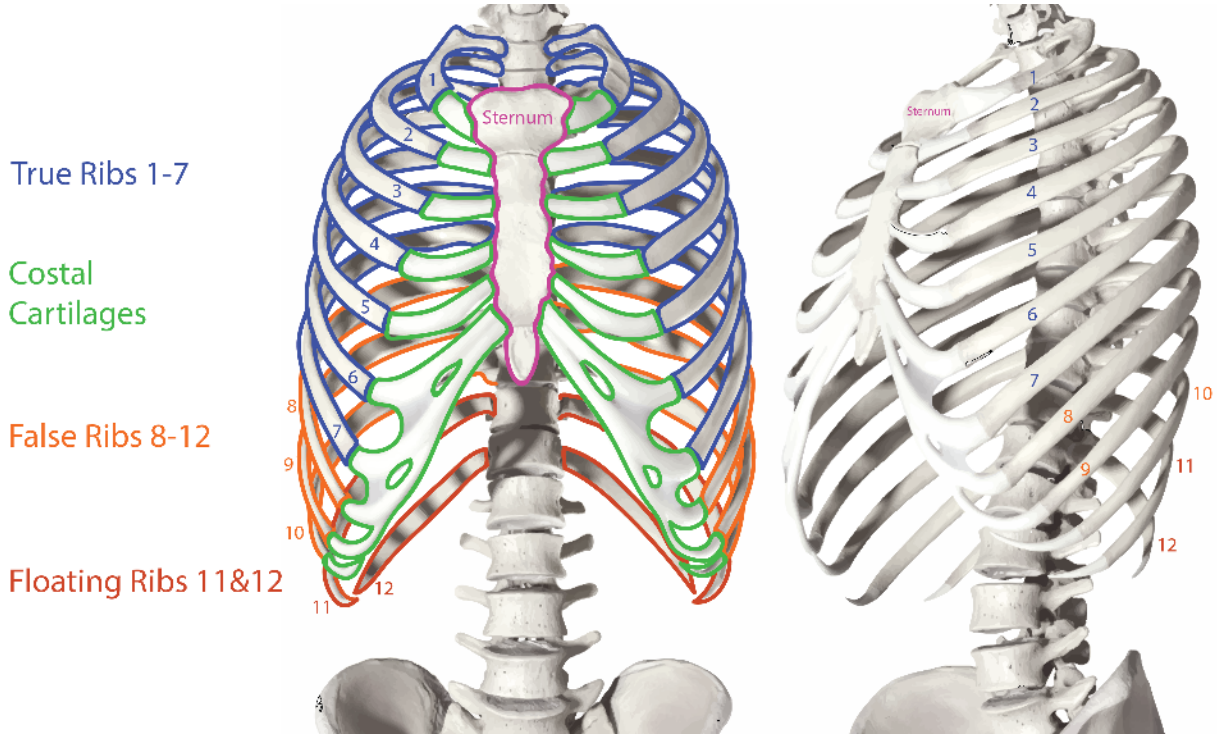


Figure 19.4.3.1: Thoracic Cage. The thoracic cage is formed by the sternum and 12 pairs of ribs with their costal cartilages. The ribs are anchored posteriorly to the 12 thoracic vertebrae. The ribs are classified as true ribs (1–7) and false ribs (8–12). The last two pairs of false ribs are also known as floating ribs (11–12). *(Image credit: "Thoracic Cage" by Gabrielle Spurlock is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.)*

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.

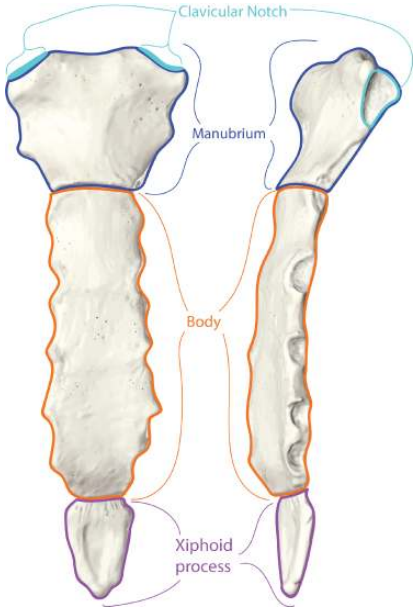


Figure 19.4.3.2: The sternum is located on the anterior midline of the thoracic cage. It is composed of three major regions: the manubrium, the body, and the xiphoid process. While the manubrium and the body begin fusing around age seven, the xiphoid process does not fuse with the body until later in life and may remain an independent bone. *(Image credit: "Sternum" by Gabrielle Spurlock is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.)*

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, or felt with the fingers through the skin. 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.

DISORDERS OF THE...

Thoracic Cage: Honeycomb sternum

The sternum develops from multiple ossification centers, typically one in the manubrium, four in the body, and one in the xiphoid process. The osteoid laid down starting at each center normally fuse together to form the singular bone region in childhood or early adulthood. A rare developmental variant of the sternum, resulting from unfused ossification centers gives a honeycomb configuration of the sternal body. This condition is usually asymptomatic and discovered incidentally during a routine exam of the chest.

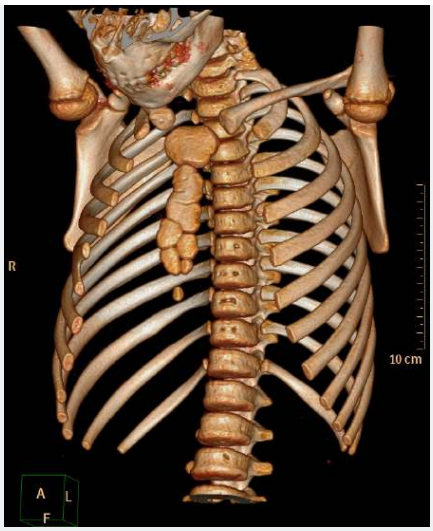


Figure 19.4.3.3: Honeycomb sternum. Case courtesy of Wesam Shamma, Radiopaedia.org. From the case rID: 174406.

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

Figure 19.4.3.4 diagrams the bone markings 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 demifacet located on the body of the same numbered thoracic vertebra and to a lesser degree, with the costal demifacet located on the body of the next higher vertebra (Figure 19.4.3.5). 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). 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. The anterior end of each rib articulates with the the costal cartilage for ribs 1-10, while the anterior end of ribs 11 and 12 are typically pointed.

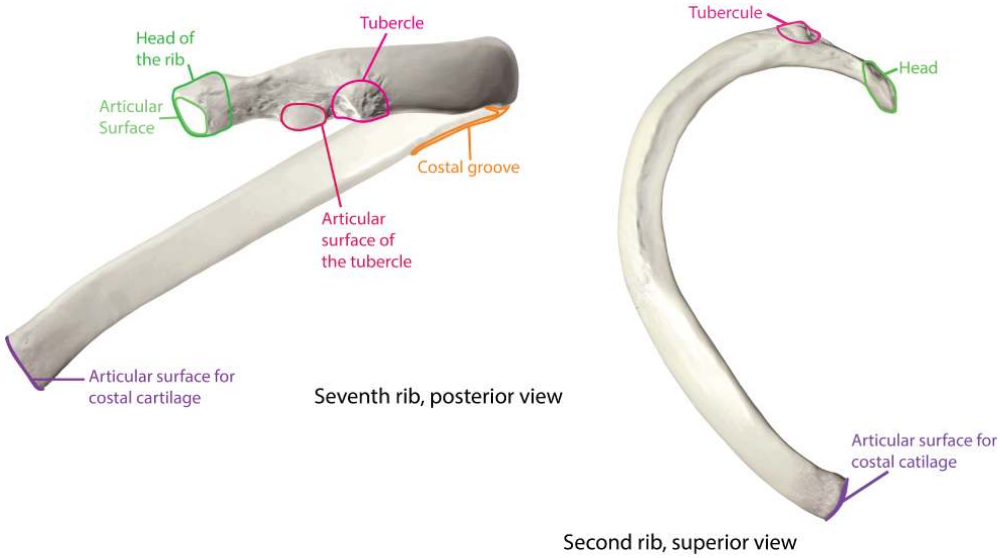


Figure 19.4.3.4: Typical ribs. Features of ribs 2-10. *(Image credit: "Typical Ribs" by Gabrielle Spurlock is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.)*

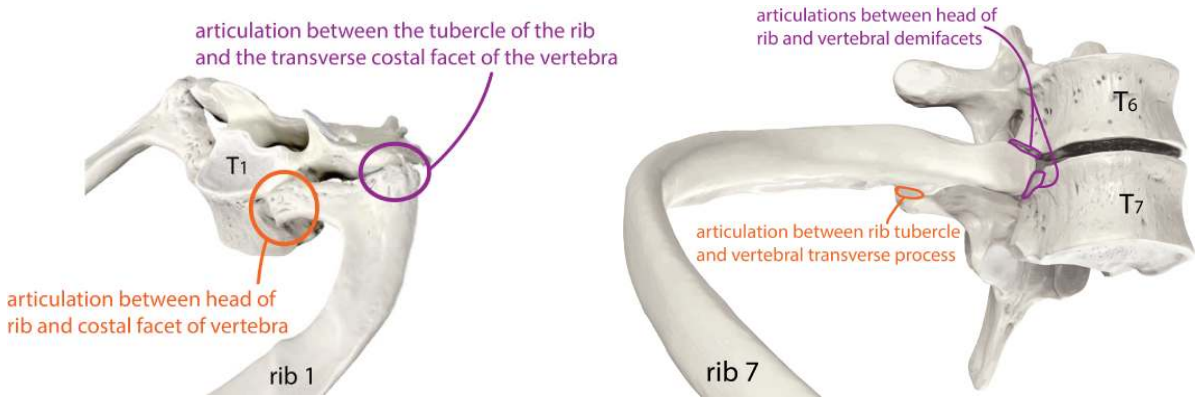


Figure 19.4.3.5: Vertebrocostal joints. The tubercle and head of the rib articulate posteriorly with the thoracic vertebrae while the anterior end articulates with the costal cartilages. *(Image credit: "Vertebrocostal Joints" by Gabrielle Spurlock is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.)*

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 19.4.3.1). 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.

Concept Review

The thoracic cage protects the heart and lungs. It is composed of 12 pairs of ribs with their costal cartilages and the sternum. The ribs are anchored posteriorly to the 12 thoracic vertebrae. The sternum consists of the manubrium, body, and xiphoid process. The manubrium and body are joined at the sternal angle, which is also the site for attachment of the second ribs.

Ribs are flattened, curved bones and are numbered 1–12. Posteriorly, the head of the rib articulates with the costal facets located on the bodies of thoracic vertebrae and the rib tubercle articulates with the facet located on the vertebral transverse process. The angle of the ribs forms the most posterior portion of the thoracic cage. The costal groove in the inferior margin of each rib carries blood vessels and a nerve. Anteriorly, each rib ends in a costal cartilage. True ribs (1–7) attach directly to the sternum via their costal cartilage. The false ribs (8–12) either attach to the sternum indirectly or not at all. Ribs 8–10 have their costal cartilages attached to the cartilage of the next higher rib. The floating ribs (11–12) are short and do not attach to the sternum or to another rib.

Review Questions

Critical Thinking Questions

Glossary

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19.4.4: The Pectoral Girdle

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

- 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. The bones that attach each upper limb to the axial skeleton form the pectoral girdle (shoulder girdle) that consists of two bones, the scapula and clavicle (Figure 19.4.4.1). 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.

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.

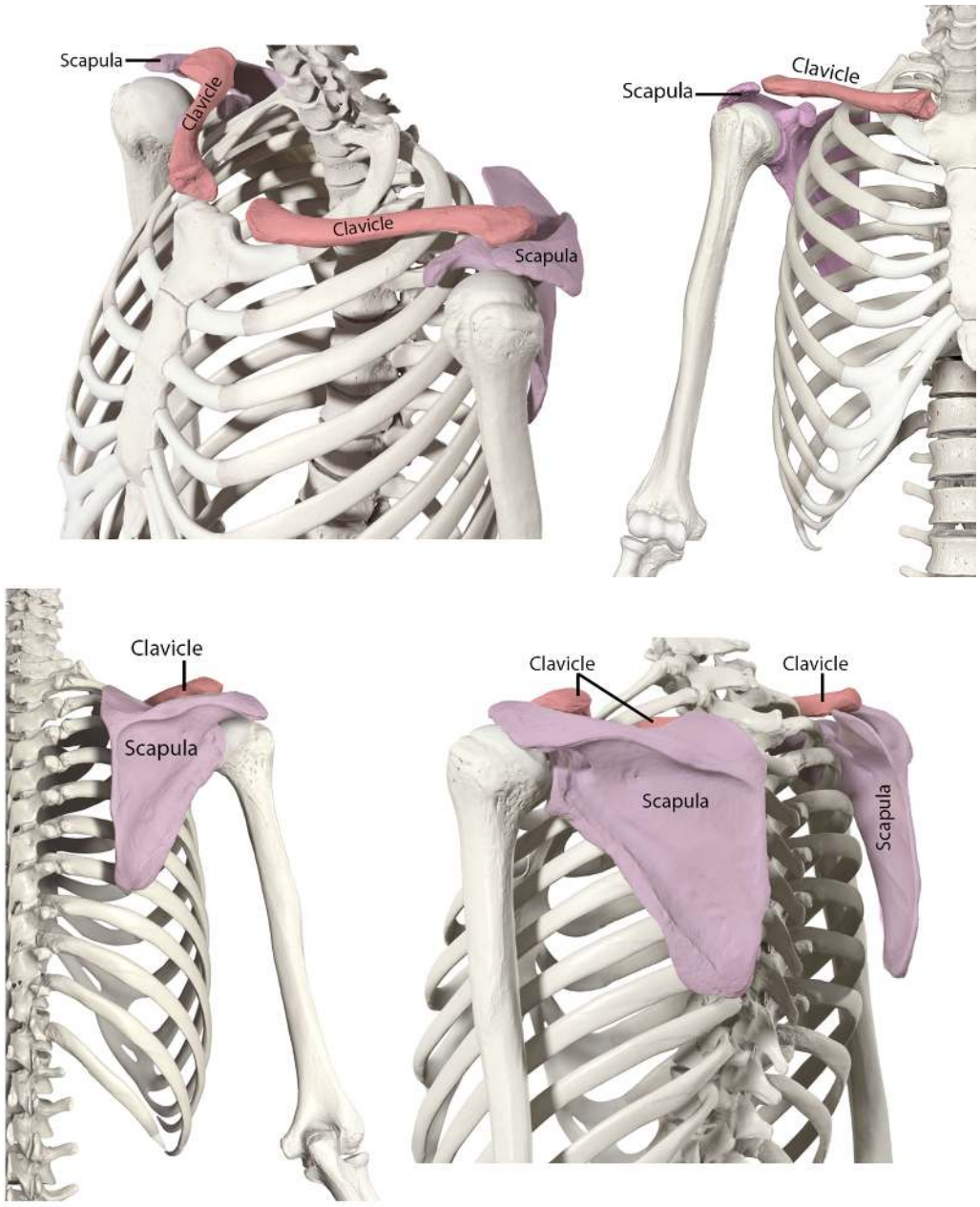


Figure 19.4.4.1: Pectoral Girdle. The pectoral girdle consists of the clavicle and the scapula, which serve to attach the upper limb to the sternum of the axial skeleton. *(Image credit: "Pectoral Girdle Bones Anterior and Posterior Views" by Jennifer Lange are licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.)*

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 (Figure 19.4.4.2). 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.

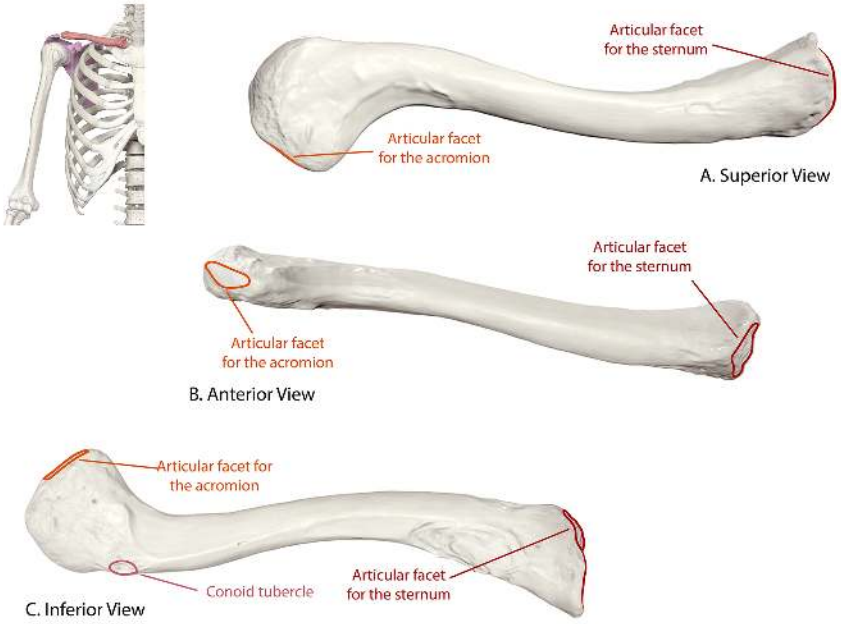


Figure 19.4.4.2: Clavicle. Each view of the clavicle shows the articular surfaces on the medial (sternal) and lateral (acromial) ends of the bone. On the inferior aspect is the conoid tubercle, which is an attachment site for the coracoclavicular ligaments of the shoulder joint. *(Image credit: "Clavicle - Superior, Anterior, Inferior" by Mark Schaeffer and Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.)*

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 19.4.4.3). 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.

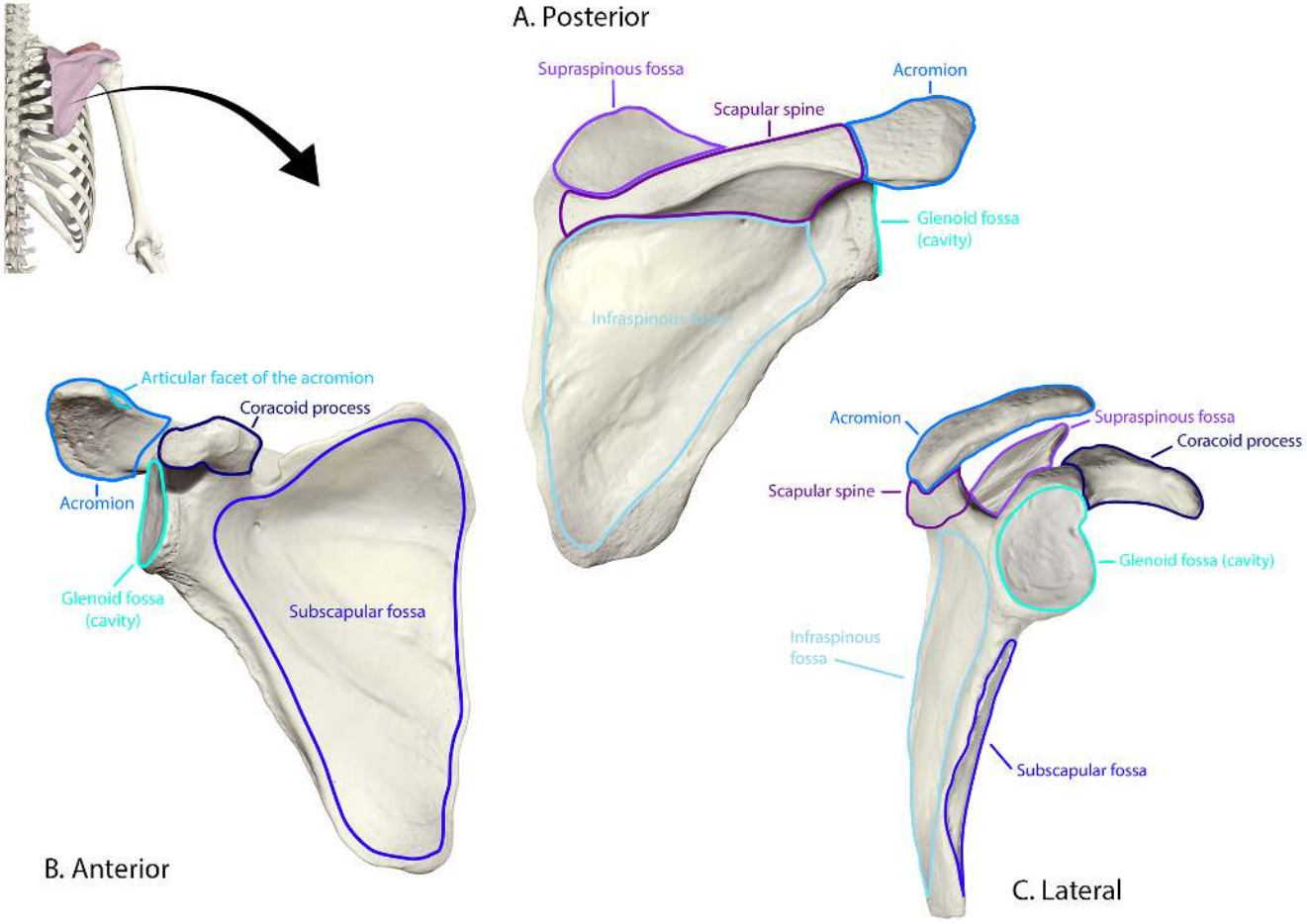


Figure 19.4.4.3: Scapula. The isolated scapula is shown here from anterior, posterior, and lateral views. *(Image credit: "Scapular Landmarks Multiple Views" by Claire McGuire and Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of images from Anatomy Standard under CC BY-NC 4.0.)*

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 19.4.4.2). 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.

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 19.4.4.2). 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.

Concept Review

The pectoral girdle, consisting of the clavicle and the scapula, attaches each upper limb to the axial skeleton. The clavicle is an anterior bone whose sternal end articulates with the manubrium of the sternum at the sternoclavicular joint. The sternal end is also anchored to the first rib by the costoclavicular ligament. The acromial end of the clavicle articulates with the acromion of the scapula at the acromioclavicular joint. This end is also anchored to the coracoid process of the scapula by the coracoclavicular ligament, which provides indirect support for the acromioclavicular joint. The clavicle supports the scapula, transmits the weight and forces from the upper limb to the body trunk, and protects the underlying nerves and blood vessels.

The scapula lies on the posterior aspect of the pectoral girdle. It mediates the attachment of the upper limb to the clavicle, and contributes to the formation of the glenohumeral (shoulder) joint. This triangular bone has three sides called the medial, lateral, and superior borders. The suprascapular notch is located on the superior border. The scapula also has three corners, two of which are the superior and inferior angles. The third corner is occupied by the glenoid cavity. Posteriorly, the spine separates the supraspinous and infraspinous fossae, and then extends laterally as the acromion. The subscapular fossa is located on the anterior surface of the scapula. The coracoid process projects anteriorly, passing inferior to the lateral end of the clavicle.

Review Questions

Critical Thinking Questions

Glossary

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19.4.5: Bones of the Upper Limb

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

- 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 upper **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 (Figure 19.4.5.1). 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** (plural = phalanges) bone of the hand.

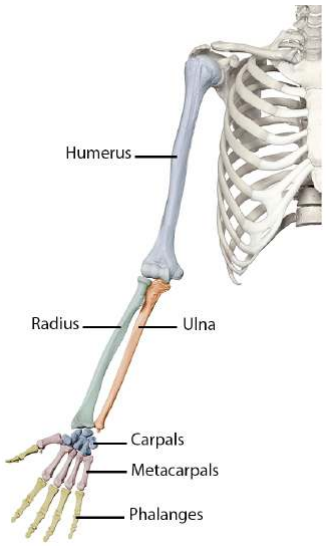


Figure 19.4.5.1: Bones of the Upper Limb. Bones of the brachial, antebrachial, and manual regions. *(Image credit: "Bones of the Upper Limb" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard.)*

Humerus

The **humerus** is the single bone of the upper arm region (Figure 19.4.5.2). 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. 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. 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.

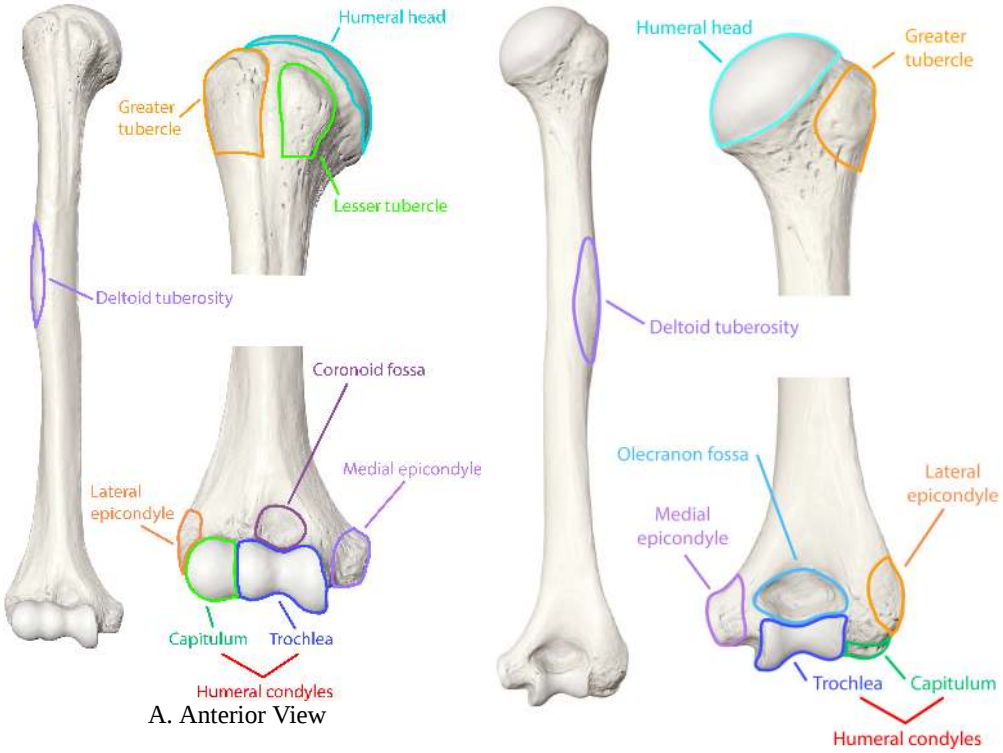
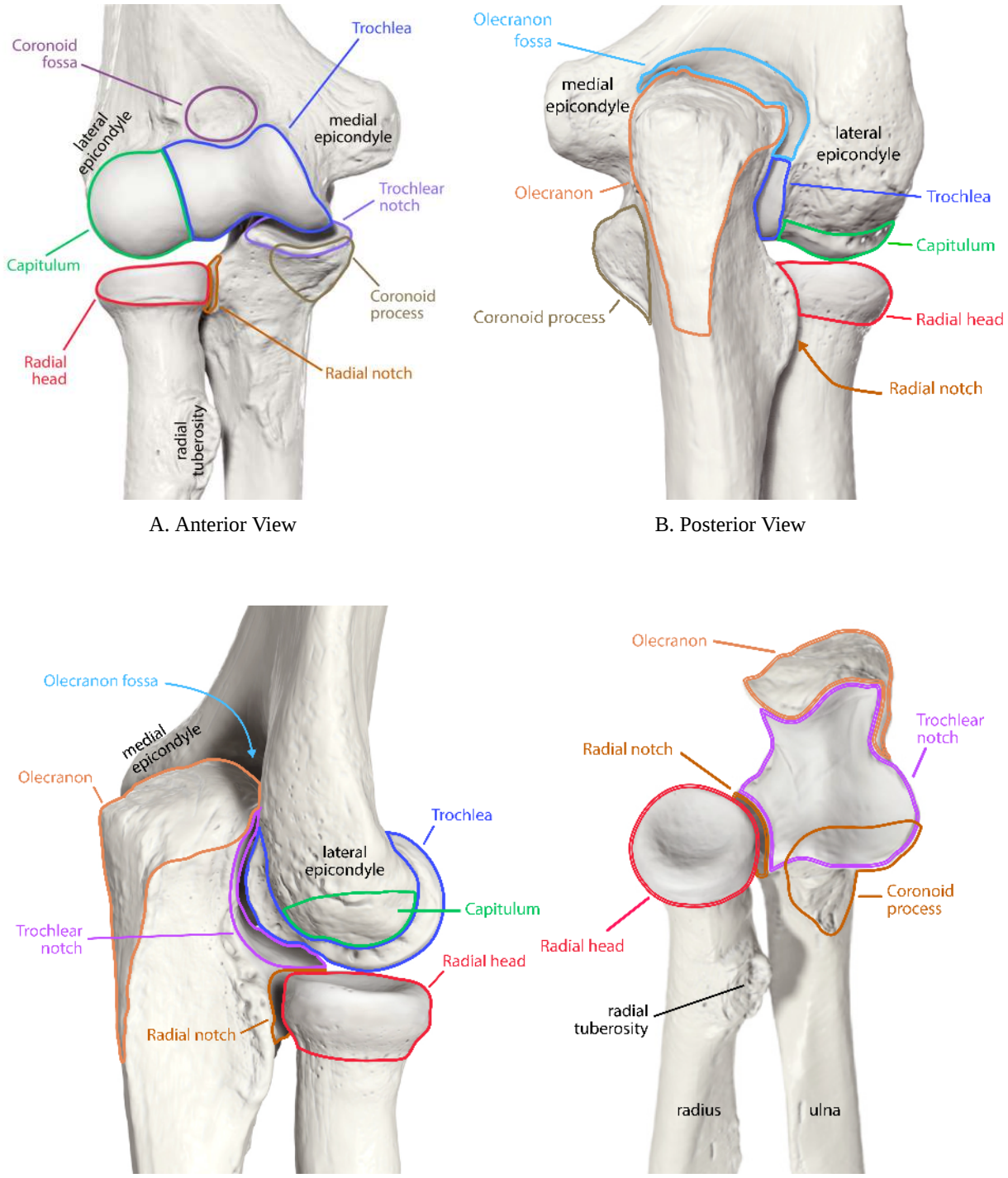


Figure 19.4.5.2: Humerus. The humerus is the single bone of the upper arm region. It articulates with the radius and ulna bones of the forearm to form the elbow joint and with the scapula to form the shoulder joint. *(Image credit: "Humerus - Anterior and Posterior" by Claire McGuire are licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard.)*

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. 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 hour glass- 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 proximal to these bony areas are spaces that accommodate the forearm bones when the elbow is fully bent (flexed) and fully straightened (extended). Superior to the trochlea on the anterior surface is the **coronoid fossa**, which receives the coronoid process of the ulna 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.



A. Anterior View

B. Posterior View

C. Lateral View

D. Proximal Radius and Ulna

Figure 19.4.5.3: Bones of the Elbow Joint. At the elbow joint the "C" shaped trochlear notch pivots around the hourglass shaped trochlea. *(Image credits: "Elbow- Anterior, Posterior, and Lateral" and "Proximal Radius and Ulna" by Claire McGuire are licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard.)*

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 19.4.5.4 and Figure 19.4.5.5). The proximal end of the ulna resembles a crescent wrench with its large, C-shaped indentation called

the **trochlear notch**. This smooth region articulates with the trochlea of the humerus at the elbow joint. The posterior and proximal portion of the ulna, containing the proximal part of the trochlear notch, is the **olecranon process.** The olecranon process forms the bony tip of the elbow that contact the table. The inferior portion of the trochlear notch is on a prominent lip of bone called the **coronoid process of the ulna**. To the lateral side and slightly inferior to the trochlear notch is a small, smooth area called the **radial notch** (this looks like a bite mark in the coronoid process). This indented area is the site of articulation between the proximal radius and ulna, forming the **proximal radioulnar joint**.

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**, also known as the antebrachial interosseous membrane, a sheet of dense connective tissue that unites the ulna and radius bones (Figure 19.4.5.6). 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.

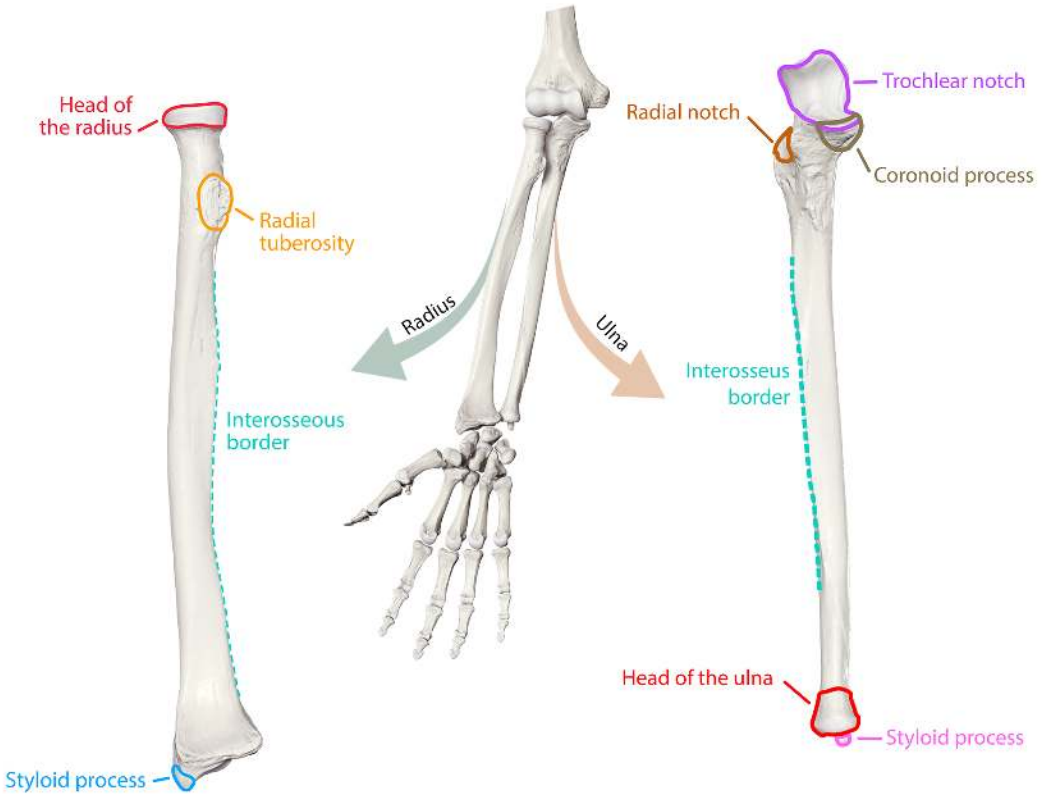


Figure 19.4.5.4: Bones of the Forearm - Anterior View. The radius and the ulna run parallel when in anatomical position. The radius is lateral (thumb side) and the ulna is medial (pinky side). *(Image credit: "Bones of the Forearm - Anterior View" by Jennifer Lange and Claire McGuire is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard.)*

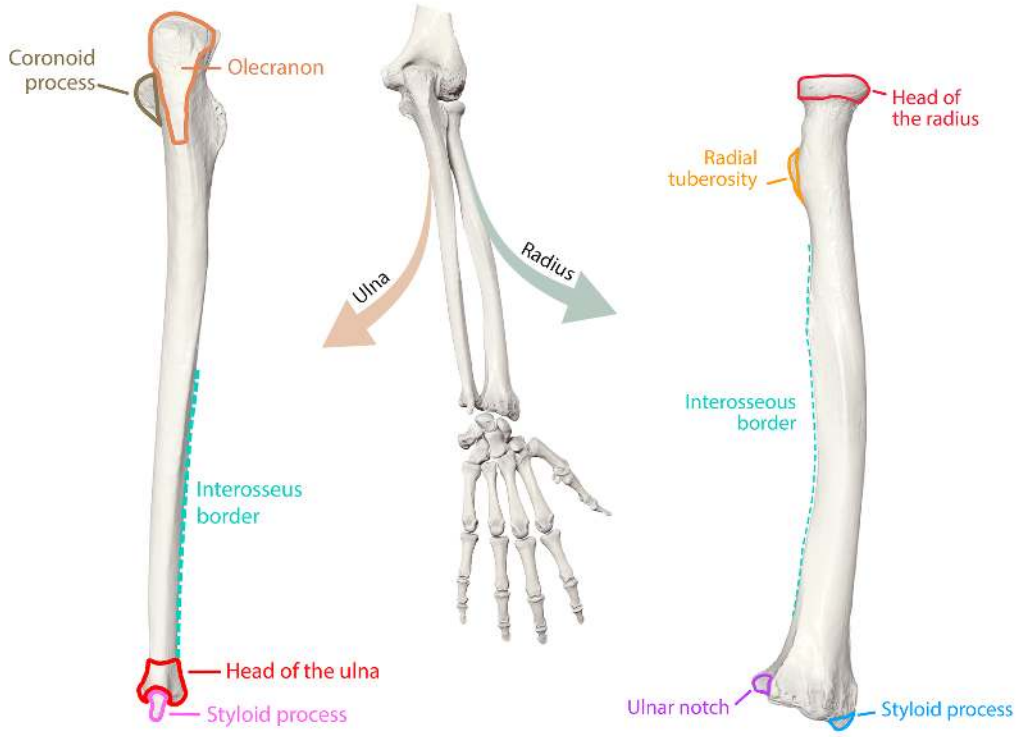


Figure 19.4.5.5: Bones of the Forearm - Posterior View. The radius articulates with the carpals at the wrist joint while the ulna articulates with the trochlea at the elbow joint. *(Image credit: "Bones of the Forearm" by Jennifer Lange and Claire McGuire is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard.)*

Radius

The **radius** runs parallel to the ulna, on the lateral (thumb) side of the forearm (see Figure 19.4.5.4 and Figure 19.4.5.5). 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. 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 (Figure 19.4.5.6). 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 19.4.5.7). 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.

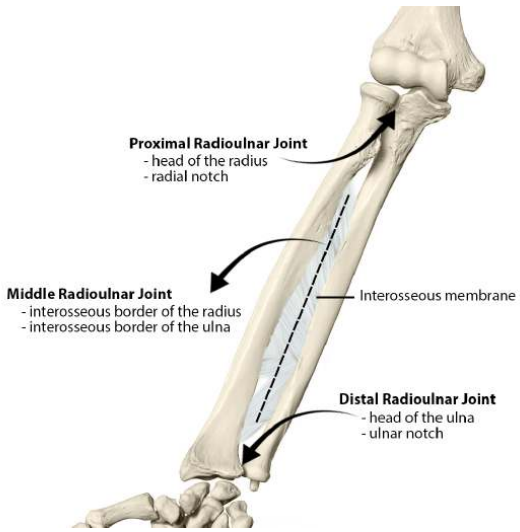


Figure 19.4.5.6: Radioulnar Joints Bone Landmarks. The radius and ulna articulate at three places - the proximal and the distal ends as well as the shafts. *(Image credit: "Radioulnar Joints Bone Landmarks" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard.)*

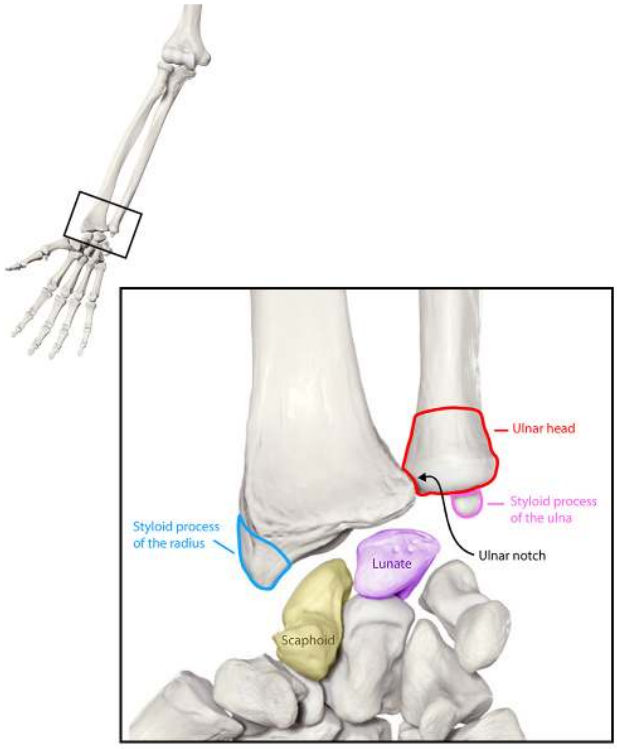


Figure 19.4.5.7: Bones of the Wrist Joint. The wrist is the radiocarpal joint, with the primary joint surfaces on the radius, scaphoid, and lunate. *(Image credit: "Wrist Joint - Anterior" by Claire McGuire is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard.)*

Carpal Bones

The wrist and base of the hand are formed by a series of eight small **carpal bones** (see Figure 19.4.5.8). 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.

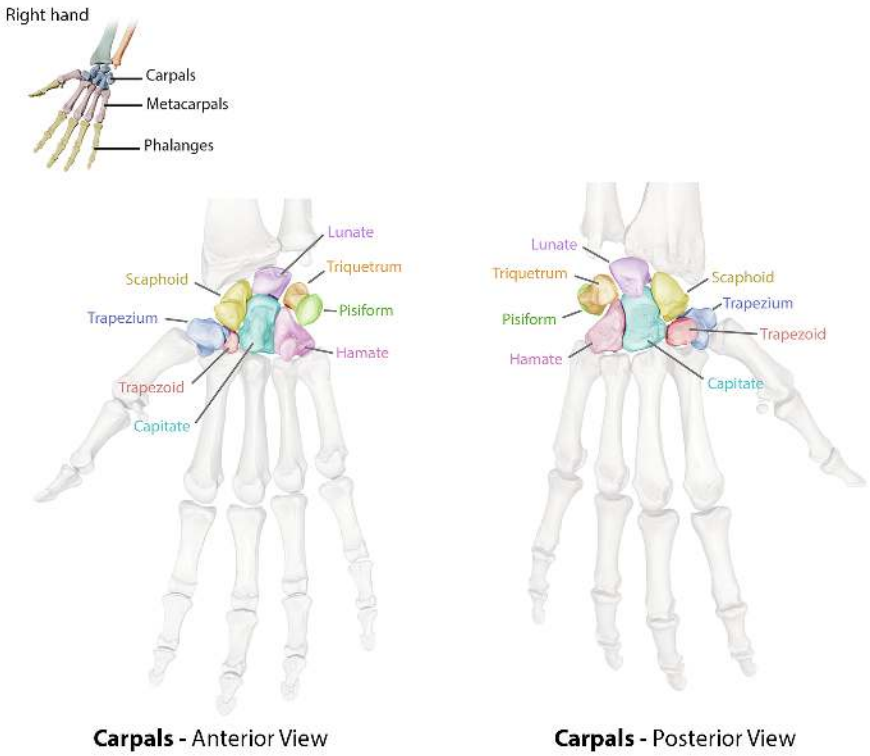


Figure 19.4.5.8: Bones of the Hand. The eight carpal bones form the base of the hand. These are arranged into proximal and distal rows of four bones each. *(Image credit: "Carpals" by Claire McGuire is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard.)*

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 19.4.5.9). 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. The four distal carpal bones are also held together as a group by ligaments. The joints between each adjacent carpal is one of the intercarpal joints. Together, the radiocarpal and intercarpal 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.

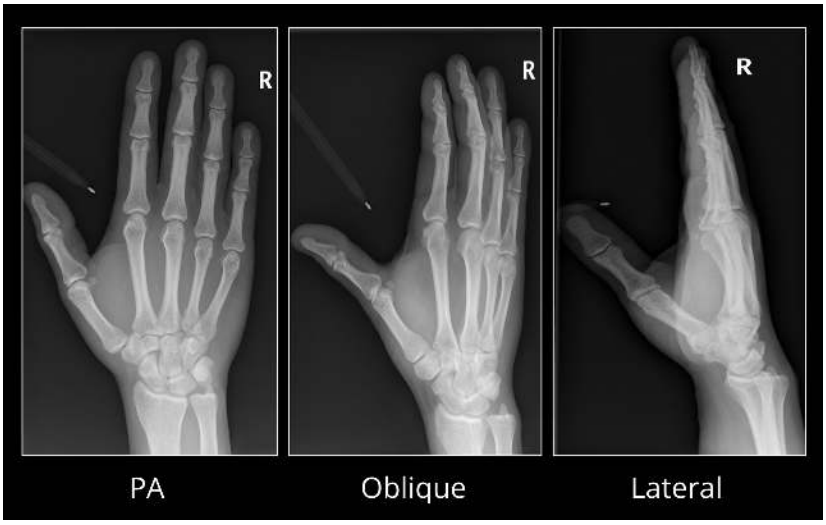


Figure 19.4.5.9: Bones of the Hand. This radiograph shows the position of the bones within the hand. Can you identify each of the carpals in each view? *(Image credit: Case courtesy of Jessica Hui Shi Ng, Radiopaedia.org. From the case rID: 70530.)*

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 (Figure 19.4.5.10). 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. 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.

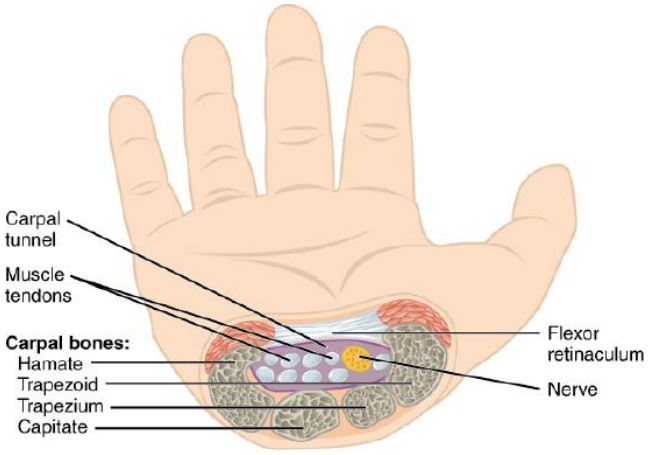


Figure 19.4.5.10: Carpal Tunnel. The carpal tunnel is the passageway by which nine muscle tendons and a major nerve enter the hand from the anterior forearm. The walls and floor of the carpal tunnel are formed by the U-shaped grouping of the carpal bones, and the roof is formed by the flexor retinaculum, a strong ligament that anteriorly unites the bones. (Image credit: "The Carpal Tunnel" by OpenStax is licensed under CC BY 3.0.)

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 19.4.5.11). The proximal end, also known as the base, of each metacarpal bone articulates with one of the distal carpal bones. Each of these articulations is a **carpometacarpal joint**. The elongated portion of the metacarpal bone is the body, or shaft. The expanded distal end, also known as the head, 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 (or moving lateral to medial).

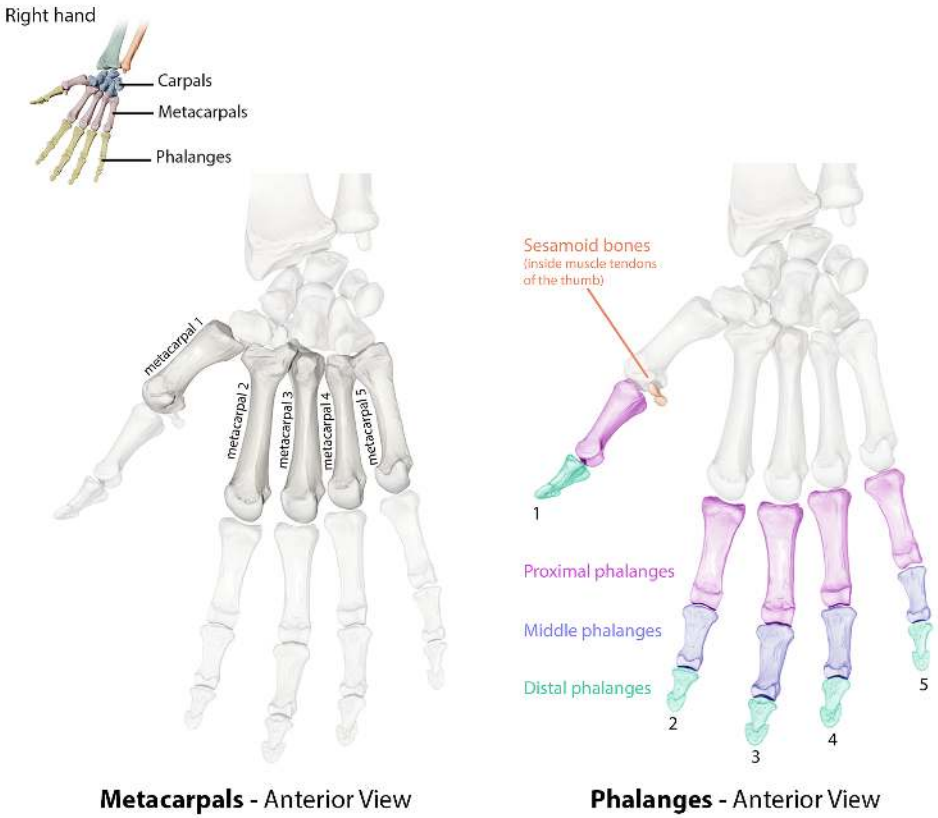


Figure 19.4.5.11: Metacarpals and Phalanges. The digits are numbered 1 to 5, with digit 1 being the thumb. Both the metacarpals and phalanges are named according to which digit they belong to. *(Image credit: "Metacarpals and Phalanges" by Claire McGuire is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard.)*

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 19.4.5.12). The anterior movement of these bones, particularly the fifth metacarpal bone, increases the strength of contact for the medial hand during gripping actions.



Figure 19.4.5.12: 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. *(Image credit: "Hand Gripping" by OpenStax is licensed under CC BY 3.0.)*

Phalanx Bones

The fingers and thumb are composed of 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 19.4.5.11). Digits 2 (index finger), 3 (middle finger), 4 (ring finger), and 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. Each phalanx bone has a base (proximal end), body (shaft), and a head (distal end).

Appendicular System: Fractures of 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.

Another frequent injury following a fall onto an outstretched hand is a Colles fracture ("col-lees") of the distal radius (see Figure 19.4.5.13). 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.



Figure 19.4.5.13: Fractures of the Upper Limb. A Colles fracture of the distal radius is the most common forearm fracture. The scaphoid is the most commonly fractured carpal. *(Image credits: Colles fracture case courtesy of Pir Abdul Ahad Aziz Qureshi, Radiopaedia.org. From the case rID: 47908. Scaphoid fracture case courtesy of David Cuete, Radiopaedia.org. From the case rID: 27557.)*

The most commonly fractured carpal bone is the scaphoid (see Figure 19.4.5.13), 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.

Concept Review

Each upper limb is divided into three regions and contains a total of 30 bones. The upper arm is the region located between the shoulder and elbow joints. This area contains the humerus. The proximal humerus consists of the head, which articulates with the scapula at the glenohumeral joint, the greater and lesser tubercles separated by the intertubercular (bicipital) groove, and the anatomical and surgical necks. The humeral shaft has the roughened area of the deltoid tuberosity on its lateral side. The distal humerus is flattened, forming a lateral supracondylar ridge that terminates at the small lateral epicondyle. The medial side of the distal humerus has the large, medial epicondyle. The articulating surfaces of the distal humerus consist of the trochlea medially and the capitulum laterally. Depressions on the humerus that accommodate the forearm bones during bending (flexing) and straightening (extending) of the elbow include the coronoid fossa, the radial fossa, and the olecranon fossa.

The forearm is the region of the upper limb located between the elbow and wrist joints. This region contains two bones, the ulna medially and the radius on the lateral (thumb) side. The elbow joint is formed by the articulation between the trochlea of the humerus and the trochlear notch of the ulna, plus the articulation between the capitulum of the humerus and the head of the radius. The proximal radioulnar joint is the articulation between the head of the radius and the radial notch of the ulna. The proximal ulna also has the olecranon process, forming an expanded posterior region, and the coronoid process and ulnar tuberosity on its anterior aspect. On the proximal radius, the narrowed region below the head is the neck; distal to this is the radial tuberosity. The shaft portions of both the ulna and radius have an interosseous border, whereas the distal ends of each bone have a pointed styloid process. The distal radioulnar joint is found between the head of the ulna and the ulnar notch of the radius. The distal end of the radius articulates with the proximal carpal bones, but the ulna does not.

The base of the hand is formed by eight carpal bones. The carpal bones are united into two rows of bones. The proximal row contains (from lateral to medial) the scaphoid, lunate, triquetrum, and pisiform bones. The scaphoid, lunate, and triquetrum bones contribute to the formation of the radiocarpal joint. The distal row of carpal bones contains (from medial to lateral) the hamate, capitate, trapezoid, and trapezium bones (“So Long To Pinky, Here Comes The Thumb”). The anterior hamate has a prominent bony hook. The proximal and distal carpal rows articulate with each other at the midcarpal joint. The carpal bones, together with the flexor retinaculum, also form the carpal tunnel of the wrist.

The five metacarpal bones form the palm of the hand. The metacarpal bones are numbered 1–5, starting with the thumb side. The first metacarpal bone is freely mobile, but the other bones are united as a group. The digits are also numbered 1–5, with the thumb being number 1. The fingers and thumb contain a total of 14 phalanges (phalanx bones). The thumb contains a proximal and a distal phalanx, whereas the remaining digits each contain proximal, middle, and distal phalanges.

Review Questions

Critical Thinking Questions

Glossary

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19.4.6: The Pelvic Girdle and Pelvis

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

- Define the pelvic girdle and describe the bones 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 two bones the right and left **os coxa** or **coxal bones** (coxal = “hip”), which serves as the attachment point for each lower limb. Each os coxa, in turn, is firmly joined to the axial skeleton via its attachment to the sacrum of the vertebral column. The right and left coxal bones also converge anteriorly to attach to each other. The bony **pelvis** is the entire structure formed by the two os coxae, the sacrum, and, attached inferiorly to the sacrum, the coccyx (Figure 19.4.6.1).

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.

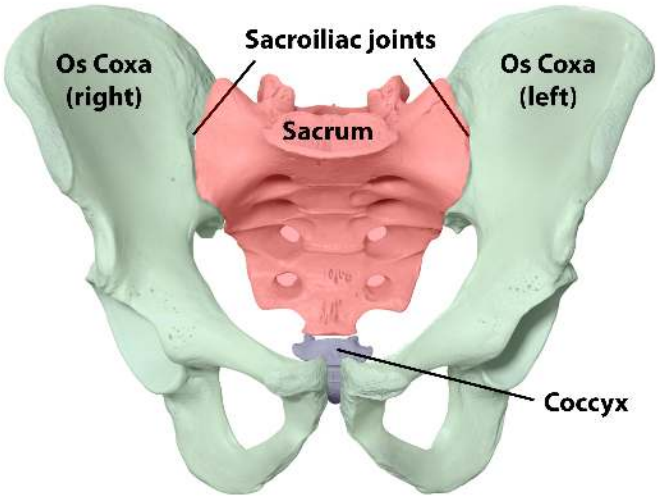


Figure 19.4.6.1: Pelvis. The pelvic girdle is formed by two coxal bones. The os coxa attaches the lower limb to the axial skeleton through its articulation with the sacrum. The right and left os coxae, plus the sacrum and the coccyx, together form the pelvis. *(Image credit: "Pelvic Girdle" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.)*

Coxal Bone

The **os coxa** or **coxal bone**, forms the pelvic girdle portion of the pelvis. The paired coxal bones are the large, curved bones that form the lateral and anterior aspects of the pelvis. Each adult coxalp 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 19.4.6.2). These names are retained and used to define the three regions of the adult coxal bone.

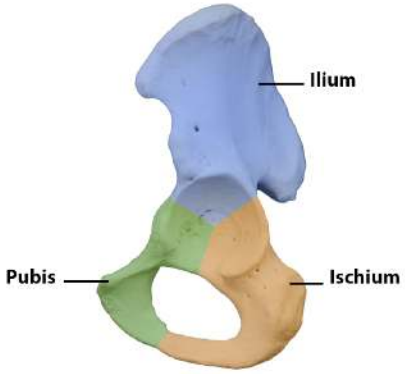


Figure 19.4.6.2: The Os Coxa. The adult coxal bone consists of three regions. The ilium forms the large, fan-shaped superior portion, the ischium forms the posteroinferior portion, and the pubis forms the anteromedial portion. *(Image credit: "Os Coxa Regions" by Jennifer Lange, modification of image from BlueLink that is licensed under CC BY-NC 4.0 with notification of the original authors.)*

The three regions of the adult os coxa can be seen in Figure 19.4.6.2. 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 19.4.6.1). 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 19.4.6.3). 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.

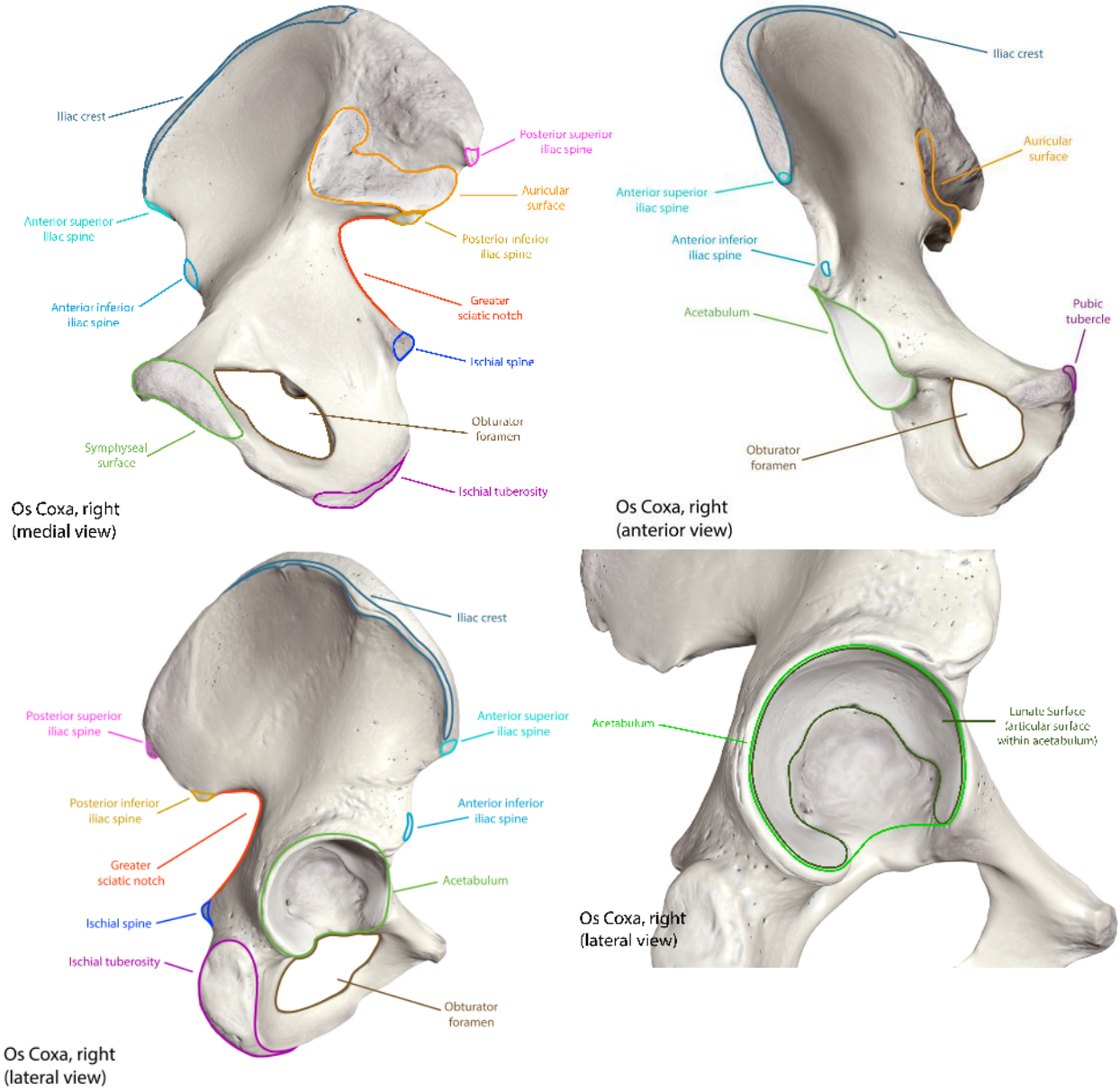


Figure 19.4.6.3: Landmarks of the os coxa as viewed medially, anteriorly, laterally. The close up of the lateral view shows the articular surface within the hip socket. *(Image credit: "Os Coxa, Multiple Views" by Mark Schaeffer is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.)*

The shallow depression located on the anteromedial (internal) surface of the upper ilium is called the **iliac fossa**. 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 19.4.6.2). The large, smooth area of the superior ischium is the **ischial body**.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.

Pubis

The pubis forms the anterior portion of the hip bone (see Figure 19.4.6.2). 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 pubic body is joined to the pubic body of the opposite hip bone by the pubic symphysis (Figure 19.4.6.1). The flattened, medial surface of the bone is the **symphyseal**

surface. The symphyseal surface of the right and left bones meet at the anterior midline of the pelvis to form the public symphysis joint.

Pelvis

The pelvis consists of four bones: the right and left os coxae, the sacrum, and the coccyx (see Figure 19.4.6.1). 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 coxal bone, the ilium, pubis, and ischium, converge centrally to form a deep, cup-shaped cavity called the **acetabulum** (Figure 19.4.6.2 and Figure 19.4.6.3). This is located on the lateral side of the os coxa and is the socket of the hip joint. The large opening in the anteroinferior coxal bone between the ischium and pubis is the **obturator foramen** (Figure 19.4.6.3). 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.

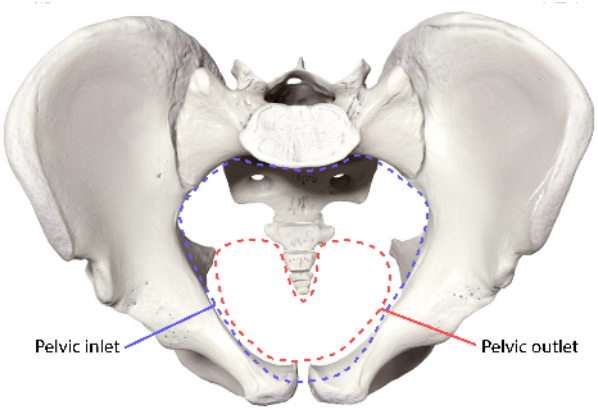


Figure 19.4.6.4: Pelvis. The pelvic follows the line of the pelvic brim and is the superior line tracing the area in which the pelvis forms a complete circle. The pelvic outlet is smaller and more inferior than the inlet. *(Image credit: "Pelvis" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.)*

The space enclosed by the bony pelvis is divided into two regions (Figure 19.4.6.4). 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.

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 19.4.6.5). 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 19.4.6.1 provides an overview of the general differences between the female and male pelvis.

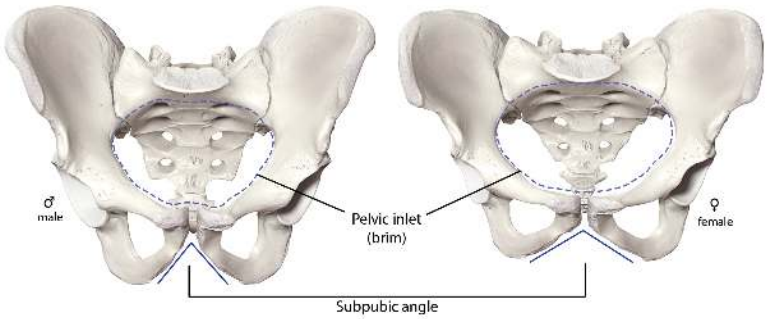


Figure 19.4.6.5: Male and Female Pelvis. The female pelvis is adapted for childbirth and is broader, with a larger subpubic angle and a wider pelvic brim than the male pelvis. *(Image credit: "Male and Female Pelvis Comparison" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.)*

Table 19.4.6.1: Overview of Differences between the Female and Male Pelvis

Characteristic	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
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 (Figure 19.4.6.6). 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.



Figure 19.4.6.6: Muhammad Nurul Islam, a UN forensic pathologist, examines human bones found on Dili beach, in the UN lab in Dili, Timor-Leste. *(Image credit: "Pathologist Examines Human Bones in Timor-Leste" by United Nations Photo is licensed under CC BY-NC-ND 2.0.)*

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 archeological 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.

Concept Review

The pelvic girdle consists of the right and left ox coxae, which serve to attach each lower limb to the axial skeleton.

Joints

1. posterior with the sacrum at the sacroiliac joint,
2. anteriorly with each other at the pubic symphysis.

Regions

1. the ilium forms the large, fan-like superior region of the bone,
    - superior margin of this area is the iliac crest
    - at either end of the iliac crest are the anterior superior and posterior superior iliac spines
    - inferior to these are the anterior inferior and posterior inferior iliac spines
    - the medial facing auricular surface of the ilium articulates with the sacrum
    - the greater sciatic notch is the posterior margin of the ilium
2. the ischium is the posterolateral portion of the bone,
    - the ischial tuberosity supports body weight when sitting
    - the ischial spine is superior to the ischial tuberosity
3. the pubis forms the anterior portion of the bone
    - the symphyseal surface of each os coxa articulates with the other at the pubic symphysis joint
    - the pubic tubercle is on the superior margin, superior to the symphyseal surface

Multiregion Landmarks

1. The lateral side of the hip bone has the cup-like acetabulum, which is part of the hip joint.
2. The large anterior opening is the obturator foramen.

Pelvic Openings

1. These superior opening is the pelvic inlet (pelvic brim).
2. The inferior opening of the pelvis is the pelvic outlet.
3. Compared to the male, the female pelvis is wider to accommodate childbirth, has a larger subpubic angle, and a broader pelvic inlet and pelvic outlet.

Pelvis

The combination of the two os coxae, the sacrum, and the coccyx forms the pelvis. The pelvis has a pronounced anterior tilt. The primary function of the pelvis is to support the upper body and transfer body weight to the lower limbs. It also serves as the site of

attachment for multiple muscles.

Review Questions

Critical Thinking Questions

Glossary

Contributors and Attributions

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19.4.7: Bones of the Lower Limb

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

- 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 (Figure 19.4.7.1). 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**.

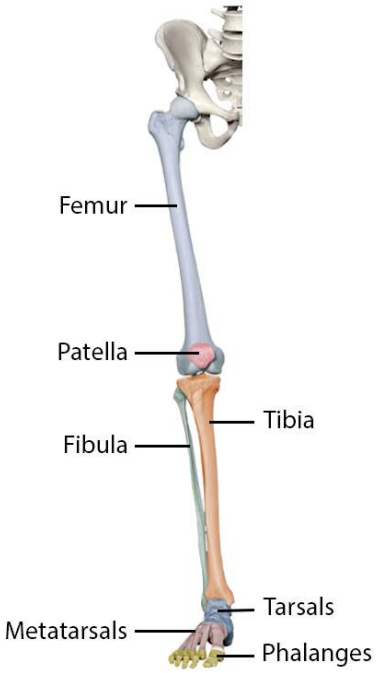


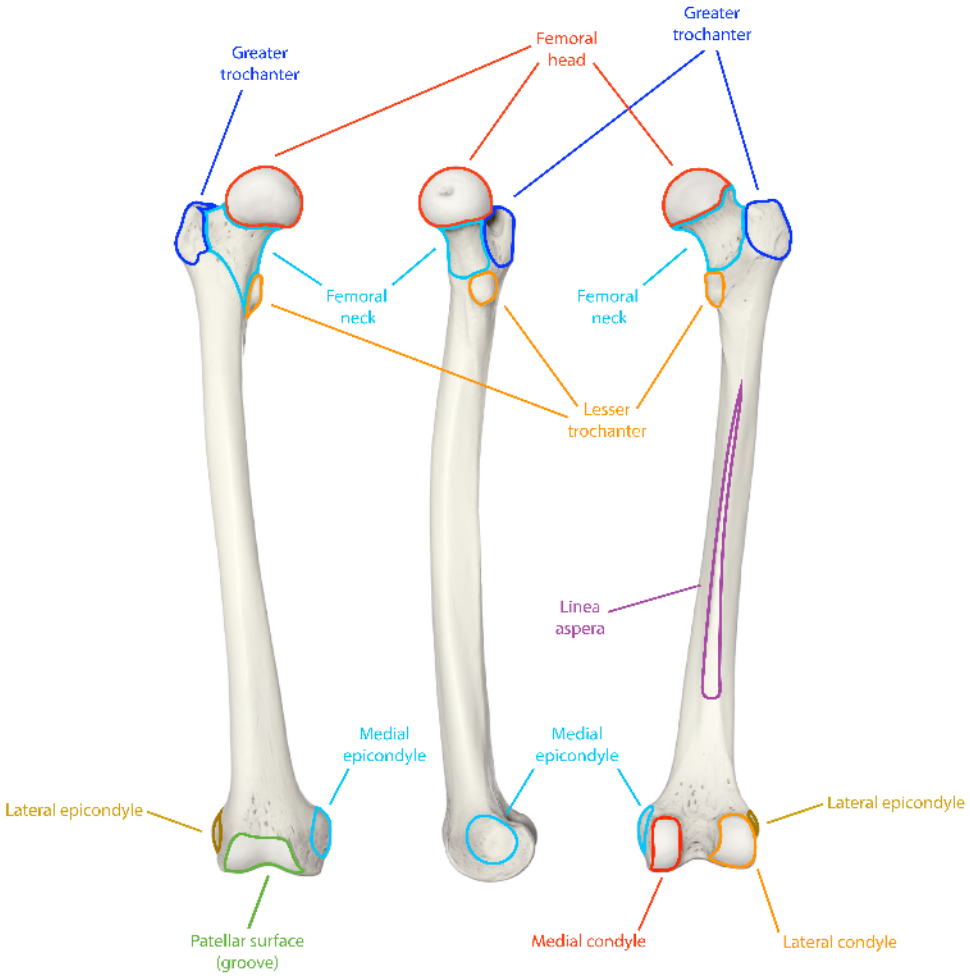
Figure 19.4.7.1: Bones of the Lower Limb. Bones of the femoral, crural, and pedal regions. *(Image credit: "Bones of the Lower Limb" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.)*

Bones of the Thigh

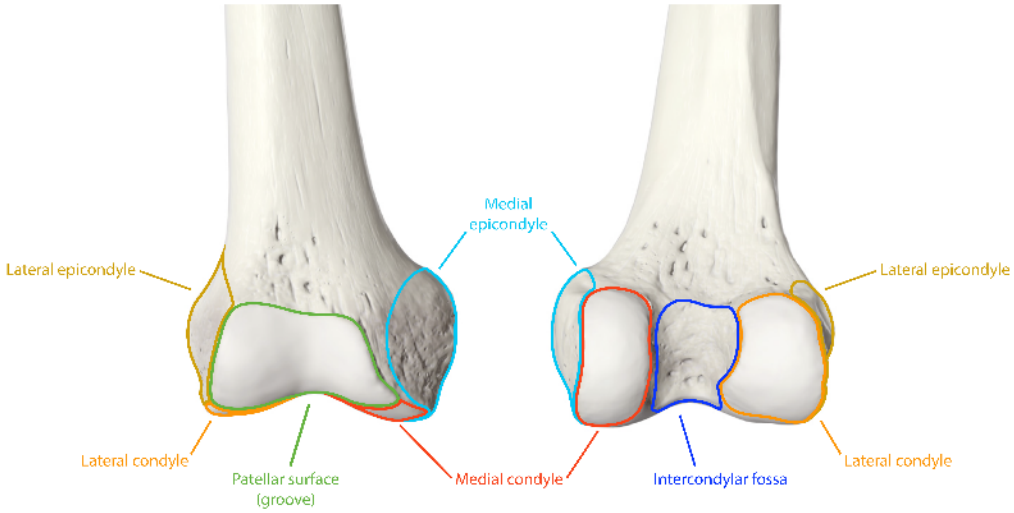
The thigh is the common name for the femoral region, the area from where the lower limb meets the trunk to the midline of the knee joint. Two bones are within this region: the femur and the patella.

Femur

The **femur**, or thigh bone, is the single bone of the thigh region (Figure 19.4.7.2) . 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.

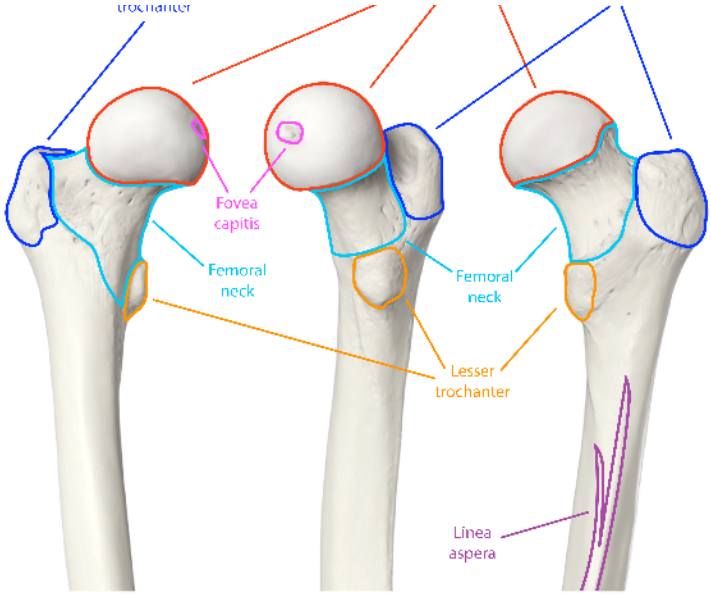


A. Anterior, Medial, and Posterior Views of the Femur



B. Anterior and Posterior Views of the Distal Femur





C. Anterior, Medial, and Posterior Views of the Proximal Femur

Figure 19.4.7.2: Femoral Landmarks. 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. *(Image credit: "Femoral Landmarks" by Mark Schaeffer are licensed under CC BY-NC-SA 4.0, modification of images from Anatomy Standard under CC BY-NC 4.0.)*

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.

The elongated body, or **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 of hip and knee joints and supporting ligaments of the knee. 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.

Patella

The triangular shaped patella (kneecap) has its pointy **apex** on the inferior side and its broader **base** on the superior side. It is largest sesamoid bone of the body (Figure 19.4.7.3) . 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 **articular surface of 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.

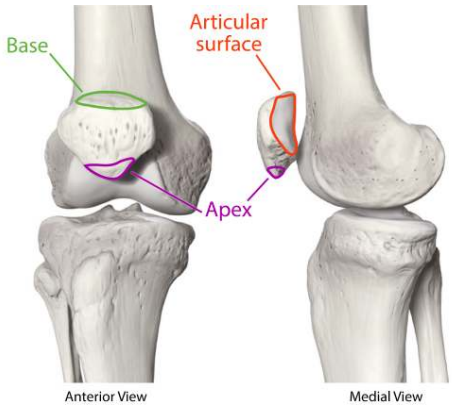


Figure 19.4.7.3: Patella. The patella sits in the patellar groove of the femur. This articulation forms the patellofemoral joint, which is a separate joint from the knee joint. *(Image credit: "Patella" by Mark Schaeffer is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.)*

DISORDER OF THE .....

Skeletal System: 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 n 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 19.4.7.2) . 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.

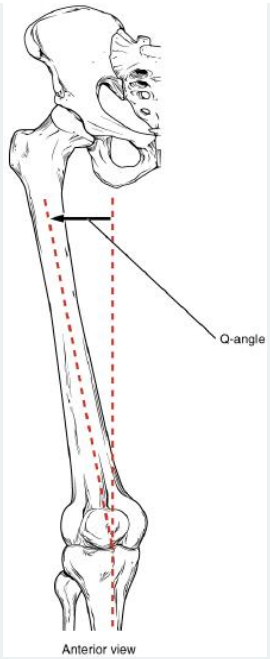


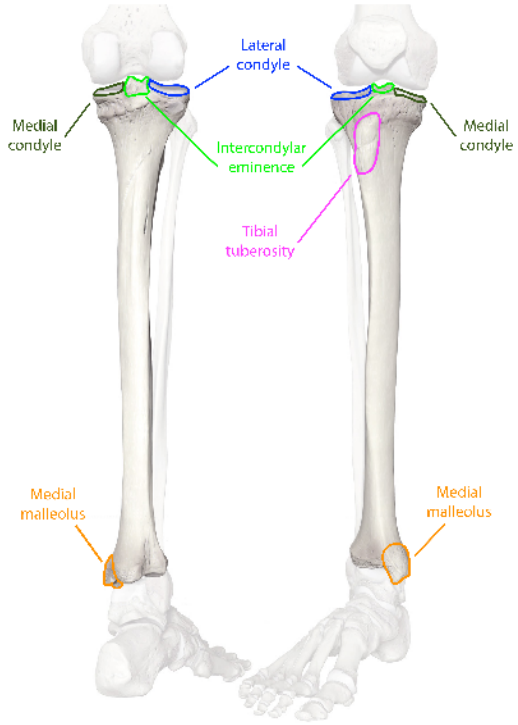
Figure 19.4.7.4: The Q-Angle. The Q-angle is a measure of the amount of lateral deviation of the femur from the vertical line of the tibia. Adult females have a larger Q-angle due to their wider pelvis than adult males. *(Image credit: "Femur Q Angle" by OpenStax is licensed under CC BY 3.0)*

Bones of the Leg

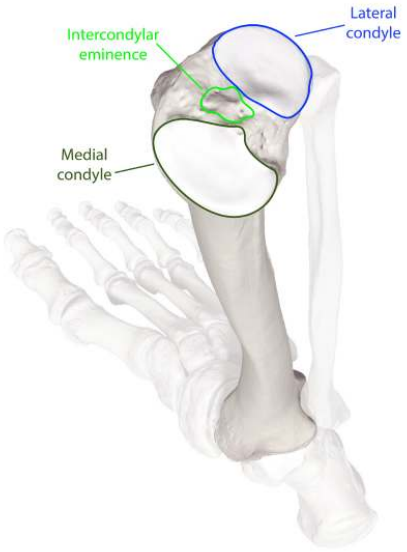
The leg is the crural region of the body, from the midline of the knee to the ankle joint. Two bones run parallel to each other in this region: the tibia is the larger, more medial bone and the fibula is the smaller, more lateral bone.

Tibia

The **tibia** (shin bone) is the larger of the two bones in the leg because all weight is transferred through it from the femur to the tarsals (Figure 19.4.7.5). It is usually the second longest bone of the body, after the femur, but occasionally its size is greater than the femur and it is the largest! The medial aspect of the tibia is located immediately under the skin, allowing it to be easily palpated down the entire length of the medial leg.



A. Anterior and Posterior Views



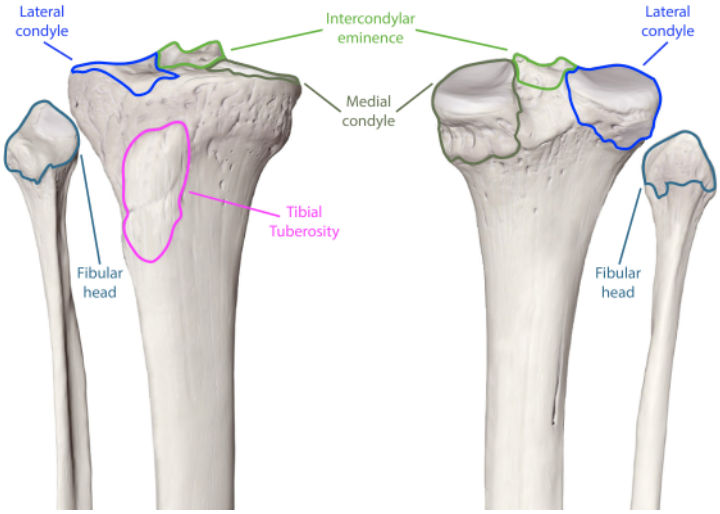
B. Superoposterior View

Figure 19.4.7.5: Tibia. The tibia is the larger, weight-bearing bone located on the medial side of the leg. *(Image credit: "Tibia Landmarks" by Mark Schaeffer is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.)*

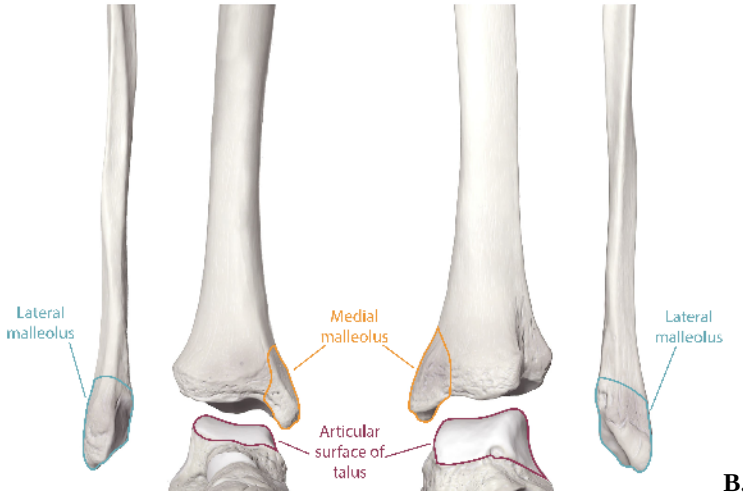
The proximal end of the tibia is greatly expanded. The two sides of this expansion form the **medial condyle of the tibia** and the **lateral condyle of the tibia**. The tibia does not have epicondyles. The top surface of each condyle is smooth and flattened, which forms an articular surface. These areas 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 the cruciate ligaments of the knee (see Figure 19.4.7.5 and Figure 19.4.7.6).

The **tibial tuberosity** is a knobby, elevated area on the anterior side of the tibia, near its proximal end. It is the attachment site for the quadriceps muscle tendon that surrounds the patella. More inferiorly, the body, or **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.

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**.



A. Proximal



B. Distal

Figure 19.4.7.6: Landmarks of the Tibia and Fibula. Major landmarks of the tibia and fibula include their articular surfaces and attachment points for muscles and ligaments. *(Image credit: "Landmarks of the Tibia and Fibula - Multiple Views" by Mark Schaeffer is licensed under CC BY-NC-SA 4.0, modification of images from Anatomy Standard under CC BY-NC 4.0.)*

Fibula

The fibula is the slender bone located on the lateral side of the leg (Figure 19.4.7.6 and Figure 19.4.7.7) . 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.

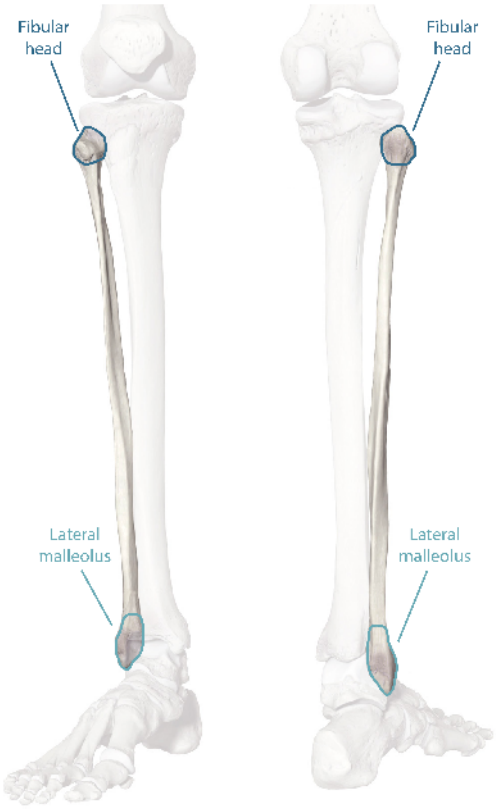


Figure 19.4.7.7: Fibula. The fibula is the lateral bone of the leg. It is slender because it is non-weightbearing. *(Image credit: "Fibula Landmarks" by Mark Schaeffer is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.)*

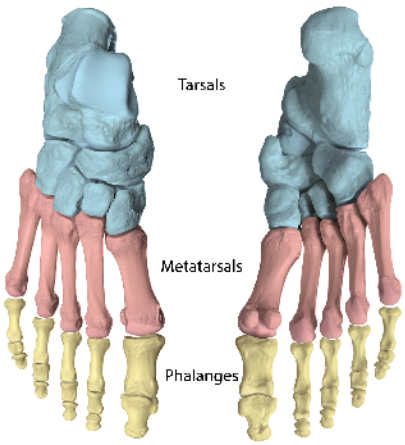
The **head of the fibula** is the small, knob-like, proximal end of the fibula. It articulates with the inferior aspect of the lateral tibial condyle, forming the **proximal tibiofibular joint**. The thin **shaft of the fibula** has the **interosseous border of the fibula**, a narrow ridge running down 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.

Bones of the Foot

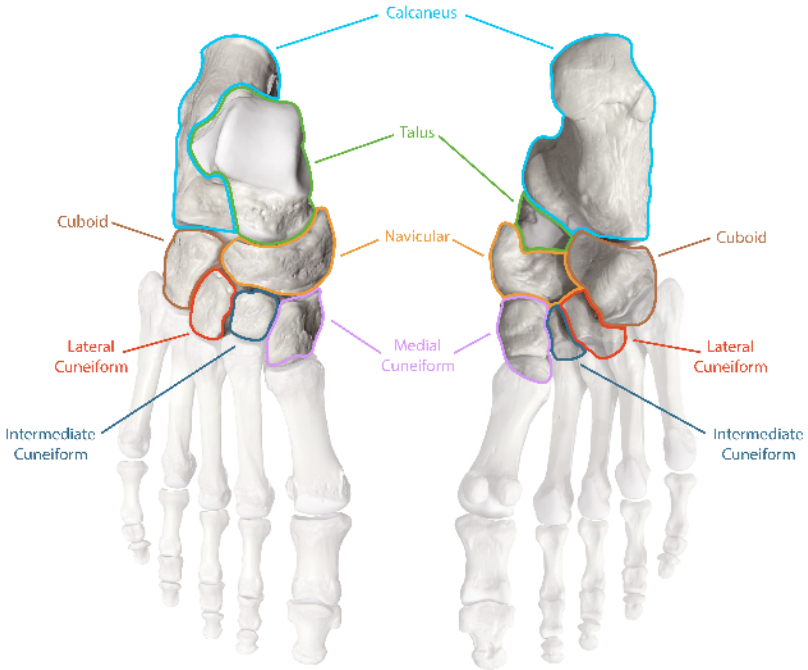
The pes, or pedal region, contains three subregions corresponding to the three types of bones found here: the tarsals, the metatarsals, and the phalanges (digits) (Figure 19.4.7.8).

Tarsals

The posterior half of the foot is formed by seven tarsal bones (Figure 19.4.7.8). 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**. 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.



A. Superior and Inferior Views



B. Superior and Inferior Views

Figure 19.4.7.8: Bones of the Foot - Tarsals. The seven individual tarsal bones make up the heel and ankle region of the foot. *(Image credit: "Bones of the Foot" and "Bones of the Foot - Tarsals" by Mark Schaeffer are licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.)*

The **cuboid** bone articulates with the anterior end of the calcaneus bone. 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 form the posterior aspect of the **transverse arch** (medial-lateral) of the foot (Figure 19.4.7.11). The navicular and lateral cuneiform bones also articulate with the medial side of the cuboid bone.

Metatarsals

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 (Figure 19.4.7.8 and Figure 19.4.7.9) . These elongated bones are numbered 1–5, starting with the medial side of the foot. The numbering of the metatarsals matches with the corresponding digit (toe) number, and the digit with only two phalanges is always number 1. In this case, the big toe is digit number 1.



Figure 19.4.7.9: Bones of the Foot - Metatarsals. The five metatarsals make up the majority of the arch of the foot. They are numbered according to which digit they attach to, with digit number 1 being medial. *(Image credit: "Bones of the Foot - Metatarsals" by Mark Schaeffer is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.)*

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 (Figure 19.4.7.10) . The toes are numbered 1–5, starting with the big toe, known as the **hallux**. The hallux has two phalanx bones, the proximal and distal phalanges. The remaining digits, numbers 2 through 5, all have proximal, middle, and distal phalanges. A joint between adjacent phalanx bones is called an interphalangeal joint.

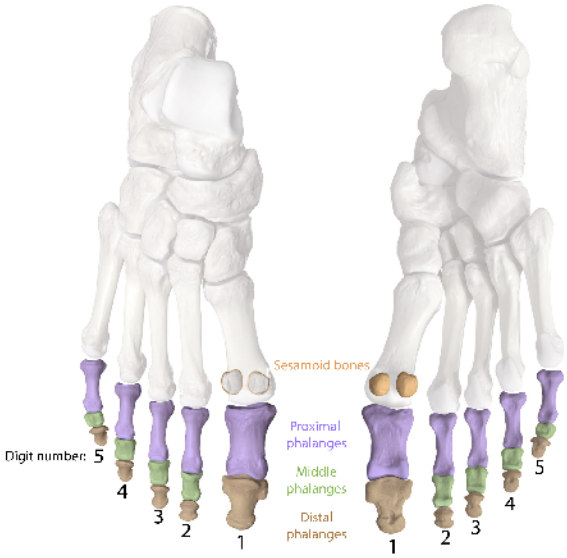


Figure 19.4.7.10: Bones of the Foot - Phalanges. The pattern and numbering system of the phalanges of the foot is the same as that of the phalanges of the hand. Digit 1 has only two phalanges (proximal and distal), while digits 2, 3, 4, and 5 have three phalanges (proximal, middle, and distal). *(Image credit: "Bones of the Foot - Phalanges" by Gabrielle Spurlock is licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.)*

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 (Figure 19.4.7.11) . 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.

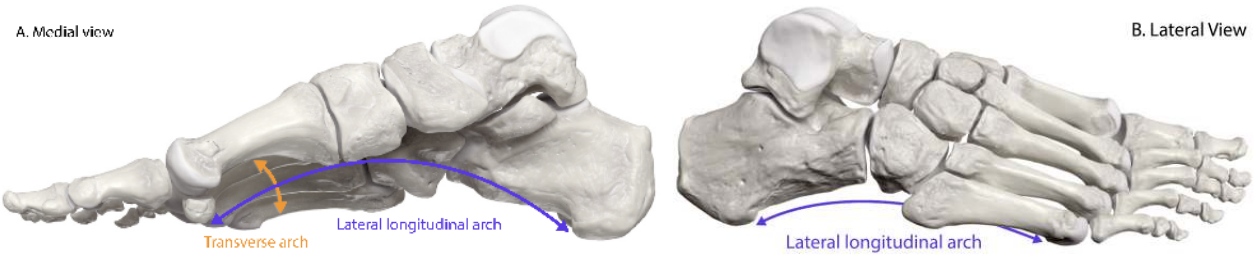


Figure 19.4.7.11: Arches of the Foot. The longitudinal arch runs anterior/posterior from the calcaneus to the heads of the metatarsals. The transverse arch runs medial/lateral underneath the metatarsals and cuneiforms. *(Image credit: "Arches of the Foot - Medial" and "Arches of the Foot - Lateral" by Mark Schaeffer are licensed under CC BY-NC-SA 4.0, modification of image from Anatomy Standard under CC BY-NC 4.0.)*

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.



Figure 19.4.7.12: Pes Planus. Comparison of x-rays of a flat longitudinal arch (A) and a normal longitudinal arch (B). Notice the depression of the lateral bones compared to normal. *(Image credit: "Pes Planus" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of images from Radiopedia.org: pes planus case courtesy of Domenico Nicoletti, rID: 40527, and normal case courtesy of Andrew Dixon, rID: 36688.)*

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 (Figure 19.4.7.12). This condition is called pes planus (“flat foot” or “fallen arches”).

Concept Review

The lower limb is divided into three regions. These are the thigh, located between the hip and knee joints; the leg, located between the knee and ankle joints; and distal to the ankle, the foot. There are 30 bones in each lower limb. These are the femur, patella, tibia, fibula, seven tarsal bones, five metatarsal bones, and 14 phalanges.

- The **femur** is the single bone of the thigh. Key landmarks include:
  - rounded **head** for articulation with the acetabulum of the os coxa to form the hip joint,
  - the **greater and lesser trochanters** on the proximal end are muscle attachment points,
  - the **linea aspera** in the posterior mid-shaft region is a muscle attachment point,
  - three articulating surfaces on the distal end: the **medial and lateral condyles**, and the **patellar surface**,
  - the **medial and lateral epicondyles** are the rough protrusions superior to the condyles that serve as muscle and ligament attachment points.
- The **patella** is a sesamoid bone located within a muscle tendon. It articulates with the patellar surface on the anterior side of the distal femur.
- The leg contains the large **tibia** on the medial side and the slender **fibula** on the lateral side. The tibia bears the weight of the body, whereas the fibula does not bear weight. Key landmarks include:
  - The **interosseous border** of each bone is the attachment site for the connective tissue sheet that unites the tibia and fibula,
  - the proximal tibia consists of the expanded **medial and lateral condyles**, which articulate with the medial and lateral condyles of the femur to form the knee joint,
  - the **intercondylar eminence** is between the tibial condyles,
  - the **tibial tuberosity** is on the anterior side of the proximal tibia,
  - on the medial side of the distal tibia is the **medial malleolus**,
  - on the lateral side of the distal tibia is the **fibular notch,**
  - the **head of the fibula** forms the proximal end

- the expanded distal end of the fibula is the **lateral malleolus**.

- The posterior foot is formed by the seven **tarsal bones**:
  - the **talus** articulates superiorly with the distal tibia to form the ankle joint,
  - the calcaneus forms the heel,
  - the **navicular**, the **cuboid**, and the **medial, intermediate, and lateral cuneiforms** are in the arch of the foot.
- The five **metatarsals** form the anterior foot.
- The **phalanges** are the bones of the toes. The big toe (digit number 1) has proximal and distal phalanx bones. The remaining toes have proximal, middle, and distal phalanges.

Review Questions

Critical Thinking Questions

Glossary

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19.5: Introduction to the Muscular System

Chapter Learning Objectives

After studying this chapter, you will be able to:

- 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 movements they cause

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. 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.

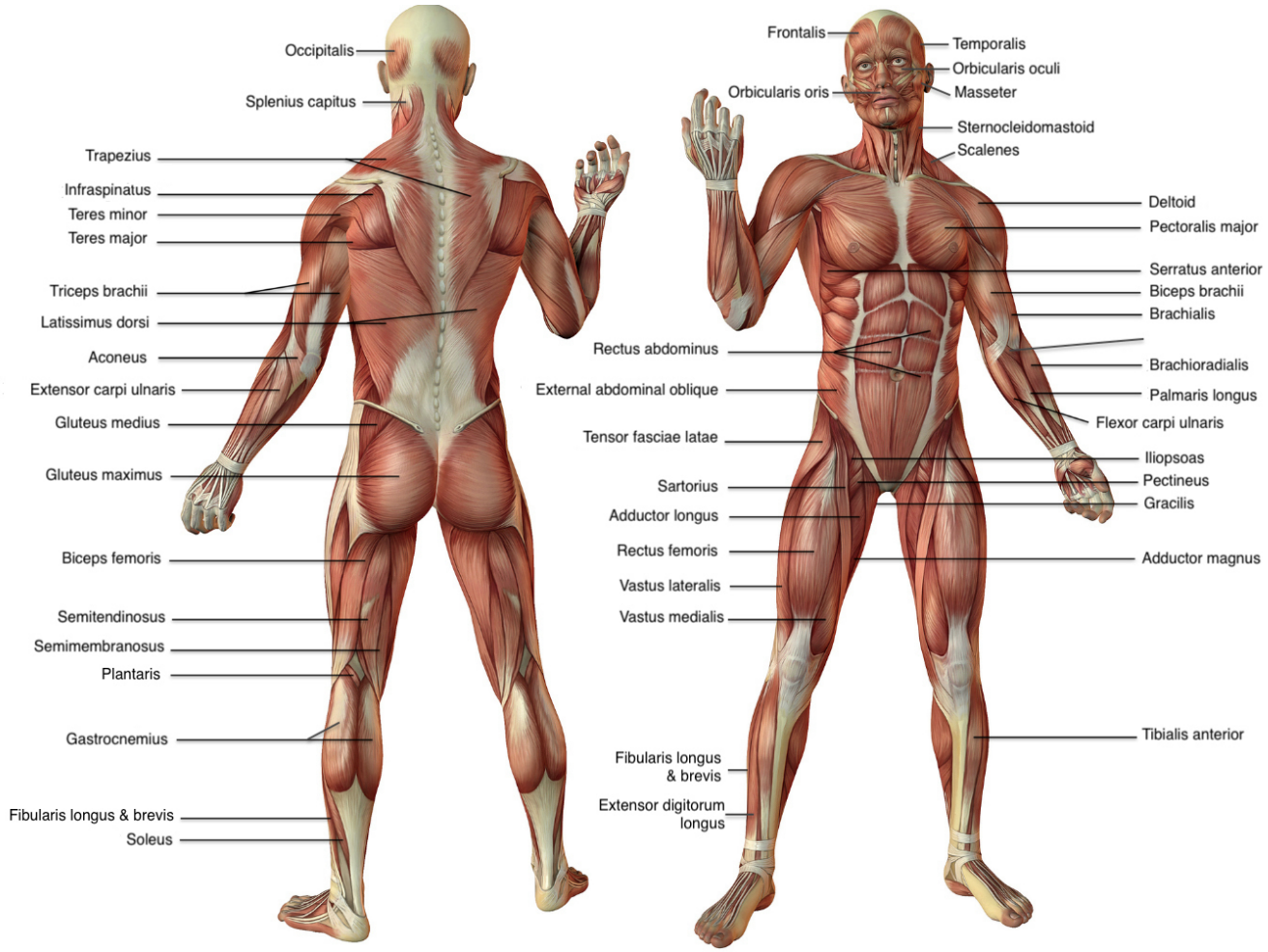


Figure 19.5.1: Muscles of the Body - Anterior and Posterior Views. *(Image credit: "Muscles of the Human Body" by Jennifer Lange, based on original by Homme en Noir is licensed by Creative Commons Attribution-Share Alike 4.0 International)*

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19.5.1: Axial Muscles of the Head, Neck, and Back

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

- Identify the major axial muscles of the face, head, neck, and vertebral column
- Identify the movement caused by these 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, including those involving eye movements and swallowing, then you will review the muscles of the vertebral column.

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 19.5.1.1).

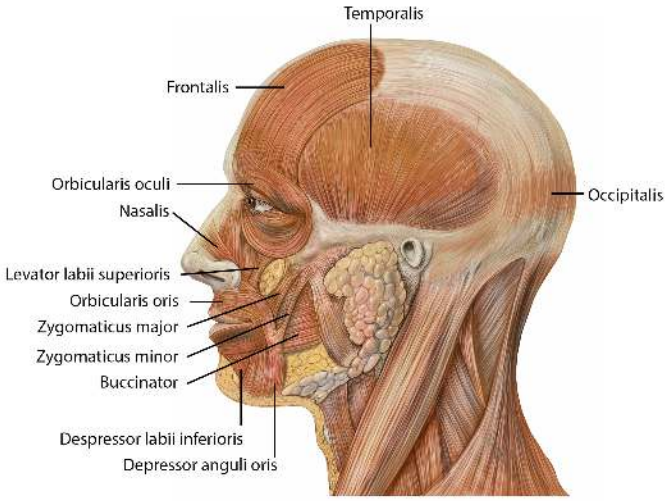


Figure 19.5.1.1: Muscles of Facial Expression. Many of the muscles of facial expression insert into the skin surrounding the eyelids, nose and mouth, producing facial expressions by moving the skin rather than bones. *(Image credit: "Muscles of Facial Expression" by Jennifer Lange, modified from original images by Patrick J. Lynch, http://patricklynch.net, licensed under CC-BY Attribution 2.5)*

Forehead and Orbit

The **occipitofrontalis** muscle moves the skin of the scalp and eyebrows in a superior direction. The muscle has a frontal belly and an occipital belly located near the respective bones. 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. This muscle is the prime mover of the eyebrows. Gently place your finger on your eyebrows then raise your eyebrows as if you were surprised and allow them to come back to rest. With these movements, you can feel the action of the occipitofrontalis. If you watch yourself in a mirror you will see that your forehead is wrinkling as the skin moves.

The **orbicularis oculi** is a circular muscle that surrounds the orbit. When this muscle contracts the eyelid closes. Pretend that a bug just flew into your eye - you will close the eyelid quickly and scrunch the skin around your eye socket using your orbicularis oculi. Want to close your eyelid gently, as if peacefully sleeping? This is caused by the relaxation of another muscle - the **levator palpebrae superioris**. When this muscle contracts is pulls your upper eyelid open, so relaxing it allows the eyelid to close.

Nose, Mouth and Cheeks

The mouth is used for both a variety of facial expressions as well as forming words while speaking and assisting in swallowing, so it has multiple muscles inserting into the surrounding skin. The largest of these muscles is the **orbicularis oris**, whose fibers encircle the lips and can keep them tightly closed. Contracting the orbicularis oris when pulling in more from the corners will produce a puckered, kissing, expression. Two primary muscles pull the skin and lips in an inferior direction - **depressor labii inferioris** pulls the lip down while **depressor anguli oris** pulls the corners of the mouth down and slightly laterally creating a frowning expression. Three primary muscles pull the skin and lips in a superior direction - the **levator labii superioris** pulls your lip upwards toward your nose while the **zygomaticus major and minor** pull the corners of the mouth up and lateral to cause you to smile. If you practice contracting the zygomaticus muscles you will get the perfect, on the spot smile for pictures!

Your nose itself does not move much, but you can flare your nostrils and compress the nasal cartilage using the **nasalis muscle**.

The largest muscle of the cheeks is the **buccinator** muscle, which compresses the cheek and allows you to whistle, blow, and suck. It also contributes to the actions of chewing and swallowing. Additional muscles of facial expression are presented in Table 19.5.1.1.

Table 19.5.1.1: Muscles of Facial Expression

Muscle	Origin	Insertion	Movement
Brow			
Occipitofrontalis (frontal belly/frontalis)	Epicranial aponeurosis	Skin of eyebrow	Furrowing (wrinkling) brow
Occipitofrontalis (occipital belly/occipitalis)	Occipital bone; mastoid process (temporal bone)	Epicranial aponeurosis	Retracts scalp
Orbit and Eyelid			
Orbicularis oculi	Medial wall of orbit	Skin surrounding eyelids	Closes eyelids (blinking, squinting, winking)
Levator palpebrae superioris	Sphenoid bone	Skin of superior eyelid	Elevates superior eyelid
Nose			
Nasalis	Maxilla	Skin of nostrils, nasal aponeurosis	Flaring nostrils
Mouth and Cheeks			
Buccinator	Maxilla, mandible	Orbicularis oris	Lateral movement of cheeks (e.g. sucking on a straw; also used to compress air in mouth while blowing)
Depressor anguli oris	Mandible	Skin at corners of mouth	Draws corners of mouth inferior and lateral (e.g. frowning)
Depressor labii inferioris	Mandible	Skin of lower lip	Lowering lower lip
Levator labii superioris	Maxilla	Skin of the of upper lip; orbicularis oris	Raising upper lip
Mentalis	Mandible	Skin of chin	Protrusion of lower lip (e.g. pouting expression)
Orbicularis oris	Maxilla, mandible; fibers of other facial muscles	Skin surrounding lips	Compresses and purses lips (e.g. kiss)
Zygomaticus major and minor	Zygomatic bone	Skin at superolateral corners of mouth and lip	Smiling

Muscles That Move the Eyes

The movement of the eyeball is under the control of the **extrinsic eye muscles** (extraocular muscles) that originate within the orbit and insert onto the superficial 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 19.5.1.2 and Table 19.5.1.2). 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.

Each of these six muscles are named for their position relative to the eyeball and the orientation of their myofibers:

- **Superior oblique muscle** - passes through fibrous trochlea, which is attached to the superiomedial aspect of the orbit
- **Inferior oblique muscle**
- **Superior rectus muscle**
- **Inferior rectus muscle**
- **Medial rectus muscle**
- **Lateral rectus muscle**

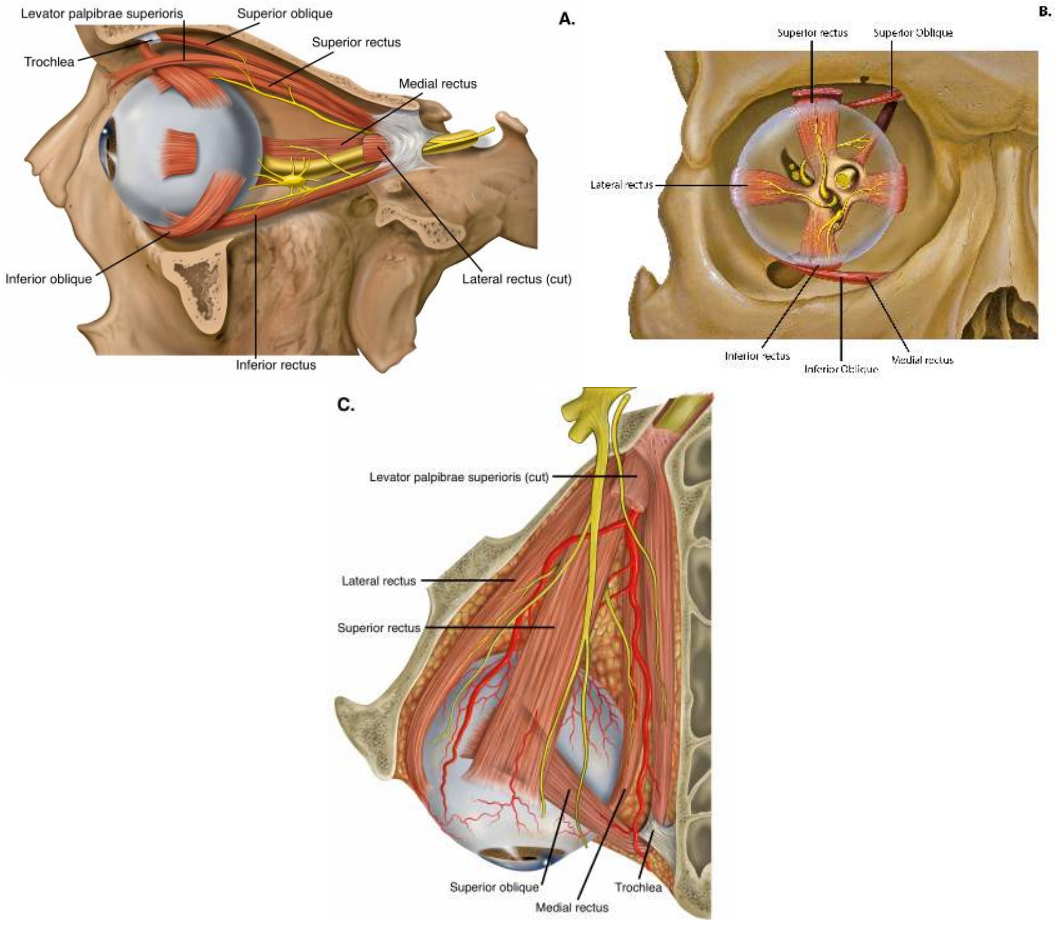
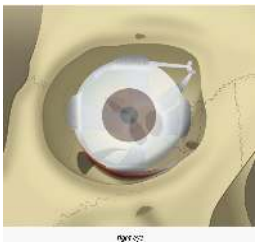
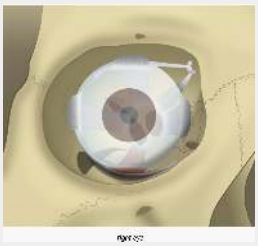
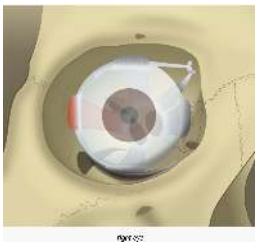
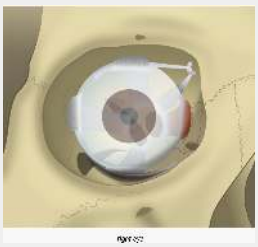
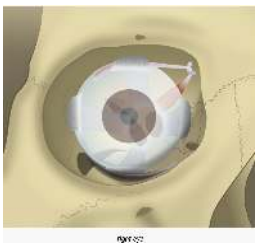
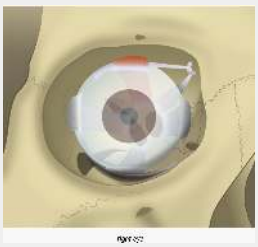


Figure 19.5.1.2: Extrinsic Eye Muscles. This six muscles control the movements of the eye within the socket. The four rectus muscles originate from a common tendon that surround the optic nerve while the two oblique muscles originate from the medial wall of the orbit. A. Left eye, lateral view. B. Right eye, superior view. C. Right eye, superior view. *(Image credit: "Extrinsic Eye Muscles" by Jennifer Lange, modified from original images by Patrick J. Lynch, http://patricklynch.net, licensed under CC-BY Attribution 2.5)*

Table 19.5.1.2: Muscles of the Eyes

Muscle	Origin	Insertion	Movement	Image(s)

Muscle	Origin	Insertion	Movement	Image(s)
Inferior oblique	Floor of orbit (maxilla)	Surface of eyeball between inferior rectus and lateral rectus	Moves eyes up and away from nose; rotates eyeball from 12 o'clock to 9 o'clock	
Inferior rectus	Common tendinous ring (ring attaches to optic foramen)	Inferior surface of eyeball	Moves eyes down and toward nose; rotates eyes from 6 o'clock to 3 o'clock	
Lateral rectus	Common tendinous ring (ring attaches to optic foramen)	Lateral surface of eyeball	Moves eyes away from nose	
Medial rectus	Common tendinous ring (ring attaches to optic foramen)	Medial surface of eyeball	Moves eyes toward nose	
Superior oblique	Sphenoid bone	Surface of eyeball between superior rectus and lateral rectus	Moves eyes down and away from nose; rotates eyeball from 6 o'clock to 9 o'clock	
Superior rectus	Common tendinous ring (ring attaches to optic foramen)	Superior surface of eyeball	Moves eyes up and toward nose; rotates eyes from 1 o'clock to 3 o'clock	

Muscles That Move the Lower Jaw at the Temporomandibular Joint

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 19.5.1.3 and Table 19.5.1.3). 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.

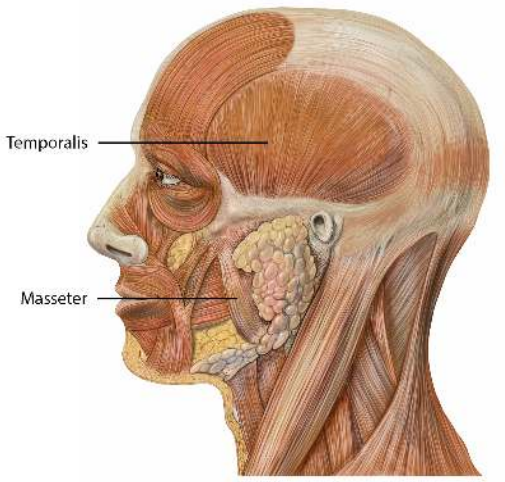


Figure 19.5.1.3: Muscles of Mastication. The muscles that move the mandible at the temporomandibular joint are typically located within the cheek and originate from processes in the skull. This provides the muscles with the large amount of leverage needed for chewing. *(Image credit: "Muscle of Mastication" by Jennifer Lange, modified from original images by Patrick J. Lynch, http://patricklynch.net, licensed under CC-BY Attribution 2.5)*

Table 19.5.1.3: Muscles of Mastication

Muscle	Origin	Insertion	Movement
Masseter	Zygomatic arch	Mandible, coronoid process and lateral surface	Closes mouth; elevation of mandible
Temporalis	Temporal bone	Mandible, coronoid process	Closes mouth; elevation and retraction of mandible

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 19.5.1.4 and Table 19.5.1.4). Because it is so moveable, the tongue facilitates complex speech patterns and sounds.

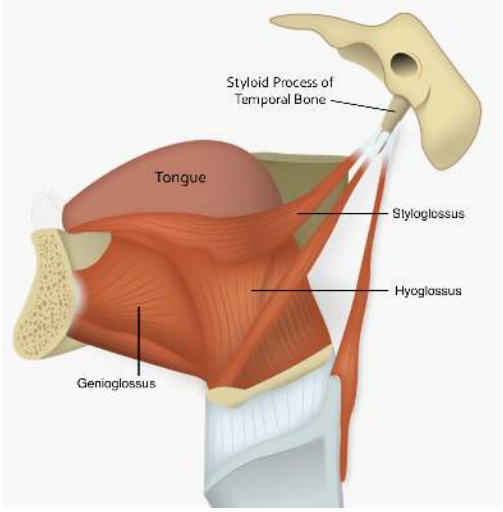


Figure 19.5.1.4: Muscles that Move the Tongue. The muscles that move the tongue allow for swallowing and speech. *(Image credit: "Extrinsic Tongue Muscles" by Jennifer Lange, modified from original by University of British Columbia Clinical Anatomy is licensed under CC BY-NC-SA 4.0)*

Table 19.5.1.4: Muscles for Tongue Movement, Swallowing, and Speech

Muscle	Origin	Insertion	Movement
Tongue			
Genioglossus	Mandible	Tongue undersurface; hyoid bone	Moves tongue down; sticks tongue out of mouth
Hyoglossus	Hyoid Bone	Sides of tongue	Flattens tongue
Styloglossus	Styloid process of temporal bone	Tongue undersurface and sides	Moves tongue up; retracts tongue back into mouth
Swallowing and Speaking			
Digastric	Mandible; temporal bone	Hyoid bone	Raises 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
Mylohyoid	Mandible	Hyoid bone; median raphe	Raises hyoid bone in a way that presses the tongue against the roof of the mouth, pushing food back into the pharynx during deglutition
Sternohyoid	Clavicle	Hyoid bone	Depresses the hyoid bone during swallowing and speaking

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 **hyoglossus** originates on the hyoid bone to move the tongue downward and flatten it.

EVERYDAY CONNECTIONS

Anesthesia and the Tongue Muscles

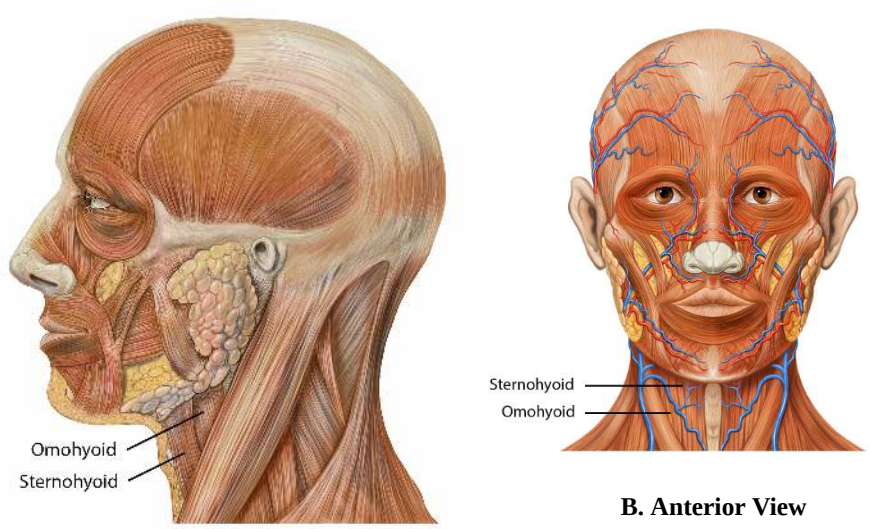
Before surgery, a patient must be made ready for general anesthesia. The normal homeostatic controls of the body are put “on hold” so that the patient can be prepped for surgery. Control of respiration must be switched from the patient’s homeostatic control to the control of the anesthesiologist. The 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 Swallowing and Speaking

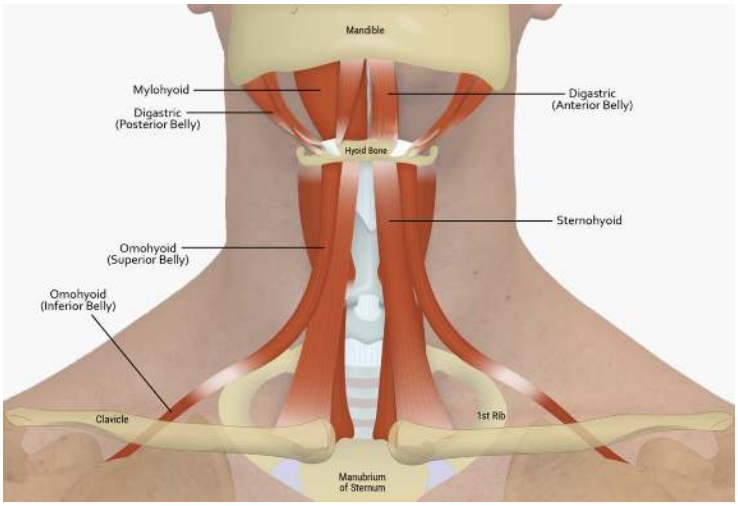
The muscles of the anterior neck assist in deglutition (swallowing) and speech by controlling the positions of the larynx (voice box), and the hyoid bone, a horseshoe-shaped bone that functions as a solid foundation on which the tongue can move. The muscles

of the neck are categorized according to their position relative to the hyoid bone (Figure 19.5.1.5). **Suprahyoid muscles** are superior to it, and the **infrahyoid muscles** are located inferiorly.



A. Lateral View

B. Anterior View



C. Anterior View of Inferior Chin

Figure 19.5.1.5: Infrahyoid and Suprahyoid Muscles. The anterior muscles of the neck facilitate swallowing and speech. Each of these muscles originate on or insert into the hyoid bone. From both anterior and lateral view points (A & B) only the superficial infrahyoid muscles can be seen. To see the suprahyoid muscles you need to view from a more inferior angle to see under the chin (C). *(Image credit: "Infrahyoid Muscles" by Jennifer Lange - A & B modified from original images by Patrick J. Lynch, http://patricklynch.net, licensed under CC-BY Attribution 2.5. Image C "Hyoid Muscles" by University of British Columbia Clinical Anatomy is licensed under CC BY-NC-SA 4.0 International.)*

The suprahyoid muscles raise the hyoid bone, the floor of the mouth, and the larynx during swallowing. Examples of 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 **mylohyoid** muscle lifts the hyoid and helps press the tongue to the top of the mouth.

The strap-like infrahyoid muscles generally depress the hyoid bone and control the position of the larynx. For example, the **omohyoid** muscle, which has superior and inferior bellies, depresses the hyoid bone in conjunction with the **sternohyoid** muscles.

Muscles That Move the Head and Vertebral Column

The skull, attached to the top of the vertebral column, is balanced, moved, and rotated by muscles located in the neck. (Table 19.5.1.5). Muscles that insert into the skull move the head at the atlanto-occipital joint and they also move the neck at the cervical intervertebral joints. Additional muscles that insert into the cervical vertebrae also cause neck movements.

When these muscles act unilaterally (on one side), the joints of the head and cervical vertebrae rotate and laterally flex. When they contract bilaterally (both right and left sides), the joints of the head and cervical vertebrae flex or extend. The major muscle that, when contracting on only one side, causes lateral flexion and rotation is the **sternocleidomastoid**. When both sides contract together the joints flex. Place your fingers on both sides of the neck and tilt your head to the left and to the right. You will feel the movement originate there. (Figure 19.5.1.6).

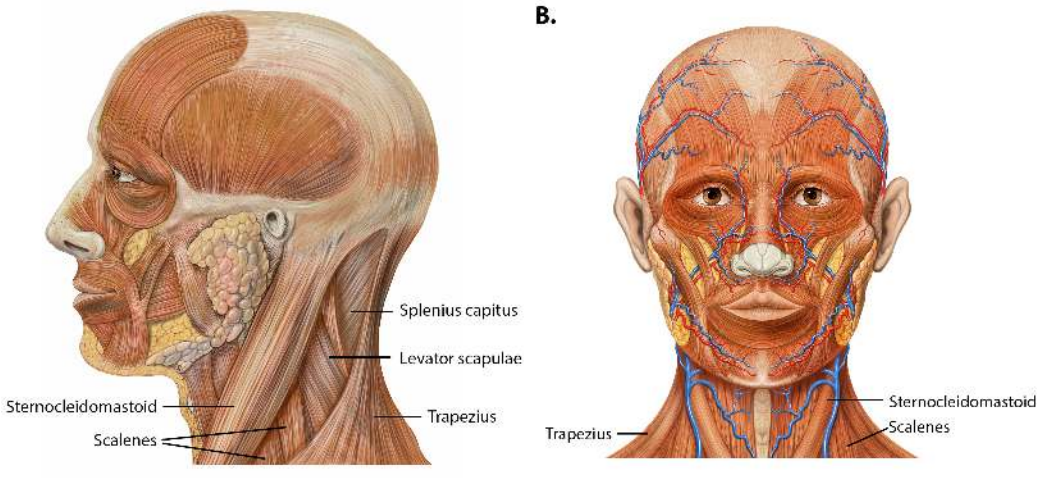
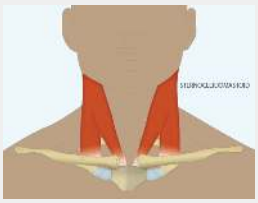


Figure 19.5.1.6: Lateral and Anterior Views of Neck Muscles. The superficial and deep muscles of the neck are responsible for moving the head, cervical vertebrae, and scapulae. (*Image credit: "Lateral and Anterior Neck Muscles" by Jennifer Lange, modified from original images by Patrick J. Lynch, http://patricklynch.net, licensed under CC-BY Attribution 2.5.*)

Table 19.5.1.5: Muscles That Move the Head

Muscle	Origin	Insertion	Movement	Image(s)
Longissimus capitis	Transverse and articular processes of cervical and thoracic vertebrae	Mastoid process of temporal bone	Rotates and tilts head to the side; tilts head backward	
Semispinalis capitis	Transverse and articular processes of cervical and thoracic vertebrae	Occipital bone	Rotates and tilts head backward	
Splenius capitis	Spinous process of cervical and thoracic vertebrae	Mastoid process of temporal bone; occipital bone	Rotates and tilts head to the side; tilts head backward	
Sternocleidomastoid	Sternum; clavicle	Mastoid process of temporal bone; occipital bone	Rotates and tilts head to the side; tilts head forward	

The muscles that insert into the skull are concerned with head movements and neck movements. The neck and back muscles that insert into vertebrae both stabilize and move the vertebral column. They 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 19.5.1.7).

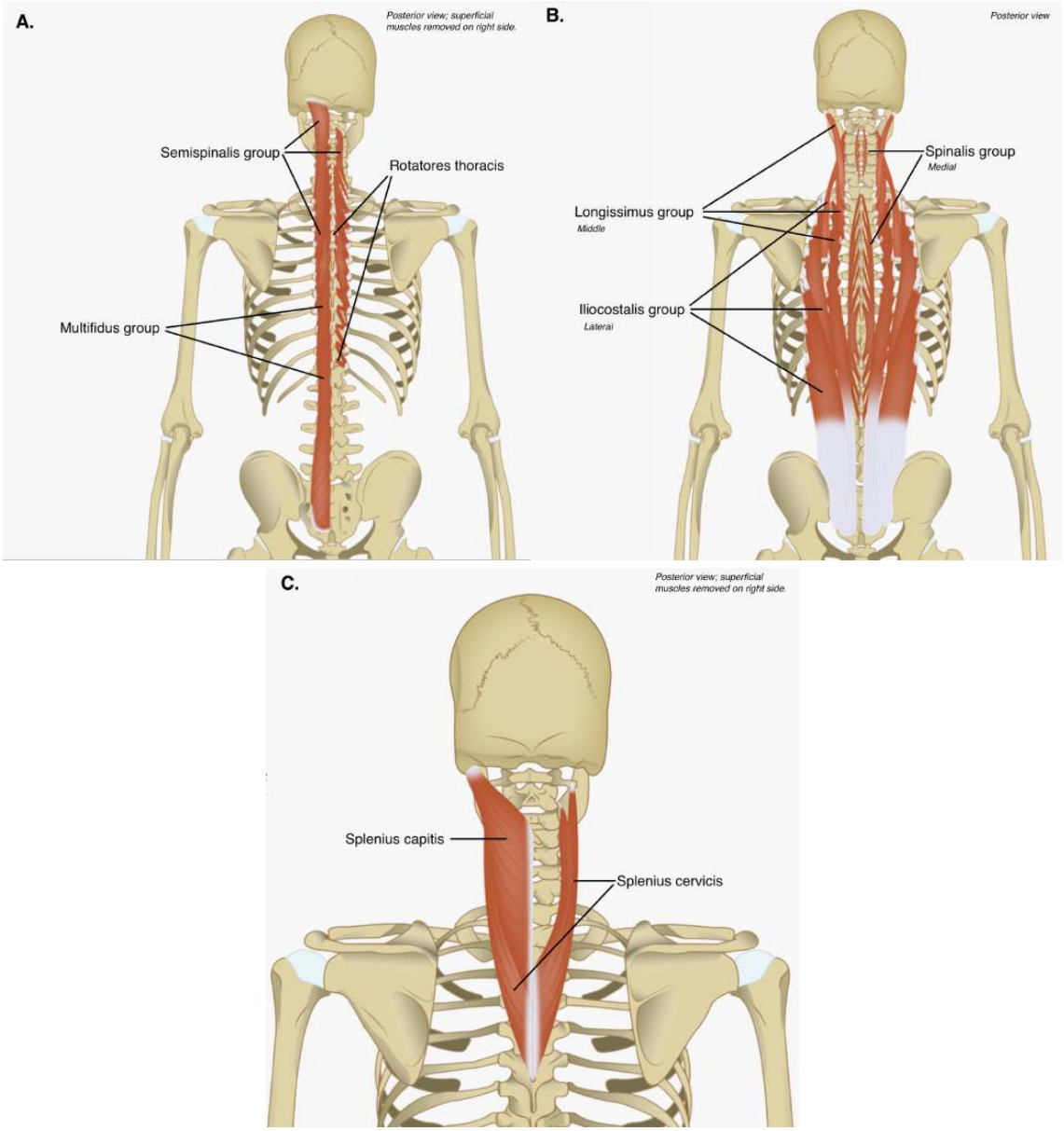


Figure 19.5.1.7: Muscles of the Posterior Neck and Back. The muscles of the along the posterior trunk work to both stabilize and move the vertebral column and some also move the head. They are arranged into two main groups based on their depth and function. A. Transversospinalis group, B. Erector spinae group, C. Splenius group. *(Image credit: "Muscles of the Posterior Neck and Back" by Jennifer Lange, modified from originals by University of British Columbia Clinical Anatomy is licensed under CC BY-NC-SA 4.0 International)*

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 muscles in the **transversospinales group** run from the transverse processes to the spinous processes of the vertebrae and they function to stabilize and move the vertebral column. Similar to the erector spinae muscles, the **semispinalis muscles** and **multifidus muscles** in this group are named for the areas of the body with which they are associated. An additional muscle, rotatores thoracis, also rotates the vertebral column. All three muscle groups extend the vertebral column.

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).

Concept Review

Muscles are either axial muscles or appendicular depending upon the location of the joints they move. The axial muscles move joints in the axial skeleton and are grouped based on location, function, or both. Groups include:

- **Facial expression:** The muscles in the face create expressions by inserting into the skin rather than onto bone.
- **Extraocular:** Muscles that move the eyeballs are extrinsic, meaning they originate outside of the eye and insert onto it.
- **Mastication:** The muscles that insert into the mandible are used for chewing, with the strongest ones elevating the mandible to close the jaw. They also play a role in speaking.
- **Tongue:** Tongue muscles are both extrinsic and intrinsic. They create complex movements that allow the tongue to move in all three planes as well as flatten and curl. These movements are used for directing food during chewing and swallowing.
- **Swallowing and speech:** The muscles of the anterior neck facilitate swallowing and speech, stabilize the hyoid bone and position the larynx.
- **Neck:** The muscles of the neck stabilize and move the head and move the joints between the cervical vertebrae.
- **Back and neck:** The muscles of the back and neck move the vertebral column can be divided into multiple groups including:
  - the splenius group in the posterior neck,
  - the erector spinae group run the length of the vertebral column to keep up upright; this group has three subgroups: the iliocostalis group, the longissimus group and the spinalis group,
  - the transversospinales group are shorter muscles that originate on the transverse processes in all regions,
  - the scalenes group in the lateral neck.

Review Questions

Critical Thinking Questions

Glossary

Contributors and Attributions

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19.5.2: Axial Muscles of the Abdominal Wall and Thorax

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

- Identify the major skeletal muscles of the abdominal wall and thorax
- Identify the movements caused by these muscles

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: the external obliques, the internal obliques, the transversus abdominis, and the rectus abdominis (Figure 19.5.2.1, Figure 19.5.2.2 and Table 19.5.2.1).

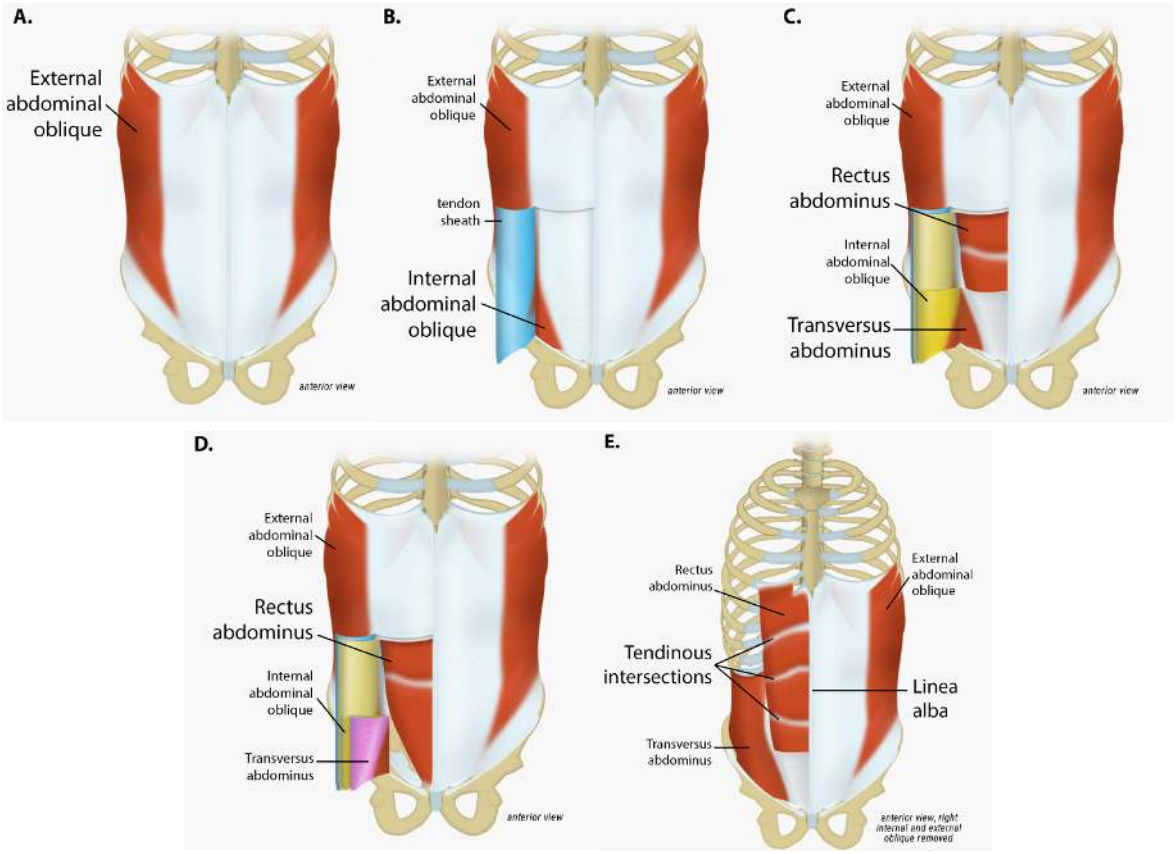


Figure 19.5.2.1: Muscles of the Abdomen. On the lateral and posterior walls the abdomen has three layers of muscles. From superficial to deep they are: A. external abdominal oblique, B. internal abdominal oblique, and C. transversus abdominus. In images C and D you can see the anteromedial muscle, the rectus abdominus. Tendon associated with these muscles are the tendinous intersections and the linea alba (image E). *(Image credits: "Abdominal Muscles" by Jennifer Lange are licensed under CC BY-NC-SA 4.0, based on images by University of British Columbia Clinical Anatomy)*

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.

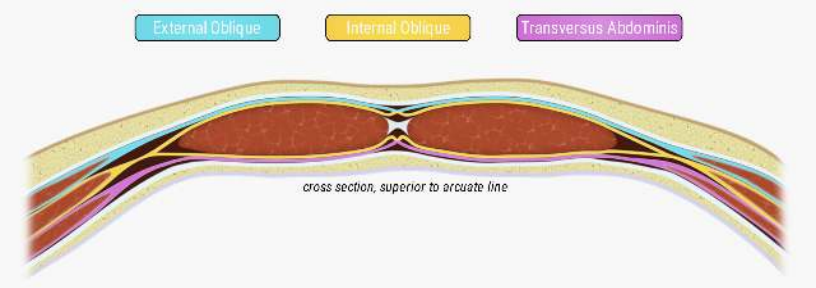


Figure 19.5.2.2: Muscles of the Abdomen - Cross Section. When viewed in cross section the relative positions of the lateral muscles can easily be seen. The tendon of the external oblique passes superficial to the rectus abdominus while the tendon of the transversus abdominus passes deep. The tendon of the internal oblique splits to pass around both sides.

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.

Table 19.5.2.1: Muscles of the Abdomen

Muscle	Origin	Insertion	Movement	Image(s)
Internal oblique	Lumbar fascia, inguinal ligament and iliac crest	Linea alba, inferior rib surfaces 9-12, costal cartilages 8-10	Bilateral: Flexes vertebral column Unilateral: Lateral flexion and rotation of vertebral column	
External oblique	Ilium; ribs 5 - 12	Ilium; linea alba; ribs 7 - 10	Bilateral: Flexes vertebral column Unilateral: Lateral flexion and rotation of vertebral column	
Rectus abdominis	Pubis	Ribs 5 and 7; sternum	Flexion of vertebral column	
Transverse abdominus	Ilium; ribs 5 - 10	Linea alba; pubis; sternum	Squeezing abdomen during forceful exhalations, defecation, urination, and childbirth	

CAREER CONNECTIONS

Physical Therapist and Physical Therapy Assistant

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 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. This plan can involve visits to the clinic to work with a Physical Therapy Assistant (PTA) who will help guide you through the appropriate exercises. Most likely, you also 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. Both Physical Therapists and Physical Therapy Assistants work closely with patients to help them get back to their normal level of physical activity.



Physical therapy technician Troy Hopkins assists retired Maj. Gen. William L. Moore Jr. at the Center for the Intrepid, Brooke Army Medical Center's outpatient rehabilitation facility on Joint Base San Antonio-Fort Sam Houston in San Antonio, Sept. 3, 2015. *(U.S. Army photo by Robert T. Shields/Released to Public Domain)*



Sierra Stout, a physical therapist with Global Outreach Doctors teaches a mobility exercise to a boy with scoliosis at a temporary medical treatment site in Point Fortin, Trinidad, Sept. 7, 2019. Comfort is working with health and government partners in Central America, South America, and the Caribbean to provide care on the ship and at land-based medical sites, helping to relieve pressure on national medical systems.

(U.S. Navy photo by Mass Communication Specialist Seaman Jordan R. Bair/Released to Public Domain)\

Muscles of Respiration

The muscles of the chest serve to facilitate breathing by changing the size of the thoracic cavity (Table 19.5.2.2). Movement of the ribs in a superior direction is called elevation of the ribs at both the sternocostal and vertebrocostal joints. Your chest expands drawing air into your lungs. Movement of the ribs in an inferior direction is called depression of the ribs, at the same joints. For your resting breathing no muscular contraction is necessary due to elasticity, but for deep exhalation muscles will pull the ribs downward and inward to decrease the size of the thoracic cavity.

Table 19.5.2.2: Muscles of the Thorax

Muscle	Origin	Insertion	Movement
Diaphragm	Lumbar vertebrae; ribs 6 - 12; sternum	Central tendon	Inhalation; compression of abdominopelvic cavity
Internal intercostals	Rib inferior to each intercostal muscle	Rib superior to each intercostal muscle	Forced exhalation
External intercostals	Rib superior to each intercostal muscle	Rib inferior to each intercostal muscle	Inhalation; elevation of ribs
Scalenes	Transverse processes of cervical vertebrae	Superior surface of 1st and 2nd rib	Elevate 1st and 2nd rib during forced inhalation

The change in volume of the thoracic cavity during breathing is due to the alternate contraction and relaxation of the **diaphragm**. It separates the thoracic and abdominal cavities, and is dome-shaped at rest (Figure 19.5.2.3). 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. 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).

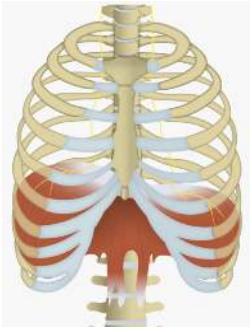


Figure 19.5.2.3: Diaphragm. The diaphragm is a dome-shaped muscle that serves as the divider between the thoracic cavity and the abdominal cavity. It is the primary muscle of breathing. *(Image credit: "The Diaphragm" by University of British Columbia Clinical Anatomy are licensed under CC BY-NC-SA 4.0 International)*

The central of the diaphragm is its tendon. 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 central tendon of the diaphragm also includes three openings for the passage of structures between the thorax and the abdomen such as the inferior vena cava, aorta, and the esophagus.

Assisting the diaphragm during deep breathing are two sets of muscles, called **intercostal muscles**, that 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 19.5.2.4).

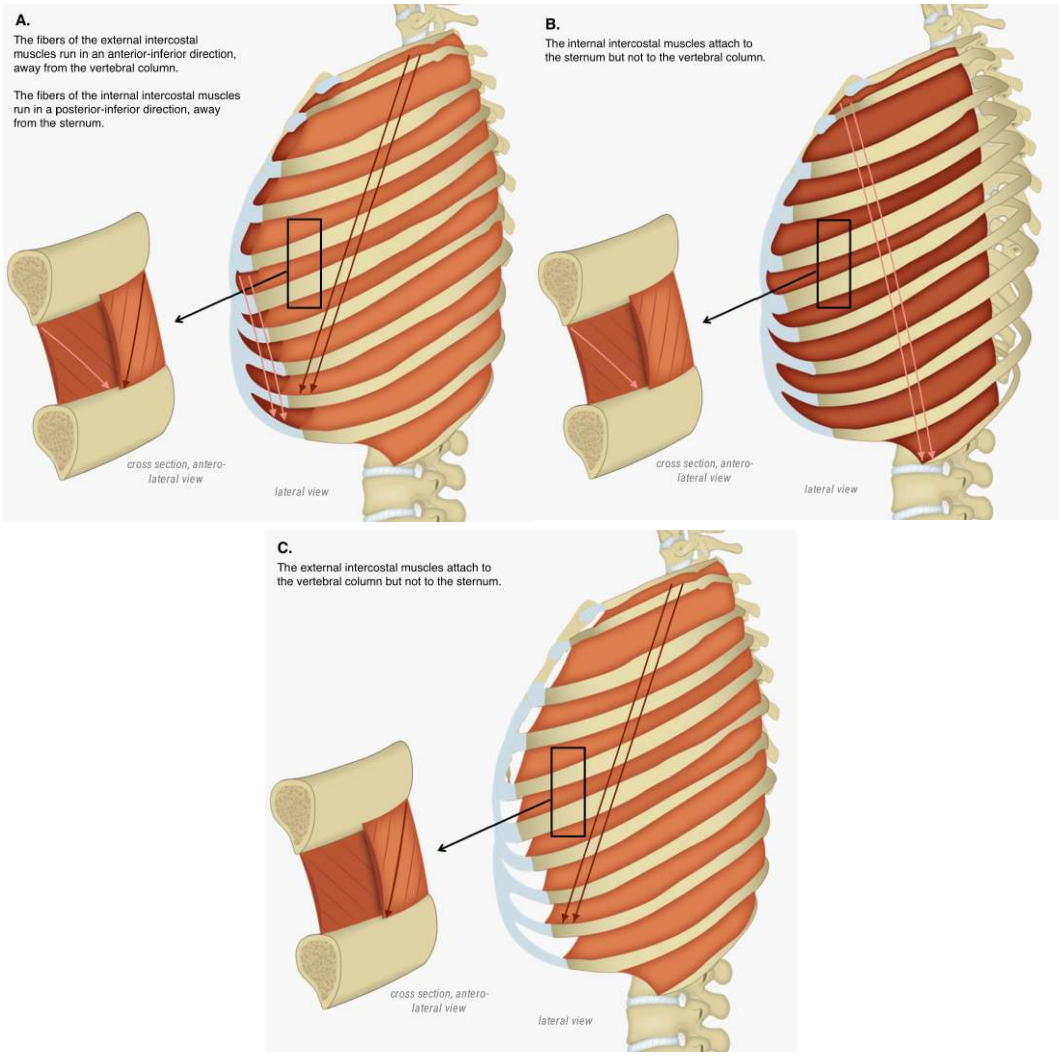


Figure 19.5.2.4: Intercostal Muscles. The internal and external intercostal muscles run between adjacent ribs. You can determine which is which by looking at their fiber angle and and their position relative to the sternum. *(Image credit: "External and Internal Intercostals" by Jennifer Lange, modified from originals by University of British Columbia Clinical Anatomy are licensed under CC BY-NC-SA 4.0 International)*

The 11 pairs of superficial **external intercostal** muscles aid in inspiration of air during breathing because when they contract, they raise the ribs, which expands the thoracic cavity. The 11 pairs of **internal intercostal** muscles, just deep to the externals, are used for forced (deep) expiration because they draw the ribs together to constrict the rib cage. The movement of the ribs caused by the intercostals is visualized using to analogies: a bucket handle and a pump handle.

Muscles of the Pelvic Floor

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 females.

The large **levator ani** consists of two skeletal muscles, the **pubococcygeus** and the **iliococcygeus** (Figure 19.5.2.5). 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 posterior muscle of the of the pelvic floor is the **coccygeus**.

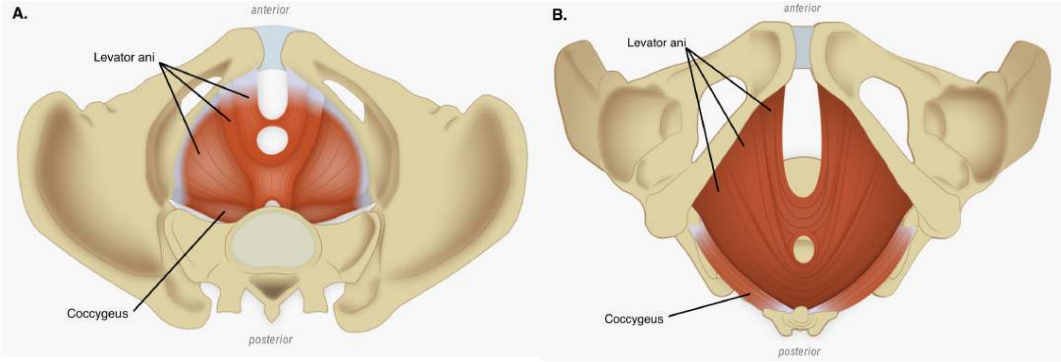


Figure 19.5.2.5: Muscles of the Pelvic Floor. The pelvic floor muscles support the pelvic organs, resist intra-abdominal pressure, and work as sphincters for the urethra, rectum, and vagina. *(Image credit: "Muscles of the Pelvic Floor" by Jennifer Lange, modified from originals by University of British Columbia Clinical Anatomy are licensed under CC BY-NC-SA 4.0 International)*

Concept Review

Made of skin, fascia, and four pairs of muscle, the anterior abdominal wall protects the organs located in the abdomen and moves the vertebral column. These muscles include the rectus abdominis, which extends through the entire length of the trunk, the external oblique, the internal oblique, and the transversus abdominus. The quadratus lumborum forms the posterior abdominal wall.

The muscles of the thorax play a large role in breathing, especially the dome-shaped diaphragm. When it contracts and flattens, the volume inside the pleural cavities increases, which decreases the pressure within them. As a result, air will flow into the lungs. The external and internal intercostal muscles span the space between the ribs and help change the shape of the rib cage and the volume-pressure ratio inside the pleural cavities during inspiration and expiration.

The perineum muscles play roles in urination in both sexes, ejaculation in men, and vaginal contraction in women. The pelvic floor muscles support the pelvic organs, resist intra-abdominal pressure, and work as sphincters for the urethra, rectum, and vagina.

Review Questions

Critical Thinking Questions

Glossary

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19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs

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

- 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 Move the Pectoral Girdle at the Sternoclavicular Joint

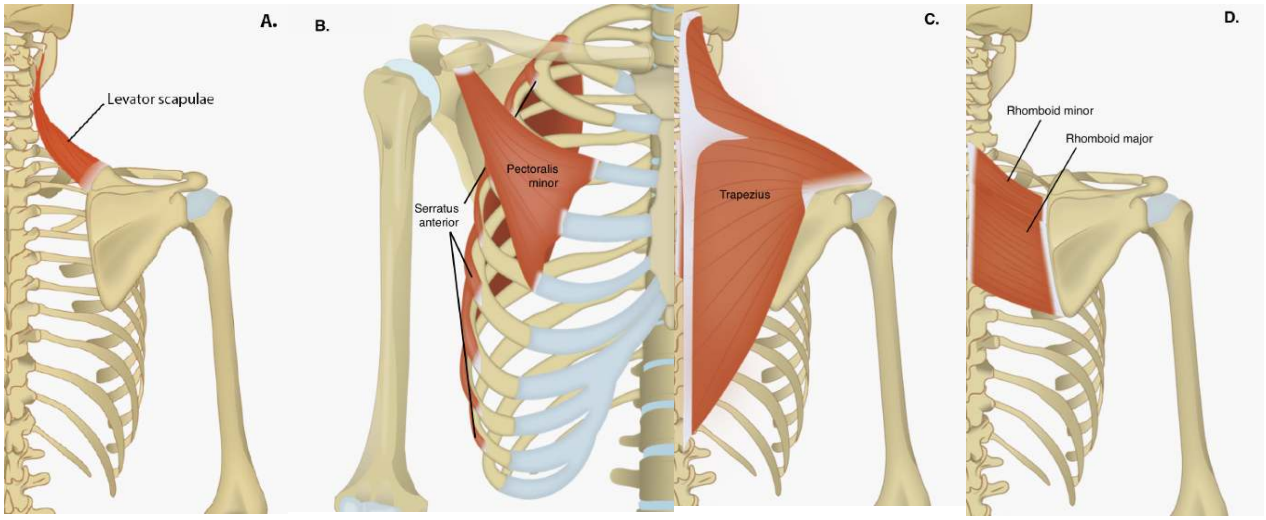


Figure 19.5.3.1: Muscles that Position the Pectoral Girdle. The muscles that stabilize the pectoral girdle make it a steady base on which other muscles can move the arm: A. Posterior muscle - deep, B. Anterior muscles - deep, C. Posterior muscles - superficial, D. Posterior muscles - deep. *(Image credit: "Muscles that Position the Pectoral Girdle" by Jennifer Lange are licensed under CC BY-NC-SA 4.0, based on images by University of British Columbia Clinical Anatomy.)*

Muscles that position the pectoral girdle are located either on the anterior thorax or on the posterior thorax (Figure 19.5.3.1 and Table 19.5.3.1). The anterior muscles include the **subclavius**, **pectoralis minor**, and **serratus anterior**. The posterior muscles include the **trapezius**, **levator scapulae, rhomboid major**, and **rhomboid minor**. When the rhomboids are contracted, your scapula moves medially, which can pull the shoulder and upper limb posteriorly.

Table 19.5.3.1: Muscles that Position the Pectoral Girdle

Muscle	Origin	Insertion	Movement	Image(s)
Levator scapulae	Transverse processes of C_1-C_4	Superior, medial border of scapula	Elevates and inferiorly rotates scapula (video)	
Pectoralis minor	Anterior surfaces of certain ribs (2 - 4 or 3 - 5)	Coracoid process of scapula	Rotates shoulder anteriorly (throwing motion); assists with inhalation	

Muscle	Origin	Insertion	Movement	Image(s)
Rhomboid major	Thoracic vertebrae (T_2 - T_5)	Medial border of scapula	Retracts scapula (video)	
Rhomboid minor	Cervical and thoracic vertebrae (C7 and T1)	Medial border of scapula	Retracts scapula (video)	
Serratus anterior	Muscle slips from certain ribs (1 - 8 or 1 - 9)	Anterior surface of vertebral border of scapula	Protracts scapula (video)	
Trapezius	Skull; vertebral column	Acromion and spine of scapula; clavicle	Dependent upon which fibers are stimulated (video): 1. Elevate and rotate scapula, 2. Depress and rotate scapula, 3. Retract scapula	

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Muscles That Move the Humerus at the Shoulder Joint

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 19.5.3.2 and Table 19.5.3.2). The two muscles that originate on the axial skeleton 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 sheath called an aponeurosis.

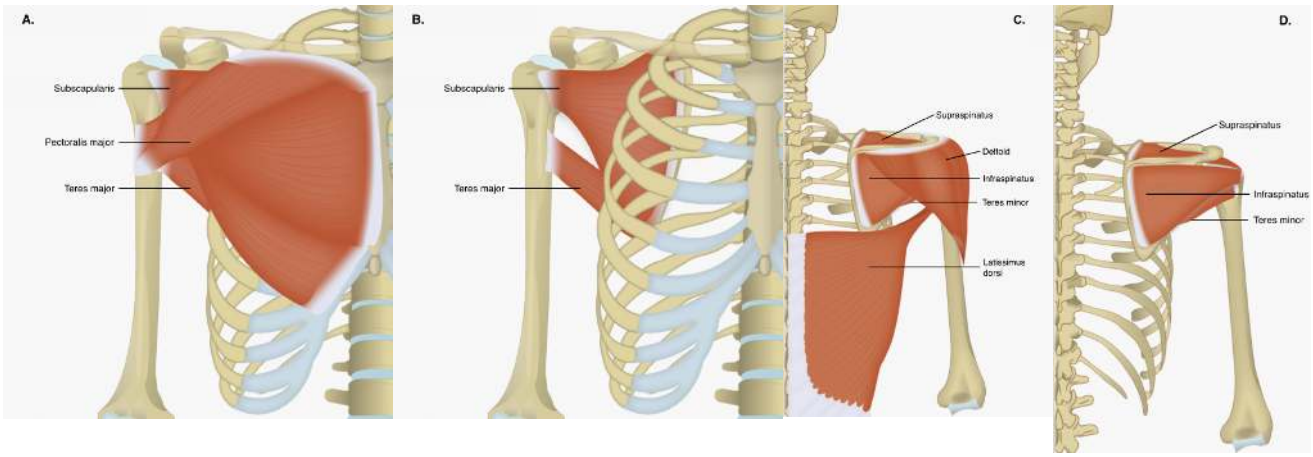
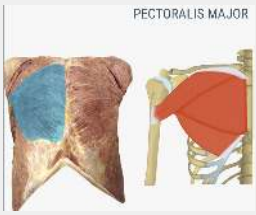
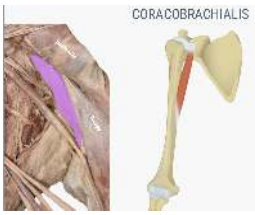


Figure 19.5.3.2: Muscles That Move the Humerus. A. Anterior view, superficial. B. Anterior view, deep. C. Posterior view, superficial. D. Posterior view, deep *(Image credit: "Muscles that Move the Humerus" by Jennifer Lange are licensed under CC BY-NC-SA 4.0, based on images by University of British Columbia Clinical Anatomy.)*

Table 19.5.3.2: Muscles that Move the Humerus at the Shoulder Joint

Muscle	Origin	Insertion	Movement	Image(s)
Latissimus dorsi	Thoracic vertebrae (T7-T12); lumbar vertebrae; lower ribs (9-12); iliac crest	Intertubercular sulcus of humerus	Extends, adducts, and internally rotates shoulder (video)	
Pectoralis major	Clavicle; sternum; cartilage of certain ribs (1-6 or 1-7); aponeurosis of external oblique muscle	Greater tubercle of humerus	Flex, adduct, and internally rotate shoulder (video)	
Coracobrachialis	Coracoid process of scapula	Medial surface of humerus shaft	Flex and adduct shoulder	
Deltoid	Trapezius; clavicle; acromion and spine of scapula	Deltoid tuberosity of humerus	Extends, abducts, and flexes shoulder (video) - motion is dependent upon which fibers are activated	
Subscapularis (part of rotator cuff)	Subscapular fossa of scapula	Lesser tubercle of humerus	Adduct and internally rotate shoulder; stabilizes shoulder joint during movement of the pectoral girdle (video)	

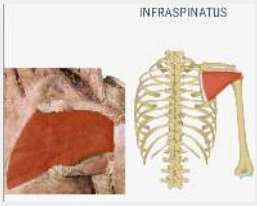
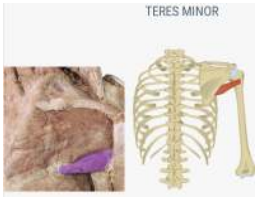
Muscle	Origin	Insertion	Movement	Image(s)
Infraspinatus (part of rotator cuff)	Infraspinous fossa of scapula	Greater tubercle of humerus	Externally rotate shoulder (video)	
Supraspinatus (part of rotator cuff)	Supraspinous fossa of scapula	Greater tubercle of humerus	Abduct shoulder (video)	
Teres major	Posterior surface of scapula	Intertubercular sulcus of humerus	Adduct and internally rotate shoulder	
Teres minor (part of rotator cuff)	Lateral border of dorsal scapular surface	Greater tubercle of humerus	Externally rotate shoulder	

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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 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 at the Elbow Joint

The forearm, containing the radius and ulna, has two actions at the hinge of the elbow joint: flexion, extension. The the muscles that cause flexion at the elbow joint include the **biceps brachii**, **brachialis**, and **brachioradialis**. The extensors are the **triceps brachii** and **anconeus**.

The biceps brachii, brachialis, and brachioradialis flex the forearm at the elbow. 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 19.5.3.3 and Table 19.5.3.3).

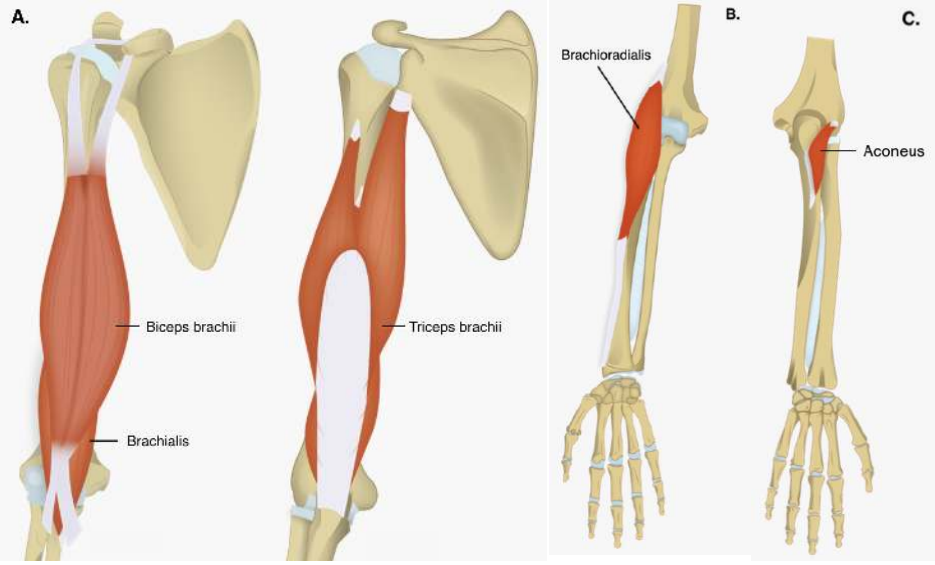


Figure 19.5.3.3: Muscles that Move the Forearm at the Elbow Joint. A. The prime movers of elbow flexion are in the anterior compartment - biceps brachii and brachialis. The prime mover of elbow extension is in the posterior compartment - triceps brachii. Muscles that assist in elbow movements are B. Brachioradialis and C. Aconeus. *(Image credit: "Muscles that Move the Forearm" by Jennifer Lange are licensed under CC BY-NC-SA 4.0, based on images by University of British Columbia Clinical Anatomy.)*

Table 19.5.3.3: Muscles that Move the Forearm at the Elbow Joint

Muscle	Origin	Insertion	Movement	Image(s)
Anterior Muscles (Flexion)				
Biceps brachii	Coracoid process; tubercle above glenoid cavity	Radial tuberosity	1. Flexion of elbow joint 2. Pronation of radioulnar joint 3. Flexion of shoulder joint	
Brachialis	Front of distal humerus	Coronoid process of ulna	Elbow flexion	
Brachioradialis	Lateral supracondylar ridge at distal end of humerus	Base of styloid process of radius	Assists in elbow flexion	
Posterior Muscles (Extension)				

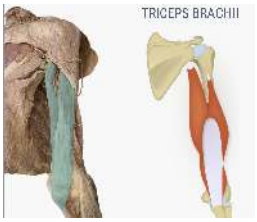
Muscle	Origin	Insertion	Movement	Image(s)
Anconeus	Lateral epicondyle of humerus	Lateral aspect of olecranon process of ulna	Assists in extending elbow joint	
Triceps brachii	Infraglenoid tubercle of scapula; posterior shaft of humerus; posterior humeral shaft distal to the radial groove	Olecranon process of ulna	Extends elbow and shoulder	

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Muscles That Move the Forearm at the Radioulnar Joints

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. (Table 19.5.3.4)

Table 19.5.3.4: Muscles that Move the Forearm at the Elbow Joint

Muscle	Origin	Insertion	Movement	Image(s)
Anterior Muscles (Pronation)				
Pronator quadratus	Distal portion of anterior ulnar shaft	Distal surface of anterior radius	Assists in turning hand palm posterior (pronation of radioulnar joint)	
Pronator teres	Medial epicondyle of humerus; coronoid process of ulna	Lateral radius	Turns hand palm posterior (pronation of radioulnar joint)	
Posterior Muscles (Supination)				
Supinator	Lateral epicondyle of humerus; proximal ulna	Proximal end of radius	Turns hand palm anterior (supinator of radioulnar joint)	

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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 Forearm 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 (Figure 19.5.3.4 and Table 19.5.3.5). 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**.

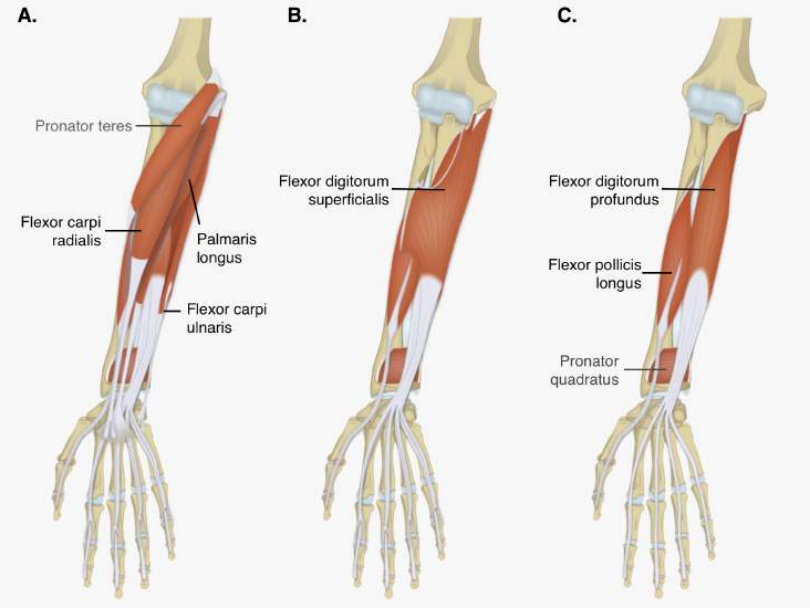


Figure 19.5.3.4: Anterior Muscles that Move the Joints of the Wrist, Hand, and Fingers. Muscles in the anterior compartment of the forearm all cause flexion. Some have additional actions depending upon their insertion point. A. Superficial layer (grey indicates muscle belongs in another group), B. Intermediate layer, C. Deep layer. (Image credit: "Muscles that Move the Joints of the Wrist, Hand, and Fingers" by Jennifer Lange *are licensed under CC BY-NC-SA 4.0, based on images by University of British Columbia Clinical Anatomy*.)

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** (Figure 19.5.3.5, Table 19.5.3.5).

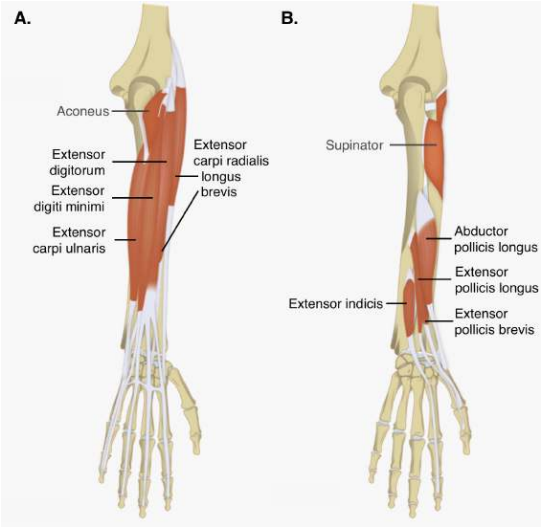


Figure 19.5.3.5: Posterior Muscles that Move the Joints of the Wrist, Hand, and Fingers. Most muscles in the posterior compartment of the forearm cause extension. Some have additional or other actions depending upon their insertion point. (Grey indicates muscle belongs in another group) A. Superficial layer, B. Deep layer. *(Image credit: "Posterior Muscles that Move the Joints of the Wrist, Hand, and Fingers" by Jennifer Lange are licensed under CC BY-NC-SA 4.0, based on images by University of British Columbia Clinical Anatomy.)*

Table 19.5.3.5: Muscles that Move the Wrist, Hands, and Forearm

Prime Mover	Origin	Insertion	Movement	Image(s)
Superficial/Intermediate Anterior Compartment of Forearm				
Flexor carpi ulnaris	Medial epicondyle of humerus; olecranon process; posterior surface of ulna	Pisiform bone; hamate bone; base of fifth metacarpal	Assists in bending hand up toward shoulder; tilts hand to side away from body; stabilizes wrist	
Flexor carpi radialis	Medial epicondyle of humerus	Base of second and third metacarpals	Bends wrist toward body; tilts hand to side away from body	
Flexor digitorum superficialis	Medial epicondyle of humerus; coronoid process of ulna; shaft of radius	Middle phalanges of fingers 2 - 5	Bends fingers to make fist	
Palmaris longus	Medical epicondyle of humerus	Palmar aponeurosis; skin and fascia of palm	Assists in bending hand up toward shoulder	
Deep Anterior Compartment of Forearm				

Prime Mover	Origin	Insertion	Movement	Image(s)
Flexor digitorum profundus	Coronoid process; anteromedial surface of ulna; interosseous membrane	Distal phalanges of fingers 2 - 5	Bends fingers to make a fist; also bends wrist toward body	
Flexor pollicus longus	Anterior surface of radius; interosseous membrane	Distal phalanx of thumb	Bends tip of thumb	
Superficial Posterior Compartment of Forearm				
Extensor carpi radialis brevis	Lateral epicondyle of humerus	Base of third metacarpal	Assists extensor radialis longus in extending and abducting wrist; also stabilizes hand during finger flexion	
Extensor carpi ulnaris	Lateral epicondyle of humerus; posterior border of ulna	Base of fifth metacarpal	Straightens wrist away from body; tilts hand to side toward body	
Extensor digiti minimi	Lateral epicondyle of humerus	Extensor expansion; distal phalanx of finger 5 (little finger)	Extends finger 5 (little finger)	
Extensor digitorum	Lateral epicondyle of humerus	Extensor expansions; distal phalanges of fingers	Opens fingers and moves them sideways away from the body	
Extensor radialis longus	Lateral supracondylar ridge of humerus	Base of second metacarpal	Straightens wrist away from body	
Deep Posterior Compartment of Forearm				
Abductor pollicis longus	Posterior surface of radius and ulna; interosseous membrane	Base of first metacarpal; trapezium	Moves thumb sideways toward body; extends thumb; moves hand sideways toward body	

Prime Mover	Origin	Insertion	Movement	Image(s)
Extensor indicis	Posterior surface of distal ulna; interosseous membrane	Tendon of extensor digitorum of finger 2 (index finger)	Extends finger 2 (index finger); straightens wrist away from body	
Extensor pollicis brevis	Dorsal shaft of radius and ulna; interosseous membrane	Base of proximal phalanx of thumb	Extends thumb	
Extensor pollicis longus	Dorsal shaft of radius and ulna; interosseous membrane	Base of distal phalanx of thumb	Extends thumb	

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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 19.5.3.6, Table 19.5.3.6). 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.

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**.

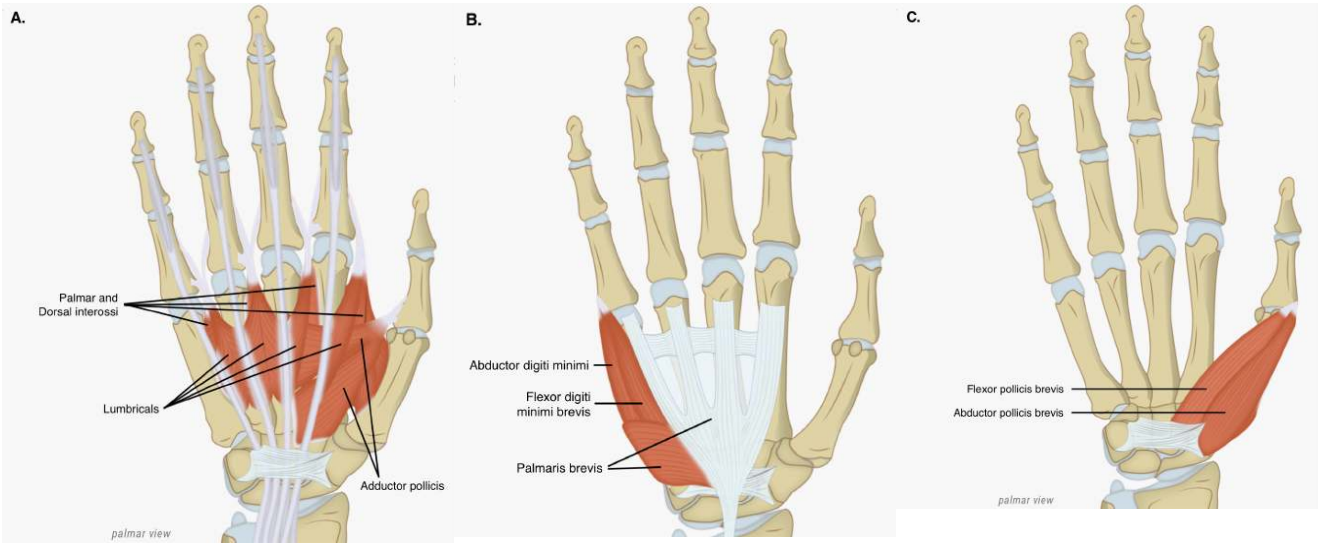


Figure 19.5.3.6: Intrinsic Muscles of the Hand. These muscles allow for fine motor control of the digits for activities such as writing and typing. A. Palmar view of the deep muscles. B. Palmar view of the hypothenar muscles. C. Palmar view of the thenar muscles. *(Image credit: "Intrinsic Muscles of the Hand" by Jennifer Lange are licensed under CC BY-NC-SA 4.0, based on images by University of British Columbia Clinical Anatomy.)*

Table 19.5.3.6: Intrinsic Muscles of the Hand

Muscle	Origin	Insertion	Movement	Image(s)
Thenar Muscles (movements video)				
Abductor pollicis brevis	Flexor retinaculum; and nearby carpals	Lateral base of proximal phalanx of thumb	Abducts and flexes thumb	
Adductor pollicis	Capitate bone; bases of metacarpals 2 - 4; front of metacarpal 3	Medial base of proximal phalanx of thumb	Adducts and flexes thumb	

Muscle	Origin	Insertion	Movement	Image(s)
Flexor pollicis brevis	Flexor retinaculum; trapezium	Lateral base of proximal phalanx of thumb	Flexes thumb	 
Opponens pollicis	Flexor retinaculum; trapezium	Anterior of first metacarpal	Opposes thumb (moves thumb across palm to touch other fingers)	
Hypothenar Muscles				
Abductor digiti minimi	Pisiform bone	Medial side of proximal phalanx of finger 5 (little finger)	Abducts and flexes MCP of 5th digit	 

Muscle	Origin	Insertion	Movement	Image(s)
Flexor digiti minimi brevis	Hamate bone; flexor retinaculum	Medial side of proximal phalanx of finger 5 (little finger)	Flexes MCP of 5th digit	
Opponens digiti minimi	Hamate bone; flexor retinaculum	Medial side of fifth metacarpal	Opposes digit 5 (moves little finger across palm to touch thumb)	
Deep Muscles				
Dorsal interossei	Sides of metacarpals	Both sides of finger 3; for each other finger, extensor expansion over first phalanx on side opposite finger 3	Abducts and flexes the three middle fingers at metacarpo-phalangeal joints; extends the three middle fingers at interphalangeal joints	
Lumbricals	Palm (lateral sides of tendons in flexor digitorum profundus)	Fingers 2–5 (lateral edges of extensional expansions on first phalanges)	Flexes each finger at metacarpo-phalangeal joints; extends each finger at interphalangeal joints	
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	Adducts and flexes each finger at metacarpo-phalangeal joints; extends each finger at interphalangeal joints	

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Concept Review

The clavicle and scapula make up the pectoral girdle, which provides a stable origin for the muscles that move the humerus. The muscles that position and stabilize the pectoral girdle are located on the thorax. The anterior thoracic muscles are the subclavius, pectoralis minor, and the serratus anterior. The posterior thoracic muscles are the trapezius, levator scapulae, rhomboid major, and rhomboid minor. Nine muscles cross the shoulder joint to move the humerus. The ones that originate on the axial skeleton are the pectoralis major and the latissimus dorsi. The deltoid, subscapularis, supraspinatus, infraspinatus, teres major, teres minor, and coracobrachialis originate on the scapula.

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. The supinator is the only one that turns the forearm anteriorly.

The extrinsic muscles of the hands originate along the forearm and insert into the hand in order to facilitate crude movements of the wrists, hands, and fingers. The superficial anterior compartment of the forearm produces flexion. These muscles are the flexor carpi radialis, palmaris longus, flexor carpi ulnaris, and the flexor digitorum superficialis. The deep anterior compartment produces flexion as well. These are the flexor pollicis longus and the flexor digitorum profundus. The rest of the compartments produce extension. The extensor carpi radialis longus, extensor carpi radialis brevis, extensor digitorum, extensor digiti minimi, and extensor carpi ulnaris are the muscles found in the superficial posterior compartment. The deep posterior compartment includes the abductor longus, extensor pollicis brevis, extensor pollicis longus, and the extensor indicis.

Finally, the intrinsic muscles of the hands allow our fingers to make precise movements, such as typing and writing. They both originate and insert within the hand. The thenar muscles, which are located on the lateral part of the palm, are the abductor pollicis brevis, opponens pollicis, flexor pollicis brevis, and adductor pollicis. The hypothenar muscles, which are located on the medial part of the palm, are the abductor digiti minimi, flexor digiti minimi brevis, and opponens digiti minimi. The intermediate muscles, located in the middle of the palm, are the lumbricals, palmar interossei, and dorsal interossei.

Review Questions

Critical Thinking Questions

Glossary

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19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs

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

- Identify the major appendicular muscles of the pelvic girdle and lower limb
- Identify the movement caused by these muscles

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 and Pelvic Muscles That Move the Femur

Most muscles that insert on the femur (the thigh bone) and move it, originate on the pelvic girdle (Table 19.5.4.1).

- The **psoas major** (the "p" is silent when pronouncing) and **iliacus** make up the **iliopsoas group**. These muscles originate on the posterior, interior of the pelvis and the vertebral column, pass over the pubis and insert into lesser trochanter of the femur. When they pass the inguinal ligament their fibers blend together so in the thigh the joined muscle is called the **iliopsoas**. Their anterior position relative to the hip joint makes them strong hip flexors (Figure 19.5.4.1).
- Some of the largest and most powerful muscles in the body are the gluteal muscles or **gluteal group**. From superficial to deep as well as largest to smallest these three muscles are the **gluteus maximus, gluteus medius**, and **gluteus minimus**. Gluteus maximus is the prime mover of hip extension as well as a lateral rotator. The gluteus medius and minimus both abduct and medially rotate the hip (Figure 19.5.4.1). The gluteus maximus has two insertion points: one in the posterior femur and one on the superior, lateral tibia via that **iliotibial (IT) band**.

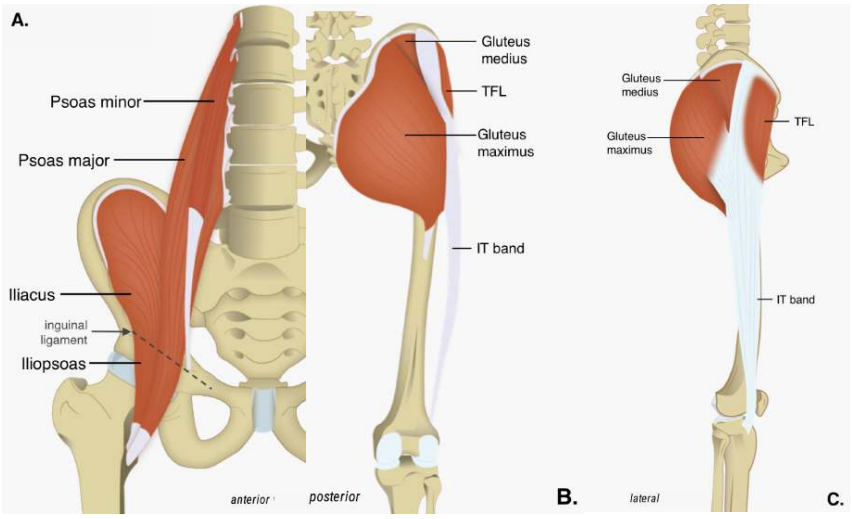


Figure 19.5.4.1: Muscles - Iliopsoas and Gluteal Groups. The primary of action of these muscles is hip flexion (A. iliopsoas group) and hip extension, abduction, and rotation (B. gluteal group). *(Image credits: "Iliopsoas and Gluteal Group Muscles" by Jennifer Lange are licensed under CC BY-NC-SA 4.0, based on images by University of British Columbia Clinical Anatomy)*

- Also in the gluteal compartment, the **tensor fasciae latae** (TFL) is a thick, squarish muscle in the superior aspect of the lateral thigh. It acts as a synergist of the gluteus medius in abducting the thigh. It also helps stabilize the lateral aspect of the knee by pulling on the iliotibial tract (band), making it taut (Figure 19.5.4.1).

- Deep to the gluteal muscles, the **piriformis**, **superior gemellus**, **obturator externus**, **inferior gemellus**, **obturator internus**, and **quadratus femoris** laterally rotate the femur at the hip (Figure 19.5.4.2).

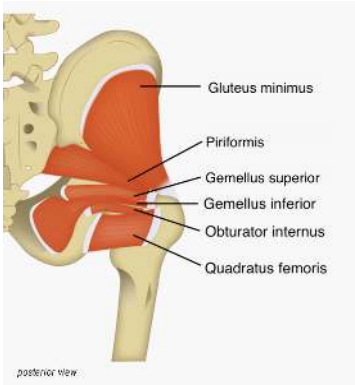


Figure 19.5.4.2: Muscles - Deep Gluteal Group. These small muscles stabilize the hip and help rotate it laterally. From superior to inferior they go in the the order of PG GO Q. *(Image credits: "Deep Gluteal Group Muscles" by Jennifer Lange are licensed under CC BY-NC-SA 4.0, based on images by University of British Columbia Clinical Anatomy)*

Muscles of the Medial Compartment

Six muscles are located in the medial compartment of the thigh (Figure 19.5.4.3). Most of these muscles perform adduction at the hip joint, and each performs other actions as well. The **adductor longus**, **adductor brevis**, **gracilis,** and **pectineus** also flex the hip joint. **Adductor magnus**, depending on which fibers are activated, can flex, extend, and laterally rotate the thigh. Gracilis is the only one of this groups of muscles that does not insert into the femur, it inserts into the posterior, medial aspect of the superior tibia which also allows it to cause flexion at the knee joint. The only muscle in this compartment that does not adduct is the **obturator externus**, this muscle's action is to laterally rotate the hip.

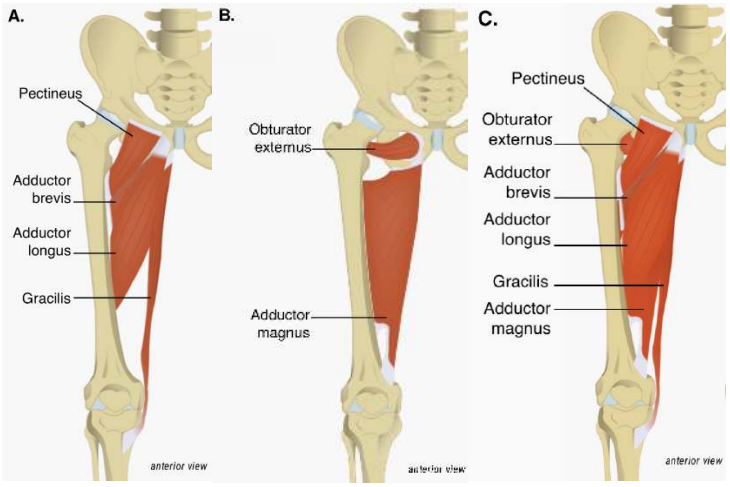


Figure 19.5.4.3: Muscles - Medial Thigh Compartment. All but one of the muscles in this group cause thigh adduction because they cross the hip joint on the medial side. Image A shows the more anterior muscles, image B shows the more posterior muscles, and image C shows them all. *(Image credits: "Medial Thigh Muscles" by Jennifer Lange are licensed under CC BY-NC-SA 4.0, based on images by University of British Columbia Clinical Anatomy)*

Table 19.5.4.1: Muscles that Move the Hip Joint

Muscle	Origin		Insertion	Movement	Image(s)
Iliopsoas group					
Iliacus	Iliac fossa; iliac crest; lateral sacrum		Lesser trochanter of femur	Flexes hip	

Muscle	Origin		Insertion	Movement	Image(s)
Psoas major	Lumbar vertebrae (L_1 - L_5); thoracic vertebrae (T_{12})		Lesser trochanter of femur	Flexes hip	
Gluteal Group					
Gluteus maximus	Dorsal ilium; sacrum; coccyx		Gluteal tuberosity of femur; iliotibial tract	Extend and laterally rotates hip	
Gluteus medius	Lateral surface of ilium		Greater trochanter of femur	Abducts and medially rotates hip	
Gluteus minimus	External surface of ilium		Greater trochanter of femur	Abducts and medially rotates hip	
Tensor fascia lata	Anterior aspect of iliac crest; anterior superior iliac spine		Iliotibial tract	Abducts and medially rotates hip	
Deep Gluteal Muscles					
Inferior gemellus	Ischial tuberosity		Greater trochanter of femur	Laterally rotates hip; maintains posture by stabilizing hip joint	
Obturator externus	Outer surfaces of obturator membrane, pubis, and ischium; margins of obturator foramen		Trochanteric fossa of posterior femur	Laterally rotates hip; maintains posture by stabilizing hip joint	
Obturator internus	Inner surface of obturator membrane; greater sciatic notch; margins of obturator foramen		Greater trochanter in front of piriformis	Laterally rotates hip; maintains posture by stabilizing hip joint	
Piriformis	Anterolateral surface of sacrum		Greater trochanter of femur	Laterally rotates hip; maintains posture by stabilizing hip joint	
Quadratus femoris	Ischial tuberosity		Trochanteric crest of femur	Laterally rotates hip; maintains posture by stabilizing hip joint	

Muscle	Origin		Insertion	Movement	Image(s)
Superior gemellus	Ischial spine		Greater trochanter of femur	Laterally rotates hip; maintains posture by stabilizing hip joint	
Medial Muscles					
Adductor brevis	Body of pubis; inferior ramus of pubis		Linea aspera above adductor longus	Adducts and flexes hip	
Adductor longus	Pubis near pubic symphysis		Linea aspera	Adducts and flexes hip	
Adductor magnus	Ischial rami; pubic rami; ischial tuberosity		Linea aspera; adductor tubercle of femur	Adducts hip Posterior fibers: extends and laterally rotates hip Anterior fibers: flex hip	
Gracilis	Inferior ramus; body of pubis; ischial ramus		Medial surface of tibia	Adducts and flexes hip; flexes knee	
Pectineus	Pectineal line of pubis		Lesser trochanter to linea aspera of posterior aspect of femur	Adducts and flexes hip	

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Muscles of the Anterior Compartment

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 (Figure 19.5.4.4). 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.

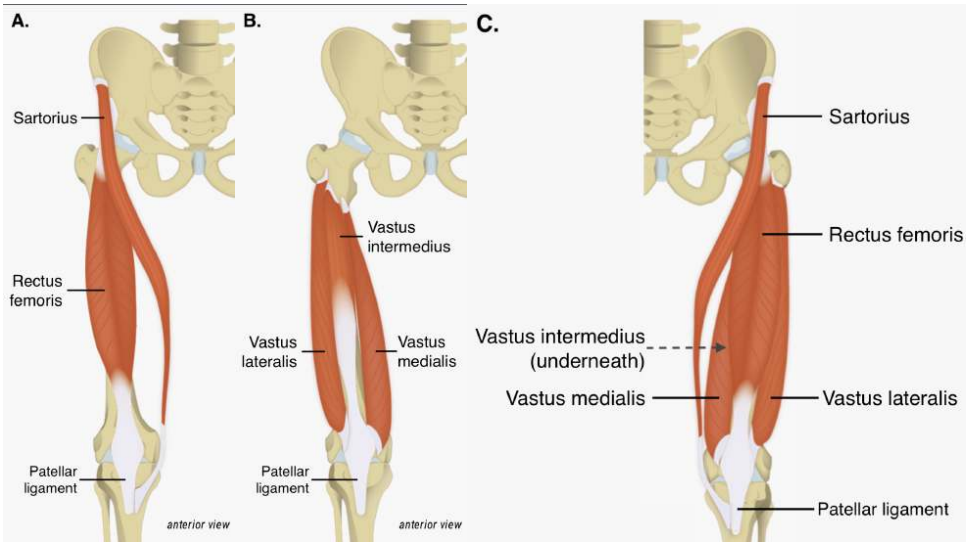


Figure 19.5.4.4: Muscles - Anterior Thigh. The two superficial muscles (A) act on both the hip and knee joints. The deeper muscles (B) only act on the knee joint. When all muscles are shown, the vastus intermedius cannot be seen (C) because it is deep to the rectus femoris. *(Image credits: "Anterior Thigh Muscles" by Jennifer Lange are licensed under CC BY-NC-SA 4.0, based on images by University of British Columbia Clinical Anatomy)*

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 (Figure 19.5.4.4). 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.

Table 19.5.4.2: Thigh Muscles That Move the Femur, Tibia, and Fibula

Muscle	Origin	Insertion	Movement	Image(s)
Anterior Compartment of Thigh: Quadricepts Femoris Group				
Rectus femoris	Anterior inferior iliac spine; superior margin of acetabulum	Patella; tibial tuberosity	Moves lower leg out in front of body, as when kicking; assists in raising knee	
Sartorius	Anterior superior iliac spine	Medial aspect of proximal tibia	Moves back of lower legs up and back toward the buttocks, as when kneeling; assists in moving thigh diagonally upward and outward as when mounting a bike	
Vastus intermedius	Proximal femur shaft	Patella; tibial tuberosity	Moves lower leg out in front of body, as when kicking	
Vastus lateralis	Greater trochanter; intertrochanteric line; linea apera	Patella; tibial tuberosity	Moves lower leg out in front of body, as when kicking	

Muscle	Origin	Insertion	Movement	Image(s)
Vastus medialis	Linea aspera; intertrochanteric line	Patella; tibial tuberosity	Moves lower leg out in front of body, as when kicking	
Posterior Compartment of Thigh: Hamstring Group				
Biceps femoris	Ischial tuberosity; linea aspera; distal femur	Head of fibula; lateral condyle of tibia	Moves back of lower legs up and back toward the buttocks, as when kneeling; moves thigh down and back; twists the thigh (and lower leg) outward	
Semimembranosus	Ischial tuberosity	Medial condyle of tibia; lateral condyle of femur	Moves back of lower legs up and back toward the buttocks, as when kneeling; moves thigh down and back; twists the thigh (and lower leg) outward	
Semitendinosus	Ischial tuberosity	Upper tibial shaft	Moves back of lower legs up and back toward the buttocks, as when kneeling; moves thigh down and back; twists the thigh (and lower leg) outward	

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Muscles of the Posterior Compartment

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 and extends the hip. These are the **biceps femoris (long head)**, **semitendinosus**, and **semimembranosus**. The biceps femoris also has a **short head** that is not considered part of the hamstrings because it only flexes the knee and does not extend the hip (Figure 19.5.4.5). The tendons of these muscles form the **popliteal fossa**, the diamond-shaped space at the back of the knee.

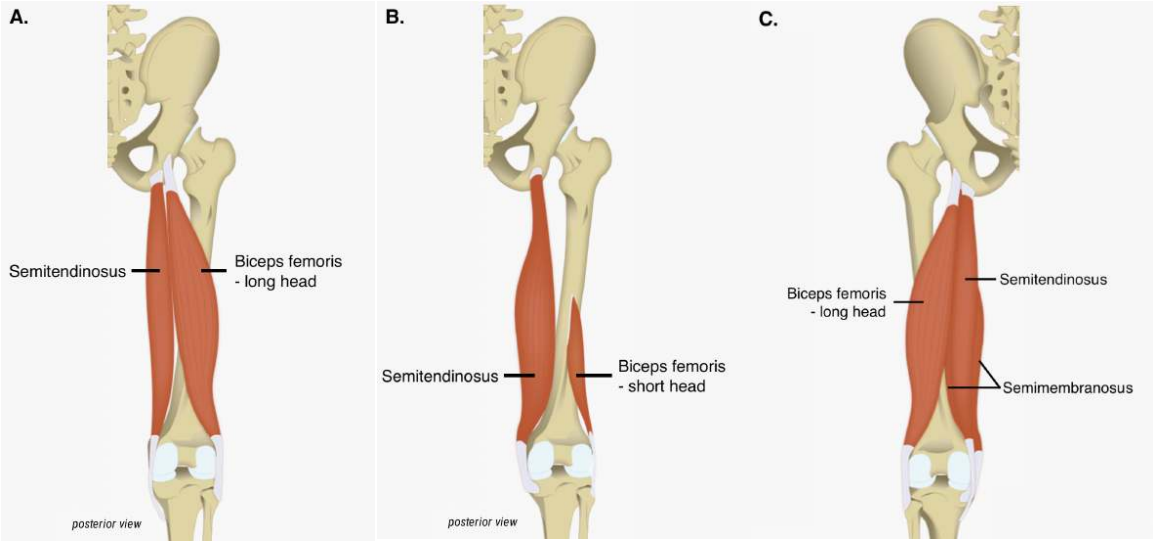


Figure 19.5.4.5: Muscles - Posterior Thigh. The superficial (A) and deep (B) muscles of the hamstring group cross both the hip and the knee joints. The short head of the biceps femoris (B) is not considered a hamstring because it does not do both of these functions, but it is located in the posterior thigh. When all muscles are shown, the short head cannot be seen (C) because it is deep to the long head. *(Image credits: "Posterior Thigh Muscles" by Jennifer Lange are licensed under CC BY-NC-SA 4.0, based on images by University of British Columbia Clinical Anatomy)*

Muscles That Move the Feet and Toes

The muscles that move the ankle, foot, and toes and are located in the leg are called the crural muscles. Similar to the thigh muscles, the muscles of the leg are divided by fascia into compartments, although the leg has three: anterior, lateral, and posterior (Table 19.5.4.3).

Muscles of the Anterior Compartment

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. Some, but not all, people have a third muscle in this group called the **fibularis tertius** (*tertius="third"*), a small muscle that originates on the anterior surface of the fibula, is associated with the extensor digitorum longus and sometimes fused to it (Figure 19.5.4.6).

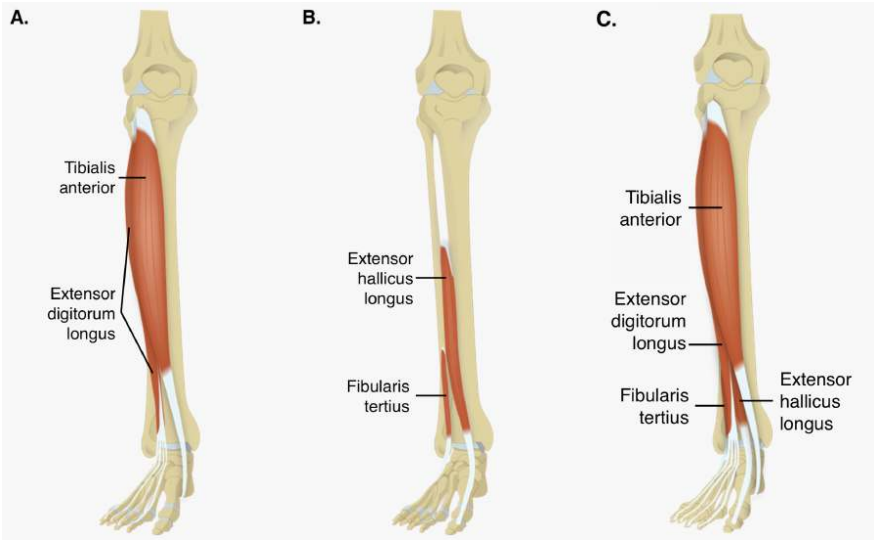


Figure 19.5.4.6: Muscles - Anterior Leg. The superficial (A) and deep (B) muscles of the anterior compartment of the leg cross both the ankle and joints in the foot. When all muscles are shown, only a small piece of the deep muscles can be seen (C), but you can easily identify the extensor hallicus longus because its tendon can be traced from the big toe. *(Image credits: "Anterior Leg Muscles" by Jennifer Lange are licensed under CC BY-NC-SA 4.0, based on images by University of British Columbia Clinical Anatomy)*

Muscles of the Lateral Compartment

The **lateral compartment of the leg** includes two muscles: the **fibularis longus** (aka peroneus longus) and the **fibularis brevis** (aka peroneus brevis) (Figure 19.5.4.7). Fibularis longus is the more superficial of the two and it originates more proximally on the fibula than does the fibularis brevis. Both are strong everters of the foot and weak plantar flexors.

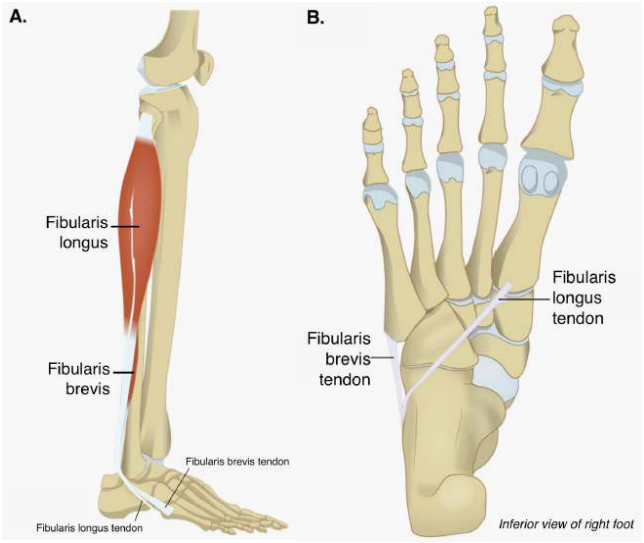


Figure 19.5.4.7: Muscles - Lateral Leg. The two muscles in the lateral compartment of the leg run along the length of the fibula (A). Based on their insertion points (B), both muscles cause eversion of the foot. *(Image credits: "Lateral Leg Muscles" by Jennifer Lange are licensed under CC BY-NC-SA 4.0, based on images by University of British Columbia Clinical Anatomy)*

Muscles of the Posterior Compartment

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 posterior aspect of the calcaneaus, and all are plantar flexors of the ankle joint. The most superficial and visible muscle of the calf is the **gastrocnemius**. This muscle originates superior to the knee and inserts into the calcaneous, so it is responsible for both knee flexion and ankle plantar flexion. The gastrocnemius has two wide muscle bellies called the **medial head** and the **lateral head**. Deep to the gastrocnemius is the wide, flat **soleus**. This muscle is named because it resembles a flatfish. The two heads of the gastrocnemius together with the soleus are collectively called the triceps surae or, more commonly, the calf muscles. The **plantaris** is a small muscle with a long tendon that runs obliquely between the two large sural muscles; some people may have two of these muscles, whereas no plantaris is observed in about seven percent of other cadaver dissections.

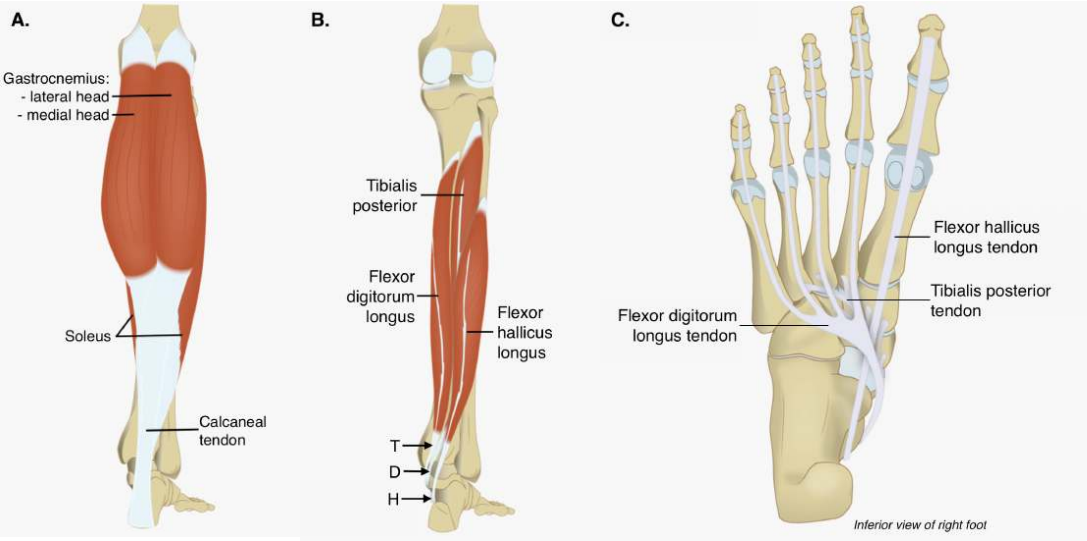


Figure 19.5.4.8: Posterior Leg Muscles. Superficial (A) and deep (B) views of the posterior compartment of the leg showing the muscles that plantar flex the ankle, invert the foot, and flex the toes as well as their tendinous insertions (C). *(Image credits: "Posterior Leg Muscles" by Jennifer Lange are licensed under CC BY-NC-SA 4.0, based on images by University of British Columbia Clinical Anatomy)*

There are four deep muscles in the posterior compartment of the leg: the **flexor digitorum longus**, **flexor hallucis longus**, **tibialis posterior** and **popliteus.** Popliteus is a small muscle that runs diagonally across the popliteal region. Its main function is to "unlock" the knee joint through slight medial rotation and flexion. The three remaining muscles are located along the posterior surface of the tibia and the fibula, deep to the

triceps surae (Figure 19.5.4.8). All plantarflex the ankle joint. As their names suggest, flexor digitorum longus also flexes digits 2-5 and flexor hallucis longus also flexes the big toe. The secondary action of the tibialis posterior is inversion of the foot. The commonly used neumonic for the order of the tendons of these three muscles as they pass posterior to the medial malleolus is Tom, Dick, And Very Nervous Harry: T = **T**ibialis posterior, Dick = flexor **D**igitorum longus, A = **a**rtery, V = **v**ein, N = **n**erve, H = flexor **H**allicus longus.

Table 19.5.4.3: Muscles That Move the Feet and Toes

Prime Mover	Origin	Insertion	Movement	Image(s)
Anterior Compartment of Leg				
Extensor digitorum longus	Lateral condyle of tibia; proximal portion of fibula; interosseous membrane	Middle and distal phalanges of toes 2 - 5	Extends toes 2-4; dorsiflexion of ankle	
Extensor hallucis longus	Anteromedial fibula shaft; interosseous membrane	Distal phalanx hallux (big toe)	Extends the big toe; dorsiflexion of ankle	
Tibialis anterior	Lateral condyle and upper tibial shaft; interosseous membrane	Interior surface of medial cuneiform; first metatarsal bone	Dorsiflexion of ankle; inversion of intertarsal	
Lateral Compartment of Leg				
Fibularis (peroneus) brevis	Distal fibula shaft	Proximal end of fifth metatarsal	Eversion of intertarsal; plantarflexion of ankle	
Fibularis (peroneus) longus	Upper portion of lateral fibula	First metatarsal; medial cuneiform	Eversion of intertarsal, plantarflexion of ankle	
Posterior Compartment of Leg: Superficial Muscles				
Gastrocnemius	Medial and lateral condyles of femur	Posterior calcaneus	Plantarflexion of ankle; flexion of knee	
Soleus	Superior tibia; fibula; interosseous membrane	Posterior calcaneus	Plantarflexion of ankle	

Prime Mover	Origin	Insertion	Movement	Image(s)
Posterior Compartment of Leg: Deep Muscles				
Flexor digitorum longus	Posterior tibia	Distal phalanges of toes 2 - 5	Flexion of digits 2-5; plantarflexion of ankle	
Flexor hallucis longus	Midshaft of fibula; interosseous membrane	Distal phalanx of hallux (big toe)	Flexes big toe; plantarflexion of ankle	
Tibialis posterior	Superior tibia; fibula; interosseous membrane	Tarsals and metatarsals 2 - 4	Plantarflexion of ankle; inversion of intertarsal	

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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. 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.

Concept Review

The pelvic girdle attaches the legs to the axial skeleton. The hip joint is where the pelvic girdle and the leg come together. The hip is joined to the pelvic girdle by many muscles. In the gluteal region, the psoas major and iliacus form the iliopsoas. The large and strong gluteus maximus, gluteus medius, and gluteus minimus extend and abduct the femur. Along with the gluteus maximus, the tensor fascia lata muscle forms the iliotibial tract. The lateral rotators of the femur at the hip are the piriformis, obturator internus, obturator externus, superior gemellus, inferior gemellus, and quadratus femoris. On the medial part of the thigh, the adductor longus, adductor brevis, and adductor magnus adduct the thigh and medially rotate it. The pectineus muscle adducts and flexes the femur at the hip.

The thigh muscles that move the femur, tibia, and fibula are divided into medial, anterior, and posterior compartments. The medial compartment includes the adductors, pectineus, and the gracilis. The anterior compartment comprises the quadriceps femoris, quadriceps tendon, patellar ligament, and the sartorius. The quadriceps femoris is made of four muscles: the rectus femoris, the vastus lateralis, the vastus medius, and the vastus intermedius, which together extend the knee. The posterior compartment of the thigh includes the hamstrings: the biceps femoris, semitendinosus, and the semimembranosus, which all flex the knee.

The muscles of the leg that move the foot and toes are divided into anterior, lateral, superficial- and deep-posterior compartments. The anterior compartment includes the tibialis anterior, the extensor hallucis longus, the extensor digitorum longus, and the fibularis (peroneus) tertius. The lateral compartment houses the fibularis (peroneus) longus and the fibularis (peroneus) brevis. The superficial posterior compartment has the gastrocnemius, soleus, and plantaris; and the deep posterior compartment has the popliteus, tibialis posterior, flexor digitorum longus, and flexor hallucis longus.

Review Questions

Critical Thinking Questions

Glossary

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19.6: Special Senses - Others

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19.7: Coronary Circulation

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

- Identify the veins and arteries of the coronary circulation system
- Describe how atherosclerosis impacts blood flow in coronary arteries and can cause a heart attack

You will recall that the heart is a remarkable pump composed largely of cardiac muscle cells that are incredibly active throughout life. Like all other cells, a **cardiomyocyte** requires a reliable supply of oxygen and nutrients, and a way to remove wastes, so it needs a dedicated, complex, and extensive coronary circulation. And because of the critical and nearly ceaseless activity of the heart throughout life, this need for a blood supply is even greater than for a typical cell. However, coronary circulation is not continuous; rather, it cycles, reaching a peak when the heart muscle is relaxed and nearly ceasing while it is contracting.

Coronary Arteries

Coronary arteries supply blood to the myocardium and other components of the heart. Immediately after the aorta emerges from the left ventricle it gives rise to the right and left coronary arteries.

The **left coronary artery** distributes blood to the left side of the heart, the left atrium and ventricle, and the interventricular septum. It runs posterior to the pulmonary trunk and almost immediately branches into two vessels: the circumflex and anterior interventricular arteries. The **circumflex artery** follows the coronary sulcus to the left and eventually fuses with the small branches of the right coronary artery. The larger **anterior interventricular artery**, also known as the left anterior descending artery (LAD), follows the anterior interventricular sulcus toward the apex of the heart. Along the way it gives rise to numerous smaller branches that interconnect with the branches of the posterior interventricular artery, forming anastomoses. An **anastomosis** is an area where vessels unite to form interconnections that normally allow blood to circulate to a region even if there may be partial blockage in another branch. The anastomoses in the heart are very small. Therefore, this ability is somewhat restricted in the heart so a coronary artery blockage often results in death of the cells (myocardial infarction) supplied by the particular vessel.

The **right coronary artery** proceeds along the coronary sulcus and distributes blood to the right atrium, portions of both ventricles, and the cardiac conducting system. On the posterior surface of the heart, the right coronary artery abruptly dips inferiorly and becomes the **posterior interventricular artery**, also known as the posterior descending artery. It runs along the posterior portion of the interventricular sulcus toward the apex of the heart, giving rise to branches that supply the posterior aspects of the interventricular septum and portions of both ventricles. Figure 19.7.1 presents the major vessels of coronary circulation from both the anterior and posterior views.

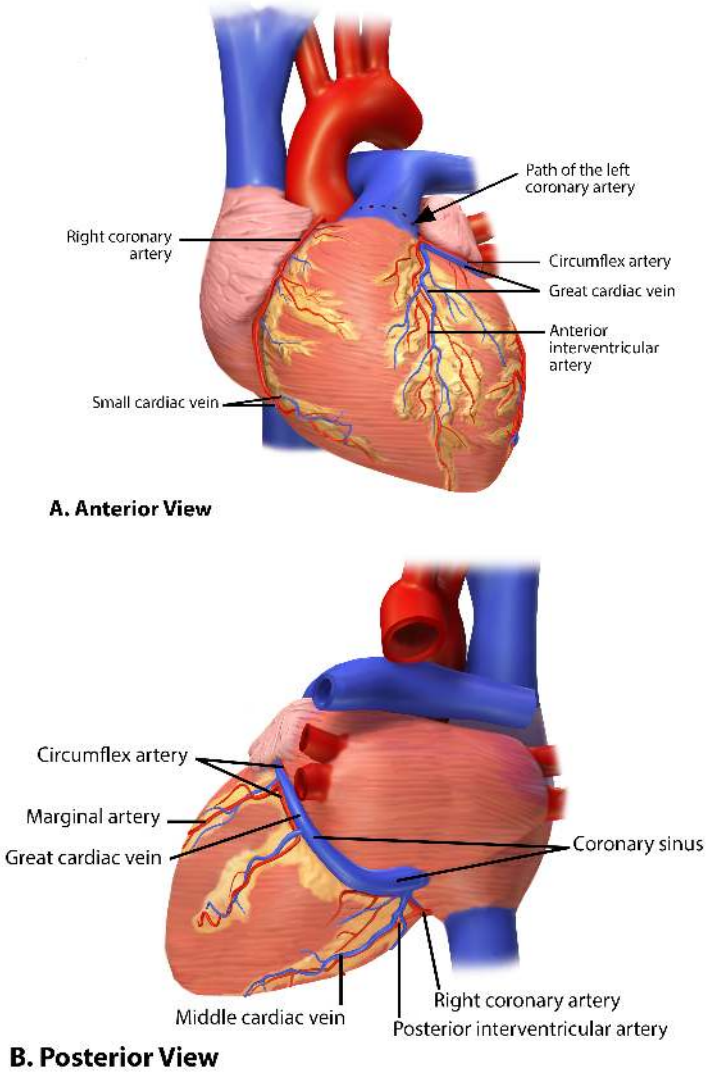


Figure 19.7.1: Coronary Arteries and Veins. The major coronary vessels shown in and anterior (A) and posterior (B) heart illustration. *(Image credits: "Coronary Vessels, Anterior View" by Jennifer Lange is licensed under CC BY-NC-SA 4.0, modification of original "Blausen 0451 - Anterior view of the heart - English labels" by Blausen Medical Communications, Inc.; "Coronary Vessels, Posterior View" by Jennifer Lange is licensed under under CC BY-NC-SA 4.0, modification of original "Blausen 0456 Heart Posterior" by Blausen Medical Communications, Inc.)*

DISORDERS OF THE...

Heart: Coronary Artery Disease

Coronary artery disease is the leading cause of death worldwide. It occurs when the buildup of plaque—a fatty material including cholesterol, connective tissue, white blood cells, and some smooth muscle cells—within the walls of the arteries obstructs the flow of blood and decreases the flexibility or compliance of the vessels. This condition is called atherosclerosis, a hardening of the arteries in which the accumulation of plaque increasingly narrows the diameter of the blood vessel. As the coronary blood vessels become occluded, the flow of blood to the tissues will be restricted, a condition called ischemia that causes the cells to receive insufficient amounts of oxygen, called hypoxia. Figure 19.7.2 shows the blockage of coronary arteries highlighted by the injection of dye. Some individuals with coronary artery disease report pain radiating from the chest called angina pectoris, but others remain asymptomatic. If untreated, coronary artery disease can lead to MI or a heart attack.

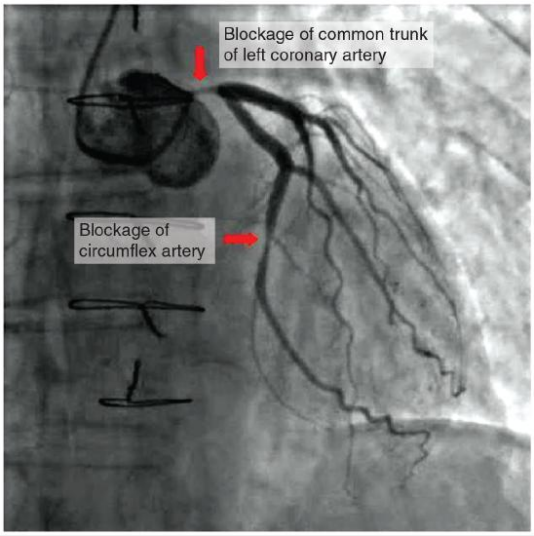


Figure 19.7.2: Atherosclerotic Coronary Arteries. In this coronary angiogram (X-ray), the dye makes visible two occluded coronary arteries, with noticeable narrowing pointed out in the circumflex artery and the common trunk of the left coronary artery. Such blockages can lead to decreased blood flow (ischemia) and insufficient oxygen (hypoxia) delivered to the cardiac tissues. If uncorrected, this can lead to cardiac muscle death (myocardial infarction). *(Image credit: "Occluded Coronay Arteries [sic]" by OpenStax is licensed under CC BY 3.0.)*

The disease progresses slowly and often begins in children and can be seen as fatty “streaks” in the vessels. It then gradually progresses throughout life. Well-documented risk factors include smoking, family history, hypertension, obesity, diabetes, high alcohol consumption, lack of exercise, stress, and hyperlipidemia or high circulating levels of lipids in the blood. Treatments may include medication, changes to diet and exercise, angioplasty with a balloon catheter, insertion of a stent, or coronary bypass procedure.

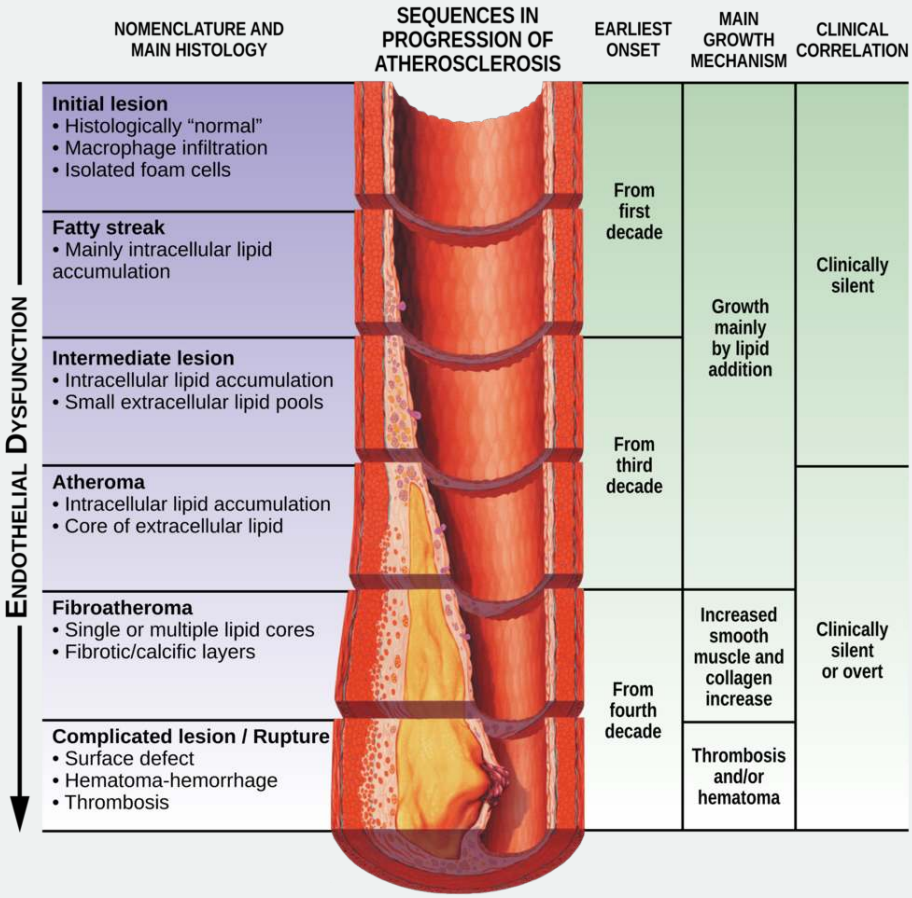


Figure 19.7.3: Atherosclerosis. Atherosclerosis is a progressive disease that narrow the diameter of an artery and restricts blood flow. *(Image credit: "Atherosclerosis Timeline - endothelial dysfunction" by YitzhakNat is licensed under CC BY-SA 4.0, via Wikimedia Commons.)*

Angioplasty is a procedure in which the occlusion is mechanically widened with a balloon (Figure 19.7.3). A specialized catheter with an expandable tip is inserted into a superficial vessel, normally in the leg, and then directed to the site of the occlusion. At this point, the balloon is inflated to compress the plaque material and to open the vessel to increase blood flow. Then, the balloon is deflated and retracted. A stent consisting of a specialized mesh is typically inserted at the site of occlusion to reinforce the weakened and damaged walls.

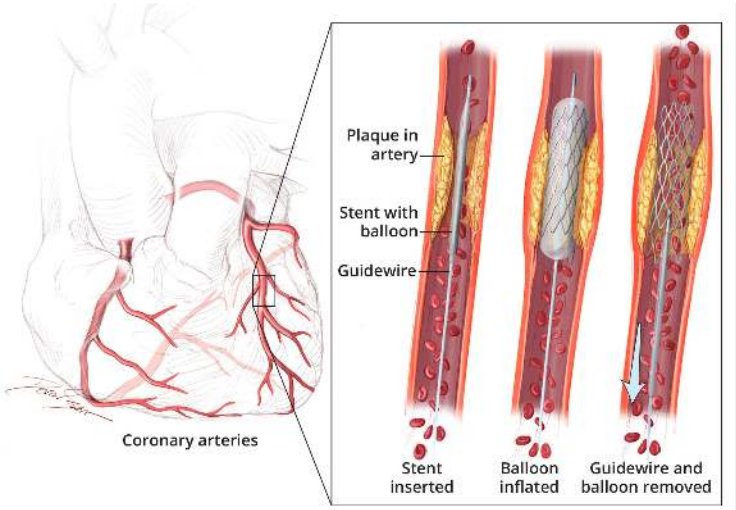


Figure 19.7.3: Angioplasty. To place a stent in a coronary artery narrowed by plaque, a catheter is inserted with an empty balloon and a stent attached at the end. The balloon is inflated to push the artery open and open the stent. Finally, the catheter and deflated balloon are removed, leaving the stent in place. (*Source: National Heart, Lung, and Blood Institute; National Institutes of Health; U.S. Department of Health and Human Services.*)

Coronary bypass surgery may also be performed. This surgical procedure grafts a replacement vessel obtained from another, less vital portion of the body to bypass the occluded area. This procedure is clearly effective in treating patients experiencing a MI, but overall does not increase longevity. Nor does it seem advisable in patients with stable although diminished cardiac capacity since frequently loss of mental acuity occurs following the procedure. Long-term changes to behavior, emphasizing diet and exercise plus a medicine regime tailored to lower blood pressure, lower cholesterol and lipids, and reduce clotting are equally as effective.

DISORDERS OF THE...

Heart: Myocardial Infarction

Myocardial infarction (MI) is the formal term for what is commonly referred to as a heart attack. It normally results from a lack of blood flow (ischemia) and oxygen (hypoxia) to a region of the heart, resulting in death of the cardiac muscle cells. An MI often occurs when a coronary artery is blocked by the buildup of atherosclerotic plaque consisting of lipids, cholesterol and fatty acids, and white blood cells, primarily macrophages. It can also occur when a portion of an unstable atherosclerotic plaque travels through the coronary arterial system and lodges in one of the smaller vessels. The resulting blockage restricts the flow of blood and oxygen to the myocardium and causes death of the tissue (Figure 19.7.4). MIs may be triggered by excessive exercise, in which the partially occluded artery is no longer able to pass sufficient quantities of blood, or severe stress, which may induce spasm of the smooth muscle in the walls of the vessel.

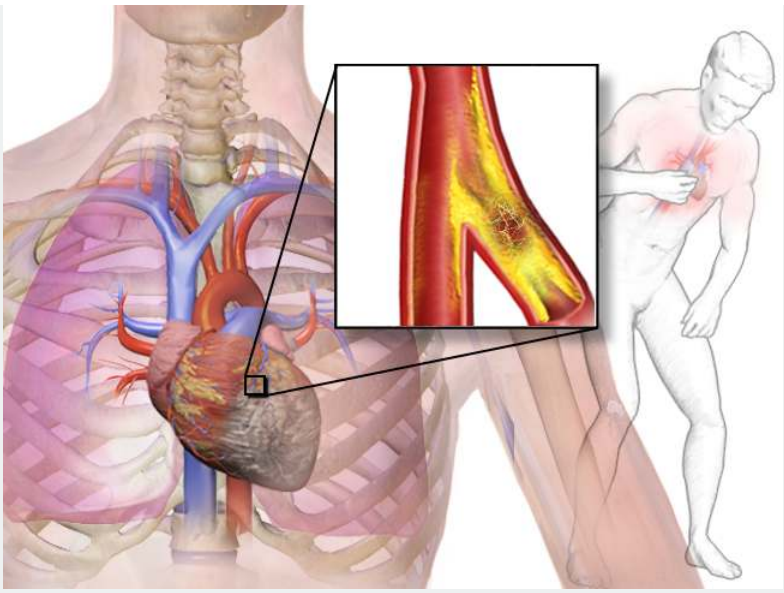


Figure 19.7.4: Myocardial Infarction. Blockage of a coronary artery results in the death of myocardium in distal regions. In men, this typically presents as a chest pain that radiates into the left arm. This pain may not be present in women. (Copyright; author via source)

In the case of acute MI, there is often sudden pain beneath the sternum (retrosternal pain) called angina pectoris, often radiating down the left arm in males but not in female patients. Until this anomaly between the sexes was discovered, many female patients suffering MIs were misdiagnosed and sent home. According to the American Heart Association, the symptoms of a heart attack are:

Symptoms in Women	Symptoms in Men
• Chest pain, but not always • Pain or pressure in the lower chest or upper abdomen • Jaw, neck or upper back pain • Nausea or vomiting • Shortness of breath • Fainting • Indigestion • Extreme fatigue	• Squeezing chest pressure or pain • Jaw, neck or back pain • Nausea or vomiting • Shortness of breath

Many of the symptoms are shared with other medical conditions, including anxiety attacks and simple indigestion, so differential diagnosis is critical. It is estimated that between 22 and 64 percent of MIs present without any symptoms.

An MI can be confirmed by examining the patient's ECG. In addition, echocardiography or cardiac magnetic resonance imaging may be employed. Common blood tests indicating an MI include elevated levels of creatine kinase MB (an enzyme that catalyzes the conversion of creatine to phosphocreatine, consuming ATP) and cardiac troponin (the regulatory protein for muscle contraction), both of which are released by damaged cardiac muscle cells.

Important risk factors for MI include cardiovascular disease, age, smoking, high blood levels of the low-density lipoprotein (LDL, often referred to as "bad" cholesterol), low levels of high-density lipoprotein (HDL, or "good" cholesterol), hypertension, diabetes mellitus, obesity, lack of physical exercise, chronic kidney disease, excessive alcohol consumption, and use of illegal drugs.

Coronary Veins

Coronary veins drain the heart and generally parallel the large surface arteries (see Figure 19.7.1). The **great cardiac vein** can be seen initially on the anterior surface of the heart following the interventricular sulcus running parallel to the anterior interventricular artery. Upon reaching the coronary sulcus it runs between the left atrium and left ventricle with the circumflex artery. The **middle cardiac vein** parallels and drains the areas supplied by the posterior interventricular artery. The **small cardiac**

vein originates on the lateral side of the right ventricle then parallels the right coronary artery in the coronary sulcus. It drains the blood from the posterior surfaces of the right atrium and ventricle. All three of these coronary veins merge with the coronary sinus - a large, thin-walled vein on the posterior surface of the heart lying within the atrioventricular sulcus and emptying directly into the right atrium. The **anterior cardiac veins** drain the anterior surface of the right ventricle but, unlike these other cardiac veins, it bypasses the coronary sinus and drains directly into the right atrium.

Concept Review

The right and left coronary arteries are the first to branch off the aorta and arise from two of the three sinuses located near the base of the aorta and are generally located in the sulci. Cardiac veins parallel the small cardiac arteries and generally drain into the coronary sinus. Coronary artery disease is caused by the build up of plaque in the walls of coronary arteries that causes ischemia and hypoxia in downstream tissues.

Review Questions

Critical Thinking Questions

Glossary

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19.8: Mean Arterial Pressure and Pulse Pressure

Pulse Pressure

As shown in Figure 19.8.1, the difference between the systolic pressure and the diastolic pressure is the pulse pressure. For example, an individual with a systolic pressure of 120 mm Hg and a diastolic pressure of 80 mm Hg would have a pulse pressure of 40 mmHg.

Generally, a pulse pressure should be at least 25 percent of the systolic pressure. A pulse pressure below this level is described as low or narrow. This may occur, for example, in patients with a low **stroke volume**, which may be seen in congestive heart failure, stenosis of the aortic valve, or significant blood loss following trauma. Stroke volume refers to the amount of blood ejected per ventricle in each heart beat.

In contrast, a high or wide pulse pressure is common in healthy people following strenuous exercise, when their resting pulse pressure of 30–40 mm Hg may increase temporarily to 100 mm Hg as stroke volume increases. A persistently high pulse pressure at or above 100 mm Hg may indicate excessive resistance in the arteries and can be caused by a variety of disorders. Chronic high resting pulse pressures can degrade the heart, brain, and kidneys, and warrant medical treatment.

Mean Arterial Pressure

Mean arterial pressure (MAP) represents the “average” pressure of blood in the arteries, that is, the average force driving blood into vessels that serve the tissues. Mean is a statistical concept and is calculated by taking the sum of the values divided by the number of values. Although complicated to measure directly and complicated to calculate, MAP can be approximated by adding the diastolic pressure to one-third of the pulse pressure or systolic pressure minus the diastolic pressure:

$$\text{MAP} = \text{ diastolic BP} + \frac{(\text{systolic BP-diastolic BP })}{3} \tag{19.8.1}$$

or

$$\text{MAP} = \text{ diastolic BP} + \frac{(\text{pulse pressure})}{3} \tag{19.8.2}$$

In Figure \(\PageIndex{1}\), this value is approximately 80 + (120 − 80) / 3, or 93.33. Normally, the MAP falls within the range of 70–110 mm Hg. If the value falls below 60 mm Hg for an extended time, blood pressure will not be high enough to ensure circulation to and through the tissues, which results in ischemia, or insufficient blood flow. A condition called hypoxia, inadequate oxygenation of tissues, commonly accompanies ischemia. The term hypoxemia refers to low levels of oxygen in systemic arterial blood. Neurons are especially sensitive to hypoxia and may die or be damaged if blood flow and oxygen supplies are not quickly restored.

mfrac

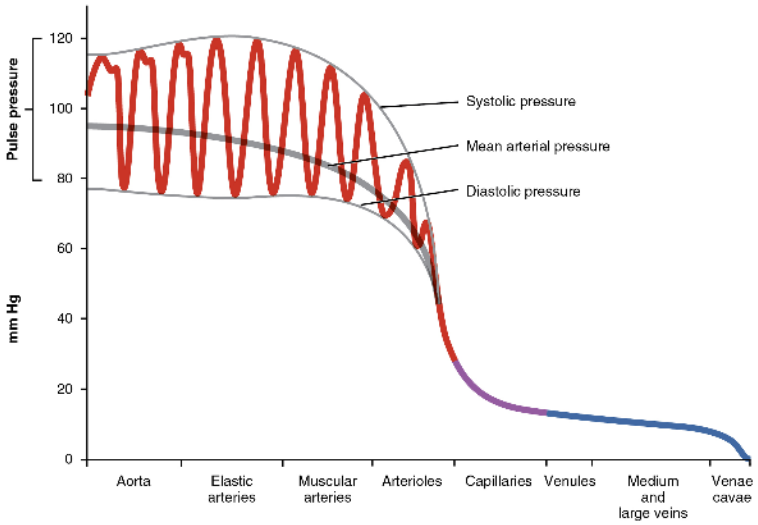


Figure 19.8.1: Systemic Blood Pressure The graph shows the components of blood pressure throughout the blood vessels, including systolic, diastolic, mean arterial, and pulse pressures.

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Index

A

abdominopelvic cavity
1.5: Anatomical Terminology
abduction
7.3: Types of Body Movements
abductor digiti minimi
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
abductor pollicis brevis
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
abductor pollicis longus
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
absorption
16: The Digestive System
16.2: Digestive System Processes and Regulation
16.3: The Stomach and the Upper Digestive Organs
abstract
1.2: Overview of the Scientific Method
accessible education
InfoPage
accessory organs
16.1: Overview of the Digestive System
accessory structures
5.1: Introduction
19: Optional Reading
acetylcholine
11.1: Introduction to the Autonomic Nervous System (ANS)
11.3: The Parasympathetic Division of the ANS
acetylcholine (ACh)
8.2: Skeletal Muscle Organ Structure
acids
2.3: Inorganic Compounds Essential to Human Functioning
acromial end of the clavicle
19.4.4: The Pectoral Girdle
acromial process
19.4.4: The Pectoral Girdle
acromioclavicular joint
19.4.4: The Pectoral Girdle
acromion
19.4.4: The Pectoral Girdle
actin
8.2: Skeletal Muscle Organ Structure
8.3: Muscle Fiber Contraction and Relaxation
8.5: Review Questions
action potential
8.2: Skeletal Muscle Organ Structure
9: Overview of the Nervous System
9.3: Synapses
9.4: The Function of Nervous Tissue
actionpotential
9.7: Review Questions
active transport
3.1: The Cell Membrane
3.4: Cell Transport and Osmosis
3.5: Review Questions
activity
14: The Cardiovascular System - Heart and Blood Vessels
adapt and share
Acknowledgements
adaptive learning
InfoPage
adduction
7.3: Types of Body Movements
adductor brevis
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
adductor longus
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
adductor magnus
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
adductor pollicis
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
adductor tubercle
19.4.7: Bones of the Lower Limb
adipocytes
4.3: Connective Tissue
adipose tissue
4.3: Connective Tissue
adrenal cortex
12.5: Adrenal Glands
adrenal glands
12: The Endocrine System
12.5: Adrenal Glands
adrenal medulla
12.5: Adrenal Glands
adrenocorticotropic hormone
12.3: The Pituitary Gland and Hypothalamus
adult skeleton
6: Bone Tissue and the Skeletal System
afferent
9.1: Organization and Functions of the Nervous System
afterload
14.6: Review Questions
agglutination
13.4: Blood Typing
aging
19.2: Functions of the Integumentary System
aging process
5.1: Introduction
agranular leukocytes
13.3: Leukocytes and Platelets
airway
15.1: Organs and Structures of the Respiratory System
alarm reaction
12.5: Adrenal Glands
albumin
13.5: Review Questions
aldosterone
12.5: Adrenal Glands
17.6: Endocrine Regulation of Kidney Function
alpha cell
12.6: Endocrine Pancreas
alveolar process of the mandible
19.4.1: The Skull
alveolar process of the maxilla
19.4.1: The Skull
alveoli
15.1: Organs and Structures of the Respiratory System
15.5: Review Questions
amphiarthrosis
7.2: Classification of Joints
anal canal
16.4: Small and Large Intestines
anal column
16.4: Small and Large Intestines
anal sinus
16.4: Small and Large Intestines
anal triangle
19.5.2: Axial Muscles of the Abdominal Wall and Thorax
anastomosis
14.1: Heart Anatomy
anatomical neck
19.4.5: Bones of the Upper Limb
anatomical planes
1.5: Anatomical Terminology
anatomical position
1.5: Anatomical Terminology
anatomical terminology
1.5: Anatomical Terminology
anatomicalposition
7.3: Types of Body Movements
anatomy
1: An Introduction to Anatomy and Physiology
1.1: Overview of Anatomy and Physiology
1.3: Structural Organization of the Human Body
1.6: Review Questions
6.2: Bone Classification
6.3: Bone Structure
9: Overview of the Nervous System
9.6: The Peripheral Nervous System
14: The Cardiovascular System - Heart and Blood Vessels
14.5: Blood Flow, Blood Pressure, and Resistance
15.1: Organs and Structures of the Respiratory System
15.2: The Lungs
15.5: Review Questions
16.3: The Stomach and the Upper Digestive Organs
16.5: Accessory Organs in Digestion- The Liver, Pancreas, and Gallbladder
16.6: Review Questions
17: The Urinary System
18: The Reproductive System
anchoring junction
4.2: Epithelial Tissue
anconeus
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
anemia
13.2: Erythrocytes
angiotensin
17.6: Endocrine Regulation of Kidney Function
angle of the mandible
19.4.1: The Skull
angle of the rib
19.4.3: The Thoracic Cage
anions
2.2: Chemical Bonds
ankle joint
19.4.7: Bones of the Lower Limb
anterior (ventral) sacral foramen
19.4.2: The Vertebral Column
anterior arch
19.4.2: The Vertebral Column
anterior border of the tibia
19.4.7: Bones of the Lower Limb
anterior cardiac veins
14.1: Heart Anatomy

anterior compartment of the arm
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
anterior compartment of the forearm
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
anterior compartment of the leg
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
anterior compartment of the thigh
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
anterior cranial fossa
19.4.1: The Skull
anterior interventricular artery
14.1: Heart Anatomy
anterior interventricular sulcus
14.1: Heart Anatomy
anterior longitudinal ligament
19.4.2: The Vertebral Column
anterior scalene
19.5.1: Axial Muscles of the Head, Neck, and Back
antibodies
13.4: Blood Typing
antigens
13.4: Blood Typing
anulus fibrosus
19.4.2: The Vertebral Column
anuria
17.7: Review Questions
aortic valve
14.1: Heart Anatomy
aortic valve stenosis
19.8: Mean Arterial Pressure and Pulse Pressure
apical
4.2: Epithelial Tissue
apocrine secretion
4.2: Epithelial Tissue
aponeurosis
8.2: Skeletal Muscle Organ Structure
appendicular
19.5.1: Axial Muscles of the Head, Neck, and Back
appendicular skeleton
19.4: Divisions of the Skeletal System
appendix
16.4: Small and Large Intestines
applied science
1.2: Overview of the Scientific Method
areolar tissue
4.3: Connective Tissue
arm
19.4.5: Bones of the Upper Limb
arterial resistance
19.8: Mean Arterial Pressure and Pulse Pressure
arteriole
14.4: Structure and Function of Blood Vessels
arteriovenous anastomosis
14.4: Structure and Function of Blood Vessels
artery
14.4: Structure and Function of Blood Vessels
articular tubercle
19.4.1: The Skull
articulation
7.2: Classification of Joints
artificial pacemaker
14.2: Cardiac Muscle and Electrical Activity
ascending colon
16.4: Small and Large Intestines
asthma
15.1: Organs and Structures of the Respiratory System
15.2: The Lungs
astrocyte
9.2: Anatomy of Nervous Tissue
atlas
19.4.2: The Vertebral Column
atomic number
2.4: Review Questions
atomic structure
2.1: Elements and Atoms - The Building Blocks of Matter
atoms
2: A Brief Overview of Chemistry
2.1: Elements and Atoms - The Building Blocks of Matter
ATP
3.2: The Cytoplasm and Cellular Organelles
8.3: Muscle Fiber Contraction and Relaxation
8.5: Review Questions
atrial_natriuretic_hormone
17.7: Review Questions
atrioventricular (AV) node
14.2: Cardiac Muscle and Electrical Activity
atrioventricular bundle
14.2: Cardiac Muscle and Electrical Activity
atrioventricular bundle branches
14.2: Cardiac Muscle and Electrical Activity
atrioventricular septum
14.1: Heart Anatomy
atrioventricular valves
14.1: Heart Anatomy
atrium
14.1: Heart Anatomy
attribution
Acknowledgements
audition
10.3: Special Senses - Ears
auditory system
10.3: Special Senses - Ears
auricle
14.1: Heart Anatomy
auscultation
14.3: Cardiac Cycle
autonomic
9.6: The Peripheral Nervous System
autonomic nervous system
11: The Autonomic Nervous System
11.1: Introduction to the Autonomic Nervous System (ANS)
11.2: The Sympathetic Division of the ANS
11.3: The Parasympathetic Division of the ANS
16.1: Overview of the Digestive System
autonomic nervous system (ANS)
9.1: Organization and Functions of the Nervous System
autonomic system
11.4: Review Questions
autorhythmicity
14.2: Cardiac Muscle and Electrical Activity
axial
19.5.1: Axial Muscles of the Head, Neck, and Back
axial skeleton
19.4: Divisions of the Skeletal System
axis
19.4.2: The Vertebral Column
axon
9.1: Organization and Functions of the Nervous System
9.2: Anatomy of Nervous Tissue
axon hillock
9.2: Anatomy of Nervous Tissue
axon segment
9.2: Anatomy of Nervous Tissue
axon terminal
9.2: Anatomy of Nervous Tissue
axoplasm
9.2: Anatomy of Nervous Tissue

B

B lymphocytes
13.3: Leukocytes and Platelets
13.5: Review Questions
Bachmann’s bundle
14.2: Cardiac Muscle and Electrical Activity
bacterial flora
16.4: Small and Large Intestines
balance
10.1: General and Special Senses
10.3: Special Senses - Ears
basal lamina
4.2: Epithelial Tissue
basal nuclei
9.5: The Central Nervous System
base of the metatarsal bone
19.4.7: Bones of the Lower Limb
basement membrane
4.2: Epithelial Tissue
bases
2.3: Inorganic Compounds Essential to Human Functioning
basic science
1.2: Overview of the Scientific Method
basophils
13.3: Leukocytes and Platelets
beta cell
12.6: Endocrine Pancreas
biaxial joint
7.2: Classification of Joints
biceps brachii
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
biceps femoris
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
bicipital groove
19.4.5: Bones of the Upper Limb
bicuspid valve
14.1: Heart Anatomy
bile
16.6: Review Questions
biological sex
1.3: Structural Organization of the Human Body
biology
1: An Introduction to Anatomy and Physiology
1.2: Overview of the Scientific Method
11: The Autonomic Nervous System
biomechanics
8: Muscle Tissue
bipolar
9.2: Anatomy of Nervous Tissue

blood
13: The Cardiovascular System - Blood
13.2: Erythrocytes
13.4: Blood Typing
13.5: Review Questions
14.6: Review Questions
17.6: Endocrine Regulation of Kidney Function
blood circulation
13.2: Erythrocytes
blood clotting
13.1: An Overview of Blood
blood composition
13.1: An Overview of Blood
blood disorders
13: The Cardiovascular System - Blood
blood flow
11.2: The Sympathetic Division of the ANS
blood glucose
1.4: Homeostasis
blood glucose regulation
12: The Endocrine System
blood groups
13: The Cardiovascular System - Blood
13.4: Blood Typing
blood pressure
1.4: Homeostasis
14.5: Blood Flow, Blood Pressure, and Resistance
blood tests
13.1: An Overview of Blood
blood typing
13: The Cardiovascular System - Blood
blood_flow
14.3: Cardiac Cycle
blood_pressure
14.3: Cardiac Cycle
body cavities
1.5: Anatomical Terminology
body movements
7: Joints
body of the rib
19.4.3: The Thoracic Cage
body temperature
1.4: Homeostasis
bodymovements
7.3: Types of Body Movements
bone
6: Bone Tissue and the Skeletal System
6.1: Functions of the Skeletal System
bone classification
6: Bone Tissue and the Skeletal System
bone development
6.4: Bone Remodeling and Calcium Homeostasis
bone formation
19: Optional Reading
bone growth
6.4: Bone Remodeling and Calcium Homeostasis
6.6: Review Questions
bone markings
6.3: Bone Structure
bone remodeling
6: Bone Tissue and the Skeletal System
bone repair
6.5: Fractures - Bone Repair
bone structure
6: Bone Tissue and the Skeletal System
bone tissue
6.6: Review Questions
bones
6.2: Bone Classification
7: Joints
brachialis
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
brachioradialis
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
brain
9: Overview of the Nervous System
9.1: Organization and Functions of the Nervous System
brain case
19.4.1: The Skull
brainstem
9.5: The Central Nervous System
breathing
15: The Respiratory System
breathing rate
11.2: The Sympathetic Division of the ANS
bronchi
15.1: Organs and Structures of the Respiratory System
15.5: Review Questions
brush border
16.4: Small and Large Intestines
buccinator
19.5.1: Axial Muscles of the Head, Neck, and Back
buffers
2.3: Inorganic Compounds Essential to Human Functioning
building blocks of matter
2: A Brief Overview of Chemistry
bundle of His
14.2: Cardiac Muscle and Electrical Activity

C

calcaneal tendon
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
calcaneus
19.4.7: Bones of the Lower Limb
calcitonin
12.4: Thyroid Gland and Parathyroid Glands
calcium ions
8.3: Muscle Fiber Contraction and Relaxation
California Community Colleges
Acknowledgements
callus formation
6.5: Fractures - Bone Repair
calvaria
19.4.1: The Skull
cancellous bone
6.6: Review Questions
cancer
1.6: Review Questions
15.2: The Lungs
capacitance
14.4: Structure and Function of Blood Vessels
capacitance vessels
14.4: Structure and Function of Blood Vessels
capillary
14.4: Structure and Function of Blood Vessels
capillary bed
14.4: Structure and Function of Blood Vessels
capitate
19.4.5: Bones of the Upper Limb
capitulum
19.4.5: Bones of the Upper Limb
carbon dioxide
15: The Respiratory System
15.1: Organs and Structures of the Respiratory System
15.3: The Process of Breathing
15.4: Gas Exchange
cardiac
14: The Cardiovascular System - Heart and Blood Vessels
cardiac cycle
14.6: Review Questions
19.7: Coronary Circulation
cardiac muscle
8: Muscle Tissue
8.1: Muscle Tissues
cardiac notch
14.1: Heart Anatomy
cardiac output
14.6: Review Questions
cardiac skeleton
14.1: Heart Anatomy
cardiac_contraction
14.3: Cardiac Cycle
cardiac_cycle
14.3: Cardiac Cycle
cardiomyocyte
14.1: Heart Anatomy
cardiovascular
13: The Cardiovascular System - Blood
cardiovascular health
14.5: Blood Flow, Blood Pressure, and Resistance
carotid canal
19.4.1: The Skull
carpal bone
19.4.5: Bones of the Upper Limb
carpal tunnel
19.4.5: Bones of the Upper Limb
carpometacarpal joint
19.4.5: Bones of the Upper Limb
cartilage
6: Bone Tissue and the Skeletal System
6.1: Functions of the Skeletal System
6.4: Bone Remodeling and Calcium Homeostasis
6.6: Review Questions
7: Joints
cartilaginous joint
7.2: Classification of Joints
cations
2.2: Chemical Bonds
caval opening
19.5.2: Axial Muscles of the Abdominal Wall and Thorax
Cecum
16.4: Small and Large Intestines
cell
3.2: The Cytoplasm and Cellular Organelles
cell differentiation
4.1: Types of Tissues
cell division
3.3: The Nucleus and DNA
cell junction
4.2: Epithelial Tissue
cell membrane
3: Cell Structure
3.1: The Cell Membrane
3.4: Cell Transport and Osmosis

cell recognition
3.1: The Cell Membrane
3.4: Cell Transport and Osmosis
cell transport
3: Cell Structure
cell types
4.1: Types of Tissues
cells
1.3: Structural Organization of the Human Body
1.6: Review Questions
cellular organization
4: Tissue Organization
cellular respiration
3.2: The Cytoplasm and Cellular Organelles
15: The Respiratory System
15.4: Gas Exchange
central nervous system
9: Overview of the Nervous System
central nervous system (CNS)
9.1: Organization and Functions of the Nervous System
centralnervoussystem
9.7: Review Questions
cerebellum
9.5: The Central Nervous System
cerebral cortex
9.4: The Function of Nervous Tissue
9.5: The Central Nervous System
cerebrospinal fluid (CSF)
9.2: Anatomy of Nervous Tissue
cerebrum
9.5: The Central Nervous System
cervical curve
19.4.2: The Vertebral Column
cervical vertebrae
19.4.2: The Vertebral Column
Chabot College
Acknowledgements
chemical bond
2.2: Chemical Bonds
chemical bonds
2: A Brief Overview of Chemistry
2.1: Elements and Atoms - The Building Blocks of Matter
2.4: Review Questions
chemical digestion
16: The Digestive System
16.1: Overview of the Digestive System
chemical reactions
2.1: Elements and Atoms - The Building Blocks of Matter
chemical synapse
9.3: Synapses
chemicals
16.3: The Stomach and the Upper Digestive Organs
chemistry
2.3: Inorganic Compounds Essential to Human Functioning
2.4: Review Questions
childbirth
1.4: Homeostasis
chondrocytes
4.3: Connective Tissue
chordae tendineae
14.1: Heart Anatomy
choroid plexus
9.2: Anatomy of Nervous Tissue
chromaffin
12.5: Adrenal Glands
chromosomes
3.3: The Nucleus and DNA
circular fold
16.4: Small and Large Intestines
circulation
14.5: Blood Flow, Blood Pressure, and Resistance
circumflex artery
14.1: Heart Anatomy
classification
6.2: Bone Classification
7: Joints
clavicle
19.4.4: The Pectoral Girdle
clavicular notch
19.4.3: The Thoracic Cage
closed reduction
6.5: Fractures - Bone Repair
coccyx
19.4: Divisions of the Skeletal System
cochlea
10.3: Special Senses - Ears
collaborative effort
InfoPage
collagen fiber
4.3: Connective Tissue
colloid
12.4: Thyroid Gland and Parathyroid Glands
colon
16.4: Small and Large Intestines
communication
12.1: An Overview of the Endocrine System
compact bone
6.3: Bone Structure
6.4: Bone Remodeling and Calcium Homeostasis
6.6: Review Questions
compatibility
13.4: Blood Typing
compounds
2.1: Elements and Atoms - The Building Blocks of Matter
2.2: Chemical Bonds
2.3: Inorganic Compounds Essential to Human Functioning
compressor urethrae
19.5.2: Axial Muscles of the Abdominal Wall and Thorax
conclusion
1.2: Overview of the Scientific Method
conducting zone
15.5: Review Questions
condylar process of the mandible
19.4.1: The Skull
congestive heart failure
19.8: Mean Arterial Pressure and Pulse Pressure
congestive_heart_failure
14.3: Cardiac Cycle
connective
4.1: Types of Tissues
6: Bone Tissue and the Skeletal System
connective tissue
4: Tissue Organization
4.4: Review Questions
7: Joints
connective tissue proper
4.3: Connective Tissue
continuous capillary
14.4: Structure and Function of Blood Vessels
continuous conduction
9.3: Synapses
contractility
8.1: Muscle Tissues
contraction
8.4: Types of Muscle Fibers and Exercise
8.5: Review Questions
control
1.2: Overview of the Scientific Method
coracobrachialis
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
coracoclavicular ligament
19.4.4: The Pectoral Girdle
coracoid process
19.4.4: The Pectoral Girdle
cornea
10.2: Special Senses - Eyes
coronary arteries
14.1: Heart Anatomy
coronary sinus
14.1: Heart Anatomy
coronary sulcus
14.1: Heart Anatomy
coronary veins
14.1: Heart Anatomy
coronoid fossa
19.4.5: Bones of the Upper Limb
coronoid process of the ulna
19.4.5: Bones of the Upper Limb
corrugator supercilii
19.5.1: Axial Muscles of the Head, Neck, and Back
cortisol
12.2: Hormones
12.5: Adrenal Glands
costal cartilage
19.4.3: The Thoracic Cage
costal facet
19.4.2: The Vertebral Column
costal groove
19.4.3: The Thoracic Cage
costoclavicular ligament
19.4.4: The Pectoral Girdle
countercurrent multiplication
17.5: Tubular Reabsorption and Secretion
covalent bonds
2.2: Chemical Bonds
cranial cavity
19.4.1: The Skull
cranial nerve
9.1: Organization and Functions of the Nervous System
10.4: Review Questions
cranial nerves
9.6: The Peripheral Nervous System
10.2: Special Senses - Eyes
cranium
19.4.1: The Skull
Creative Commons
Acknowledgements
cribriform plate
19.4.1: The Skull
crista galli
19.4.1: The Skull
cuboid
19.4.7: Bones of the Lower Limb
curriculum development
InfoPage

cycle
18.2: Anatomy and Physiology of the Female Reproductive System
cytoplasm
3: Cell Structure
cytoskeleton
3.2: The Cytoplasm and Cellular Organelles

D

deductive reasoning
1.2: Overview of the Scientific Method
deep anterior compartment
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
deep posterior compartment of the forearm
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
deep transverse perineal
19.5.2: Axial Muscles of the Abdominal Wall and Thorax
defensins
13.3: Leukocytes and Platelets
deglutition
19.5.1: Axial Muscles of the Head, Neck, and Back
delta cell
12.6: Endocrine Pancreas
deltoid
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
deltoid tuberosity
19.4.5: Bones of the Upper Limb
dendrite
9.1: Organization and Functions of the Nervous System
9.2: Anatomy of Nervous Tissue
dens
19.4.2: The Vertebral Column
dense connective tissue
4.3: Connective Tissue
depolarize
8.2: Skeletal Muscle Organ Structure
dermis
5.2: Layers of the Skin
descending colon
16.4: Small and Large Intestines
descriptive science
1.2: Overview of the Scientific Method
diabetes
12.7: Review Questions
diabetes mellitus
12.6: Endocrine Pancreas
diabetes_insipidus
17.7: Review Questions
diabetes_mellitus
17.7: Review Questions
diagnostics
13.1: An Overview of Blood
diapedesis
13.3: Leukocytes and Platelets
diaphragm
15.3: The Process of Breathing
19.5.2: Axial Muscles of the Abdominal Wall and Thorax
diarthrosis
7.2: Classification of Joints
diastole
19.7: Coronary Circulation
diastolic pressure
14.5: Blood Flow, Blood Pressure, and Resistance
19.8: Mean Arterial Pressure and Pulse Pressure
diencephalon
9.5: The Central Nervous System
differentiation
4.4: Review Questions
diffusion
3.1: The Cell Membrane
3.4: Cell Transport and Osmosis
3.5: Review Questions
digastric
19.5.1: Axial Muscles of the Head, Neck, and Back
digestion
16: The Digestive System
16.2: Digestive System Processes and Regulation
16.3: The Stomach and the Upper Digestive Organs
16.5: Accessory Organs in Digestion- The Liver, Pancreas, and Gallbladder
16.6: Review Questions
digestive
16.3: The Stomach and the Upper Digestive Organs
16.6: Review Questions
digestive enzymes
16.2: Digestive System Processes and Regulation
digestive glands
16.1: Overview of the Digestive System
digestive hormones
16.2: Digestive System Processes and Regulation
digestive organs
16.2: Digestive System Processes and Regulation
digestive processes
16.1: Overview of the Digestive System
digestive system
11.2: The Sympathetic Division of the ANS
16: The Digestive System
16.1: Overview of the Digestive System
16.2: Digestive System Processes and Regulation
16.5: Accessory Organs in Digestion- The Liver, Pancreas, and Gallbladder
dilated pupils
11.4: Review Questions
directional terms
1.5: Anatomical Terminology
discussion
1.2: Overview of the Scientific Method
disease
15.2: The Lungs
diseases
5.1: Introduction
19.2: Functions of the Integumentary System
dissection
1.1: Overview of Anatomy and Physiology
distal radioulnar joint
19.4.5: Bones of the Upper Limb
distal tibiofibular joint
19.4.7: Bones of the Lower Limb
DNA
3: Cell Structure
3.3: The Nucleus and DNA
3.5: Review Questions
dorsal group
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
duodenal gland
16.4: Small and Large Intestines
duodenum
16.4: Small and Large Intestines

E

ear anatomy
10.3: Special Senses - Ears
ear ossicles
19.4: Divisions of the Skeletal System
ECG
14.3: Cardiac Cycle
14.6: Review Questions
ecosystems
1: An Introduction to Anatomy and Physiology
effector
9.1: Organization and Functions of the Nervous System
efferent
9.1: Organization and Functions of the Nervous System
elastic artery
14.4: Structure and Function of Blood Vessels
elastic cartilage
4.3: Connective Tissue
elastic fiber
4.3: Connective Tissue
elasticity
8.1: Muscle Tissues
elbow joint
19.4.5: Bones of the Upper Limb
electrical
14: The Cardiovascular System - Heart and Blood Vessels
electrical charge
2.2: Chemical Bonds
electrical synapse
9.3: Synapses
electrocardiogram (ECG)
14.2: Cardiac Muscle and Electrical Activity
electrochemicalgradient
3.5: Review Questions
electrolyte balance
17.3: Microscopic Anatomy of the Kidney
electrolytes
17.5: Tubular Reabsorption and Secretion
elements
2: A Brief Overview of Chemistry
2.1: Elements and Atoms - The Building Blocks of Matter
2.4: Review Questions
embryonic
4.4: Review Questions
embryonic development
19: Optional Reading
embryonic origin
4: Tissue Organization
emigration
13.3: Leukocytes and Platelets
end diastolic volume (EDV)
19.7: Coronary Circulation
end systolic volume (ESV)
19.7: Coronary Circulation
endocardium
14.1: Heart Anatomy
endochondral ossification
6.5: Fractures - Bone Repair
19.3: Bone Formation and Development
endocrine
12.7: Review Questions
endocrine gland
4.2: Epithelial Tissue

endocrine glands
12.2: Hormones
endocrine regulation
17: The Urinary System
endocrine system
1.4: Homeostasis
12: The Endocrine System
12.1: An Overview of the Endocrine System
12.3: The Pituitary Gland and Hypothalamus
endomysium
8.2: Skeletal Muscle Organ Structure
endoplasmic reticulum
3.2: The Cytoplasm and Cellular Organelles
endothelium
4.2: Epithelial Tissue
14.1: Heart Anatomy
energy
2.4: Review Questions
8.4: Types of Muscle Fibers and Exercise
enteric nervous system
16.1: Overview of the Digestive System
enteric nervous system (ENS)
9.1: Organization and Functions of the Nervous System
enzymes
16.5: Accessory Organs in Digestion- The Liver, Pancreas, and Gallbladder
16.6: Review Questions
eosinophils
13.3: Leukocytes and Platelets
ependymal cell
9.2: Anatomy of Nervous Tissue
epicardial coronary arteries
14.1: Heart Anatomy
epicardium
14.1: Heart Anatomy
epicranial aponeurosis
19.5.1: Axial Muscles of the Head, Neck, and Back
epidermis
5.2: Layers of the Skin
epimysium
8.2: Skeletal Muscle Organ Structure
epinephrine
12.5: Adrenal Glands
epiphyseal line
19.3: Bone Formation and Development
epiploic appendage
16.4: Small and Large Intestines
epithelial
4.1: Types of Tissues
4.4: Review Questions
epithelial tissue
4: Tissue Organization
EPO
13.2: Erythrocytes
erectile dysfunction
18.1: Anatomy and Physiology of the Male Reproductive System
erector spinae group
19.5.1: Axial Muscles of the Head, Neck, and Back
erythrocytes
13: The Cardiovascular System - Blood
13.1: An Overview of Blood
13.2: Erythrocytes
13.5: Review Questions
erythropoietin
13.5: Review Questions
ethmoid air cell
19.4.1: The Skull
eukaryotic cells
3: Cell Structure
3.2: The Cytoplasm and Cellular Organelles
excitability
8.1: Muscle Tissues
exercise
1.6: Review Questions
8: Muscle Tissue
8.5: Review Questions
19.8: Mean Arterial Pressure and Pulse Pressure
exhalation
15.5: Review Questions
exocrine gland
4.2: Epithelial Tissue
extensibility
8.1: Muscle Tissues
extension
7.3: Types of Body Movements
extensor carpi radialis brevis
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
extensor carpi ulnaris
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
extensor digiti minimi
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
extensor digitorum
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
extensor digitorum brevis
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
extensor digitorum longus
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
extensor hallucis longus
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
extensor indicis
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
extensor pollicis brevis
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
extensor pollicis longus
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
extensor radialis longus
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
extensor retinaculum
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
external acoustic meatus
19.4.1: The Skull
external anal sphincter
16.4: Small and Large Intestines
external elastic membrane
14.4: Structure and Function of Blood Vessels
external intercostal
19.5.2: Axial Muscles of the Abdominal Wall and Thorax
external oblique
19.5.2: Axial Muscles of the Abdominal Wall and Thorax
external occipital protuberance
19.4.1: The Skull
external respiration
15.4: Gas Exchange
extraocular muscles
10.2: Special Senses - Eyes
extrinsic eye muscles
19.5.1: Axial Muscles of the Head, Neck, and Back
extrinsic muscles of the hand
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
eye anatomy
10.2: Special Senses - Eyes

F

facet
19.4.2: The Vertebral Column
facial bones
19.4.1: The Skull
false ribs
19.4.3: The Thoracic Cage
falsifiable
1.2: Overview of the Scientific Method
fascicle
8.2: Skeletal Muscle Organ Structure
fast
8.4: Types of Muscle Fibers and Exercise
fatigue
8.5: Review Questions
feces
16.4: Small and Large Intestines
feedback loops
12.2: Hormones
female reproductive system
18: The Reproductive System
femoral triangle
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
femur
19.4.7: Bones of the Lower Limb
fenestrated capillary
14.4: Structure and Function of Blood Vessels
fertilization
18.2: Anatomy and Physiology of the Female Reproductive System
fibers
8.4: Types of Muscle Fibers and Exercise
fibroblast
4.3: Connective Tissue
fibrocartilage
4.3: Connective Tissue
fibrocyte
4.3: Connective Tissue
fibrous joint
7.2: Classification of Joints
fibula
19.4.7: Bones of the Lower Limb
fibular notch
19.4.7: Bones of the Lower Limb
fibularis brevis
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
fibularis longus
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
fibularis tertius
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
fight or flight response
11.1: Introduction to the Autonomic Nervous System (ANS)
11.2: The Sympathetic Division of the ANS

filtration
17.3: Microscopic Anatomy of the Kidney
17.4: Urine Formation and Glomerular Filtration Rate (GFR)
filtration_membrane
17.7: Review Questions
flat bones
6.2: Bone Classification
flatus
16.4: Small and Large Intestines
flexion
7.3: Types of Body Movements
flexor carpi radialis
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
flexor carpi ulnaris
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
flexor digiti minimi brevis
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
flexor digitorum longus
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
flexor digitorum profundus
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
flexor digitorum superficialis
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
flexor hallucis longus
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
flexor pollicis brevis
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
flexor pollicis longus
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
flexor retinaculum
19.4.5: Bones of the Upper Limb
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
floating ribs
19.4.3: The Thoracic Cage
fluid connective tissue
4.3: Connective Tissue
foot
19.4.7: Bones of the Lower Limb
foramen magnum
19.4.1: The Skull
foramen ovale
14.1: Heart Anatomy
foramen ovale of the middle cranial fossa
19.4.1: The Skull
foramen rotundum
19.4.1: The Skull
foramen spinosum
19.4.1: The Skull
forearm
19.4.5: Bones of the Upper Limb
fossa
19.4.4: The Pectoral Girdle
fossa ovalis
14.1: Heart Anatomy
fovea capitis
19.4.7: Bones of the Lower Limb
fracture
6.6: Review Questions
fracture hematoma
6.5: Fractures - Bone Repair
fractures
6.5: Fractures - Bone Repair
free to use
Acknowledgements
frontal bone
19.4.1: The Skull
frontal sinus
19.4.1: The Skull
frontalis
19.5.1: Axial Muscles of the Head, Neck, and Back
function
17.6: Endocrine Regulation of Kidney Function
functional classification
7: Joints
functions
6: Bone Tissue and the Skeletal System
functions of tissues
4: Tissue Organization

G

gallbladder
16.5: Accessory Organs in Digestion- The Liver, Pancreas, and Gallbladder
gamete
18.1: Anatomy and Physiology of the Male Reproductive System
gametes
18: The Reproductive System
ganglia
11.3: The Parasympathetic Division of the ANS
ganglion
9.1: Organization and Functions of the Nervous System
gap junction
4.2: Epithelial Tissue
gas
15.3: The Process of Breathing
gas exchange
13.2: Erythrocytes
15: The Respiratory System
15.2: The Lungs
15.4: Gas Exchange
15.5: Review Questions
gasexchange
15.1: Organs and Structures of the Respiratory System
gastric
16.3: The Stomach and the Upper Digestive Organs
gastrocnemius
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
gastrocolic reflex
16.4: Small and Large Intestines
gastroileal reflex
16.4: Small and Large Intestines
gastrointestinal
16.6: Review Questions
gastrointestinal system
16.2: Digestive System Processes and Regulation
gastrointestinal tract
16.1: Overview of the Digestive System
gender identity
1.3: Structural Organization of the Human Body
general adaptation syndrome (GAS)
12.5: Adrenal Glands
general sense
9.1: Organization and Functions of the Nervous System
genetic instructions
3: Cell Structure
3.3: The Nucleus and DNA
genetic material
3.3: The Nucleus and DNA
genioglossus
19.5.1: Axial Muscles of the Head, Neck, and Back
geniohyoid
19.5.1: Axial Muscles of the Head, Neck, and Back
germ layers
4.1: Types of Tissues
glabella
19.4.1: The Skull
glenohumeral joint
19.4.4: The Pectoral Girdle
glenoid cavity
19.4.4: The Pectoral Girdle
glial cell
9.1: Organization and Functions of the Nervous System
glial cells
9: Overview of the Nervous System
glialcells
9.7: Review Questions
glomerular filtration rate
17: The Urinary System
17.4: Urine Formation and Glomerular Filtration Rate (GFR)
glomerulus
17.3: Microscopic Anatomy of the Kidney
glucagon
12.2: Hormones
12.6: Endocrine Pancreas
glucocorticoids
12.5: Adrenal Glands
glucose
17.5: Tubular Reabsorption and Secretion
gluteal group
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
gluteal tuberosity
19.4.7: Bones of the Lower Limb
gluteus maximus
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
gluteus medius
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
gluteus minimus
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
glycolytic
8.4: Types of Muscle Fibers and Exercise
goblet cell
4.2: Epithelial Tissue
goiter
12.4: Thyroid Gland and Parathyroid Glands
Golgi apparatus
3.2: The Cytoplasm and Cellular Organelles
gracilis
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
graded potential
9.4: The Function of Nervous Tissue
granular leukocytes
13.3: Leukocytes and Platelets

gray matter
9.1: Organization and Functions of the Nervous System
9.5: The Central Nervous System
great cardiac vein
14.1: Heart Anatomy
greater trochanter
19.4.7: Bones of the Lower Limb
greater tubercle
19.4.5: Bones of the Upper Limb
greater wings of sphenoid bone
19.4.1: The Skull
gross anatomy
1.1: Overview of Anatomy and Physiology
ground substance
4.3: Connective Tissue
growth hormone
12.2: Hormones
12.3: The Pituitary Gland and Hypothalamus
gustation
10.1: General and Special Senses

H

hair
19.1: Accessory Structures of the Skin
hair cells
10.3: Special Senses - Ears
hair growth
19.1: Accessory Structures of the Skin
hallux
19.4.7: Bones of the Lower Limb
hamate
19.4.5: Bones of the Upper Limb
hamstring group
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
hand
19.4.5: Bones of the Upper Limb
hard palate
19.4.1: The Skull
haustral contraction
16.4: Small and Large Intestines
haustrum
16.4: Small and Large Intestines
head of the femur
19.4.7: Bones of the Lower Limb
head of the fibula
19.4.7: Bones of the Lower Limb
head of the humerus
19.4.5: Bones of the Upper Limb
head of the metatarsal bone
19.4.7: Bones of the Lower Limb
head of the radius
19.4.5: Bones of the Upper Limb
head of the rib
19.4.3: The Thoracic Cage
Head of the ulna
19.4.5: Bones of the Upper Limb
healing process
6.5: Fractures - Bone Repair
health
12.1: An Overview of the Endocrine System
12.7: Review Questions
15.2: The Lungs
19.2: Functions of the Integumentary System
hearing
10.1: General and Special Senses
heart
14: The Cardiovascular System - Heart and Blood Vessels
14.6: Review Questions
heart block
14.2: Cardiac Muscle and Electrical Activity
heart health
19.8: Mean Arterial Pressure and Pulse Pressure
heart muscle
19: Optional Reading
heart rate
11.2: The Sympathetic Division of the ANS
11.4: Review Questions
14.5: Blood Flow, Blood Pressure, and Resistance
heart sounds
19.7: Coronary Circulation
heart_sounds
14.3: Cardiac Cycle
heart_valves
14.3: Cardiac Cycle
hematopoiesis
6.1: Functions of the Skeletal System
hemoglobin
13.2: Erythrocytes
13.5: Review Questions
15.4: Gas Exchange
15.5: Review Questions
hemolysis
13.4: Blood Typing
hemostasis
13: The Cardiovascular System - Blood
hepatopancreatic ampulla
16.4: Small and Large Intestines
hepatopancreatic sphincter
16.4: Small and Large Intestines
hip joint
19.4.7: Bones of the Lower Limb
histology
1.1: Overview of Anatomy and Physiology
4.1: Types of Tissues
6.3: Bone Structure
holocrine secretion
4.2: Epithelial Tissue
homeostasis
1: An Introduction to Anatomy and Physiology
1.1: Overview of Anatomy and Physiology
1.4: Homeostasis
2.3: Inorganic Compounds Essential to Human Functioning
5.1: Introduction
9.6: The Peripheral Nervous System
11.1: Introduction to the Autonomic Nervous System (ANS)
11.4: Review Questions
12: The Endocrine System
12.1: An Overview of the Endocrine System
13.1: An Overview of Blood
hook of the hamate bone
19.4.5: Bones of the Upper Limb
horizontal plate
19.4.1: The Skull
hormone receptors
12.2: Hormones
hormones
12: The Endocrine System
12.1: An Overview of the Endocrine System
12.2: Hormones
12.3: The Pituitary Gland and Hypothalamus
12.7: Review Questions
16.3: The Stomach and the Upper Digestive Organs
16.5: Accessory Organs in Digestion- The Liver, Pancreas, and Gallbladder
17.6: Endocrine Regulation of Kidney Function
18.2: Anatomy and Physiology of the Female Reproductive System
human anatomy
1.1: Overview of Anatomy and Physiology
11: The Autonomic Nervous System
human body
1: An Introduction to Anatomy and Physiology
1.3: Structural Organization of the Human Body
1.5: Anatomical Terminology
human functioning
2: A Brief Overview of Chemistry
humerus
19.4.5: Bones of the Upper Limb
hyaline cartilage
4.3: Connective Tissue
hydrogen bonds
2.2: Chemical Bonds
hyoglossus
19.5.1: Axial Muscles of the Head, Neck, and Back
hyoid bone
19.4: Divisions of the Skeletal System
hyperglycemia
12.6: Endocrine Pancreas
hypertrophic cardiomyopathy
14.1: Heart Anatomy
hypodermis
5.2: Layers of the Skin
hypoglossal canal
19.4.1: The Skull
hypophyseal (pituitary) fossa
19.4.1: The Skull
hypothalamus
12: The Endocrine System
12.3: The Pituitary Gland and Hypothalamus
hypothesis
1.2: Overview of the Scientific Method
hypothyroidism
12.4: Thyroid Gland and Parathyroid Glands

I

ileocecal sphincter
16.4: Small and Large Intestines
Ileum
16.4: Small and Large Intestines
iliacus
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
iliococcygeus
19.5.2: Axial Muscles of the Abdominal Wall and Thorax
iliocostalis cervicis
19.5.1: Axial Muscles of the Head, Neck, and Back
iliocostalis group
19.5.1: Axial Muscles of the Head, Neck, and Back
iliocostalis lumborum
19.5.1: Axial Muscles of the Head, Neck, and Back
iliocostalis thoracis
19.5.1: Axial Muscles of the Head, Neck, and Back

iliopsoas group
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
iliotibial tract
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
immune response
13.4: Blood Typing
inductive reasoning
1.2: Overview of the Scientific Method
inferior angle of the scapula
19.4.4: The Pectoral Girdle
inferior articular process
19.4.2: The Vertebral Column
inferior extensor retinaculum
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
inferior gemellus
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
inferior nasal concha
19.4.1: The Skull
inferior vena cava
14.1: Heart Anatomy
inflammation
4.4: Review Questions
infraglenoid fossa
19.4.4: The Pectoral Girdle
infraglenoid tubercle
19.4.4: The Pectoral Girdle
infrahyoid muscles
19.5.1: Axial Muscles of the Head, Neck, and Back
infraorbital foramen
19.4.1: The Skull
infraspinatus
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
infraspinous fossa
19.4.4: The Pectoral Girdle
infratemporal fossa
19.4.1: The Skull
ingestion
16: The Digestive System
inhalation
15.5: Review Questions
innermost intercostal
19.5.2: Axial Muscles of the Abdominal Wall and Thorax
inorganic compounds
2: A Brief Overview of Chemistry
insulin
1.4: Homeostasis
12.2: Hormones
12.6: Endocrine Pancreas
12.7: Review Questions
integral proteins
3.1: The Cell Membrane
3.4: Cell Transport and Osmosis
integration
9.1: Organization and Functions of the Nervous System
integumentary system
5.1: Introduction
5.2: Layers of the Skin
19: Optional Reading
19.1: Accessory Structures of the Skin
19.2: Functions of the Integumentary System
interatrial band
14.2: Cardiac Muscle and Electrical Activity
interatrial septum
14.1: Heart Anatomy
intercalated disc
14.2: Cardiac Muscle and Electrical Activity
intercondylar eminence
19.4.7: Bones of the Lower Limb
intercondylar fossa
19.4.7: Bones of the Lower Limb
intercostal muscles
19.5.2: Axial Muscles of the Abdominal Wall and Thorax
intermediate cuneiform
19.4.7: Bones of the Lower Limb
internal anal sphincter
16.4: Small and Large Intestines
internal elastic membrane
14.4: Structure and Function of Blood Vessels
internal intercostal
19.5.2: Axial Muscles of the Abdominal Wall and Thorax
internal oblique
19.5.2: Axial Muscles of the Abdominal Wall and Thorax
internal organs
1.5: Anatomical Terminology
internal respiration
15.4: Gas Exchange
interneuron
9.2: Anatomy of Nervous Tissue
internodal pathways
14.2: Cardiac Muscle and Electrical Activity
interosseous border of the fibula
19.4.7: Bones of the Lower Limb
interosseous border of the radius
19.4.5: Bones of the Upper Limb
interosseous border of the tibia
19.4.7: Bones of the Lower Limb
interosseous border of the ulna
19.4.5: Bones of the Upper Limb
interosseous membrane of the forearm
19.4.5: Bones of the Upper Limb
interosseous membrane of the leg
19.4.7: Bones of the Lower Limb
interphalangeal joint
19.4.5: Bones of the Upper Limb
intertrochanteric crest
19.4.7: Bones of the Lower Limb
intertrochanteric line
19.4.7: Bones of the Lower Limb
intertubercular groove (sulcus)
19.4.5: Bones of the Upper Limb
interventricular septum
14.1: Heart Anatomy
intervertebral disc
19.4.2: The Vertebral Column
intervertebral foramen
19.4.2: The Vertebral Column
intestinal gland
16.4: Small and Large Intestines
intestinal juice
16.4: Small and Large Intestines
intestines
16.6: Review Questions
intramembranous ossification
19.3: Bone Formation and Development
intrinsic muscles of the hand
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
introduction
1.2: Overview of the Scientific Method
ionchannels
3.5: Review Questions
ionic bonds
2.2: Chemical Bonds
ionpumps
3.5: Review Questions
ions
2.2: Chemical Bonds
irregular bones
6.2: Bone Classification
ischiococcygeus
19.5.2: Axial Muscles of the Abdominal Wall and Thorax
Islets of Langerhans
12.6: Endocrine Pancreas
isotopes
2.1: Elements and Atoms - The Building Blocks of Matter
isovolumic contraction
19.7: Coronary Circulation
isovolumic ventricular relaxation phase
19.7: Coronary Circulation

J

jejunum
16.4: Small and Large Intestines
joint
7.2: Classification of Joints
joint cavity
7.2: Classification of Joints
jointmovements
7.3: Types of Body Movements
joints
7: Joints
jugular (suprasternal) notch
19.4.3: The Thoracic Cage
jugular foramen
19.4.1: The Skull

K

keratin
19.1: Accessory Structures of the Skin
kidney
17.4: Urine Formation and Glomerular Filtration Rate (GFR)
17.6: Endocrine Regulation of Kidney Function
kidney failure
17.4: Urine Formation and Glomerular Filtration Rate (GFR)
kidney function
17.3: Microscopic Anatomy of the Kidney
kidney_functional_unit
17.7: Review Questions
kidneys
17: The Urinary System
knee joint
19.4.7: Bones of the Lower Limb
kyphosis
19.4.2: The Vertebral Column

L

lacrimal bone
19.4.1: The Skull
lacrimal fossa
19.4.1: The Skull
lacteal
16.4: Small and Large Intestines
lacunae
4.3: Connective Tissue
lambdoid suture
19.4.1: The Skull
lamina
19.4.2: The Vertebral Column
large intestine
16: The Digestive System
16.4: Small and Large Intestines
lateral border of the scapula
19.4.4: The Pectoral Girdle
lateral compartment of the leg
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
lateral condyle of the femur
19.4.7: Bones of the Lower Limb
lateral condyle of the tibia
19.4.7: Bones of the Lower Limb
lateral cuneiform
19.4.7: Bones of the Lower Limb
lateral epicondyle of the femur
19.4.7: Bones of the Lower Limb
lateral epicondyle of the humerus
19.4.5: Bones of the Upper Limb
lateral malleolus
19.4.7: Bones of the Lower Limb
lateral pterygoid
19.5.1: Axial Muscles of the Head, Neck, and Back
lateral pterygoid plate
19.4.1: The Skull
lateral sacral crest
19.4.2: The Vertebral Column
lateral supracondylar ridge
19.4.5: Bones of the Upper Limb
latissimus dorsi
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
learning
2.3: Inorganic Compounds Essential to Human Functioning
15.2: The Lungs
15.3: The Process of Breathing
16.3: The Stomach and the Upper Digestive Organs
17.6: Endocrine Regulation of Kidney Function
18.2: Anatomy and Physiology of the Female Reproductive System
learning objectives
11.1: Introduction to the Autonomic Nervous System (ANS)
11.2: The Sympathetic Division of the ANS
left atrioventricular valve
14.1: Heart Anatomy
left colic flexure
16.4: Small and Large Intestines
leg
19.4.7: Bones of the Lower Limb
lens
10.2: Special Senses - Eyes
lesser trochanter
19.4.7: Bones of the Lower Limb
lesser tubercle
19.4.5: Bones of the Upper Limb
lesser wings of the sphenoid bone
19.4.1: The Skull
leukemia
13.3: Leukocytes and Platelets
leukocyte
13.3: Leukocytes and Platelets
leukocytes
13: The Cardiovascular System - Blood
13.1: An Overview of Blood
13.5: Review Questions
leukocytosis
13.3: Leukocytes and Platelets
leukopenia
13.3: Leukocytes and Platelets
levator ani
19.5.2: Axial Muscles of the Abdominal Wall and Thorax
LibreTexts
InfoPage
life science
1.2: Overview of the Scientific Method
ligament of the head of the femur
19.4.7: Bones of the Lower Limb
ligamentum flavum
19.4.2: The Vertebral Column
linea alba
19.5.2: Axial Muscles of the Abdominal Wall and Thorax
linea aspera
19.4.7: Bones of the Lower Limb
lingula
19.4.1: The Skull
liver
16.5: Accessory Organs in Digestion- The Liver, Pancreas, and Gallbladder
living organisms
1: An Introduction to Anatomy and Physiology
long bones
6.2: Bone Classification
6.6: Review Questions
longissimus capitis
19.5.1: Axial Muscles of the Head, Neck, and Back
longissimus group
19.5.1: Axial Muscles of the Head, Neck, and Back
longissimus thoracis
19.5.1: Axial Muscles of the Head, Neck, and Back
loop of Henle
17.5: Tubular Reabsorption and Secretion
loose connective tissue
4.3: Connective Tissue
lordosis
19.4.2: The Vertebral Column
lumbar curve
19.4.2: The Vertebral Column
lumbar vertebrae
19.4.2: The Vertebral Column
Lumen
14.4: Structure and Function of Blood Vessels
lunate
19.4.5: Bones of the Upper Limb
lungs
15: The Respiratory System
luteinizing hormone
12.3: The Pituitary Gland and Hypothalamus
lymphocytes
13.3: Leukocytes and Platelets
lymphoma
13.3: Leukocytes and Platelets
Lysozyme
13.3: Leukocytes and Platelets

M

main pancreatic duct
16.4: Small and Large Intestines
major duodenal papilla
16.4: Small and Large Intestines
makeup
5.1: Introduction
male gonads
18.1: Anatomy and Physiology of the Male Reproductive System
male reproductive system
18: The Reproductive System
18.1: Anatomy and Physiology of the Male Reproductive System
mandible
19.4.1: The Skull
mandibular foramen
19.4.1: The Skull
mandibular fossa
19.4.1: The Skull
mandibular notch
19.4.1: The Skull
manubrium
19.4.3: The Thoracic Cage
marginal arteries
14.1: Heart Anatomy
mass
2.1: Elements and Atoms - The Building Blocks of Matter
mass movement
16.4: Small and Large Intestines
masseter
19.5.1: Axial Muscles of the Head, Neck, and Back
mastication
19.5.1: Axial Muscles of the Head, Neck, and Back
mastoid process
19.4.1: The Skull
materials and methods
1.2: Overview of the Scientific Method
matrix
4.3: Connective Tissue
matter
2.1: Elements and Atoms - The Building Blocks of Matter
maxillary bone
19.4.1: The Skull
maxillary sinus
19.4.1: The Skull
mean arterial pressure
14.5: Blood Flow, Blood Pressure, and Resistance
19.8: Mean Arterial Pressure and Pulse Pressure
mechanical digestion
16: The Digestive System
16.1: Overview of the Digestive System
mechanoreception
10.3: Special Senses - Ears
medial border of the scapula
19.4.4: The Pectoral Girdle
medial compartment of the thigh
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
medial condyle of the femur
19.4.7: Bones of the Lower Limb
medial condyle of the tibia
19.4.7: Bones of the Lower Limb

medial cuneiform
19.4.7: Bones of the Lower Limb
medial epicondyle of the femur
19.4.7: Bones of the Lower Limb
medial epicondyle of the humerus
19.4.5: Bones of the Upper Limb
medial malleolus
19.4.7: Bones of the Lower Limb
medial pterygoid
19.5.1: Axial Muscles of the Head, Neck, and Back
medial pterygoid plate
19.4.1: The Skull
medical lab technology
13.1: An Overview of Blood
medical terminology
1.5: Anatomical Terminology
medical treatment
12.1: An Overview of the Endocrine System
megakaryocyte
13.3: Leukocytes and Platelets
melanin
19.1: Accessory Structures of the Skin
melanocytes
5.2: Layers of the Skin
membrane structure
3.1: The Cell Membrane
3.4: Cell Transport and Osmosis
membranes
3.5: Review Questions
memory
9.5: The Central Nervous System
memory cell
13.3: Leukocytes and Platelets
menstrual
18.2: Anatomy and Physiology of the Female Reproductive System
mental foramen
19.4.1: The Skull
mental protuberance
19.4.1: The Skull
merocrine secretion
4.2: Epithelial Tissue
mesenchymal cell
4.3: Connective Tissue
mesenchyme
4.3: Connective Tissue
mesoappendix
16.4: Small and Large Intestines
mesothelium
4.2: Epithelial Tissue
14.1: Heart Anatomy
metabolism
1.6: Review Questions
8.4: Types of Muscle Fibers and Exercise
8.5: Review Questions
12.7: Review Questions
16.5: Accessory Organs in Digestion- The Liver, Pancreas, and Gallbladder
metacarpal bone
19.4.5: Bones of the Upper Limb
metacarpophalangeal joint
19.4.5: Bones of the Upper Limb
metarteriole
14.4: Structure and Function of Blood Vessels
metatarsal bone
19.4.7: Bones of the Lower Limb
metatarsophalangeal joint
19.4.7: Bones of the Lower Limb
microcirculation
14.4: Structure and Function of Blood Vessels
microglia
9.2: Anatomy of Nervous Tissue
Microscopic Anatomy
1.1: Overview of Anatomy and Physiology
microvillus
16.4: Small and Large Intestines
midcarpal joint
19.4.5: Bones of the Upper Limb
middle cardiac vein
14.1: Heart Anatomy
middle cranial fossa
19.4.1: The Skull
middle nasal concha
19.4.1: The Skull
middle scalene
19.5.1: Axial Muscles of the Head, Neck, and Back
migrating motility complex
16.4: Small and Large Intestines
mineralocorticoids
12.5: Adrenal Glands
mitochondria
3.2: The Cytoplasm and Cellular Organelles
3.5: Review Questions
mitral valve
14.1: Heart Anatomy
mobility
7.3: Types of Body Movements
modeling
19.3: Bone Formation and Development
moderator band
14.1: Heart Anatomy
molecular biology
3.3: The Nucleus and DNA
molecules
2.2: Chemical Bonds
2.4: Review Questions
monocytes
13.3: Leukocytes and Platelets
morphological features
4: Tissue Organization
motilin
16.4: Small and Large Intestines
motor neuron
9.2: Anatomy of Nervous Tissue
motor neurons
9.6: The Peripheral Nervous System
10.4: Review Questions
motor response
9.4: The Function of Nervous Tissue
movement
7: Joints
19: Optional Reading
mucous connective tissue
4.3: Connective Tissue
mucous gland
4.2: Epithelial Tissue
multiaxial joint
7.2: Classification of Joints
multicellular organisms
4: Tissue Organization
multifidus
19.5.1: Axial Muscles of the Head, Neck, and Back
multipolar
9.2: Anatomy of Nervous Tissue
murmur
19.7: Coronary Circulation
muscarinic receptors
11.3: The Parasympathetic Division of the ANS
muscle
4.1: Types of Tissues
4.4: Review Questions
8: Muscle Tissue
8.4: Types of Muscle Fibers and Exercise
8.5: Review Questions
14: The Cardiovascular System - Heart and Blood Vessels
muscle contraction
8: Muscle Tissue
8.3: Muscle Fiber Contraction and Relaxation
muscle relaxation
8: Muscle Tissue
muscle tissue
8: Muscle Tissue
muscular artery
14.4: Structure and Function of Blood Vessels
muscular system
19: Optional Reading
myelin
9.1: Organization and Functions of the Nervous System
9.7: Review Questions
myelin sheath
9.2: Anatomy of Nervous Tissue
myelinated
9.2: Anatomy of Nervous Tissue
mylohyoid
19.5.1: Axial Muscles of the Head, Neck, and Back
mylohyoid line
19.4.1: The Skull
myocardial conducting cells
14.2: Cardiac Muscle and Electrical Activity
myocardial contractile cells
14.2: Cardiac Muscle and Electrical Activity
myocardium
14.1: Heart Anatomy
14.6: Review Questions
myofibril
8.2: Skeletal Muscle Organ Structure
8.3: Muscle Fiber Contraction and Relaxation
myosin
8.2: Skeletal Muscle Organ Structure
8.3: Muscle Fiber Contraction and Relaxation

N

nails
19.1: Accessory Structures of the Skin
nasal cavity
19.4.1: The Skull
nasal conchae
19.4.1: The Skull
nasal septum
19.4.1: The Skull
nasolacrimal canal
19.4.1: The Skull
natriuretic_hormones
17.7: Review Questions
natural killer (NK) cells
13.3: Leukocytes and Platelets
natural science
1.2: Overview of the Scientific Method
navicular
19.4.7: Bones of the Lower Limb

neck of the femur
19.4.7: Bones of the Lower Limb
neck of the radius
19.4.5: Bones of the Upper Limb
neck of the rib
19.4.3: The Thoracic Cage
negative feedback
1.4: Homeostasis
neonatal hypothyroidism
12.4: Thyroid Gland and Parathyroid Glands
nephron
17: The Urinary System
17.3: Microscopic Anatomy of the Kidney
17.4: Urine Formation and Glomerular Filtration Rate (GFR)
17.5: Tubular Reabsorption and Secretion
nerve
9.1: Organization and Functions of the Nervous System
nerve impulse
4.4: Review Questions
nervi vasorum
14.4: Structure and Function of Blood Vessels
nervous
4.1: Types of Tissues
4.4: Review Questions
nervous system
9: Overview of the Nervous System
9.4: The Function of Nervous Tissue
nervoussystem
9.7: Review Questions
neural signals
10.3: Special Senses - Ears
neuromuscular junction (NMJ)
8.2: Skeletal Muscle Organ Structure
neuron
9.1: Organization and Functions of the Nervous System
9.7: Review Questions
neuronal polarity
9.2: Anatomy of Nervous Tissue
neurons
9: Overview of the Nervous System
11.1: Introduction to the Autonomic Nervous System (ANS)
neurophysiology
9.4: The Function of Nervous Tissue
neuroscience
11: The Autonomic Nervous System
neurotransmitter
8.2: Skeletal Muscle Organ Structure
9.3: Synapses
9.7: Review Questions
11.1: Introduction to the Autonomic Nervous System (ANS)
neurotransmitters
9: Overview of the Nervous System
9.4: The Function of Nervous Tissue
11.3: The Parasympathetic Division of the ANS
11.4: Review Questions
12.1: An Overview of the Endocrine System
neutrophil
13.5: Review Questions
neutrophils
13.3: Leukocytes and Platelets
nociceptor
10.4: Review Questions
node of Ranvier
9.2: Anatomy of Nervous Tissue
NonCommercial
Acknowledgements
norepinephrine
12.5: Adrenal Glands
nuchal ligament
19.4.2: The Vertebral Column
nucleic acids
2.4: Review Questions
nucleus
3: Cell Structure
3.3: The Nucleus and DNA
9.1: Organization and Functions of the Nervous System
nucleus pulposus
19.4.2: The Vertebral Column
nutrient absorption
16.1: Overview of the Digestive System
nutrients
1.6: Review Questions
16: The Digestive System
nutrition
16.2: Digestive System Processes and Regulation
16.5: Accessory Organs in Digestion- The Liver, Pancreas, and Gallbladder

O

objectives
2.3: Inorganic Compounds Essential to Human Functioning
15.3: The Process of Breathing
16.3: The Stomach and the Upper Digestive Organs
17.6: Endocrine Regulation of Kidney Function
obturator externus
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
obturator internus
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
occipital bone
19.4.1: The Skull
occipital condyle
19.4.1: The Skull
occipitalis
19.5.1: Axial Muscles of the Head, Neck, and Back
occipitofrontalis
19.5.1: Axial Muscles of the Head, Neck, and Back
OER
InfoPage
Acknowledgements
olecranon fossa
19.4.5: Bones of the Upper Limb
olecranon process
19.4.5: Bones of the Upper Limb
olfaction
10.1: General and Special Senses
oligodendrocyte
9.2: Anatomy of Nervous Tissue
oliguria
17.7: Review Questions
omohyoid
19.5.1: Axial Muscles of the Head, Neck, and Back
ongissimus cervicis
19.5.1: Axial Muscles of the Head, Neck, and Back
oogenesis
18.2: Anatomy and Physiology of the Female Reproductive System
open education
Acknowledgements
open reduction
6.5: Fractures - Bone Repair
opponens digiti minimi
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
opponens pollicis
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
orbicularis oculi
19.5.1: Axial Muscles of the Head, Neck, and Back
orbicularis oris
19.5.1: Axial Muscles of the Head, Neck, and Back
organ function
4.1: Types of Tissues
organ systems
1.3: Structural Organization of the Human Body
1.6: Review Questions
organelles
3: Cell Structure
3.2: The Cytoplasm and Cellular Organelles
organic compounds
2.4: Review Questions
organization levels
1.3: Structural Organization of the Human Body
organs
1.3: Structural Organization of the Human Body
1.6: Review Questions
16.6: Review Questions
orthopedist
6.1: Functions of the Skeletal System
osmosis
3: Cell Structure
osseous tissue
6.1: Functions of the Skeletal System
ossification
6.4: Bone Remodeling and Calcium Homeostasis
19: Optional Reading
19.3: Bone Formation and Development
ossification center
19.3: Bone Formation and Development
osteoblasts
6.3: Bone Structure
6.4: Bone Remodeling and Calcium Homeostasis
osteoclasts
6.3: Bone Structure
osteocytes
6.3: Bone Structure
6.4: Bone Remodeling and Calcium Homeostasis
6.6: Review Questions
osteogenic cells
6.3: Bone Structure
osteoid
19.3: Bone Formation and Development
ovarian
18.2: Anatomy and Physiology of the Female Reproductive System
overview
1: An Introduction to Anatomy and Physiology
oxidative
8.4: Types of Muscle Fibers and Exercise
oxygen
15: The Respiratory System
15.1: Organs and Structures of the Respiratory System
15.3: The Process of Breathing
15.4: Gas Exchange
oxygen transport
13.1: An Overview of Blood
13.2: Erythrocytes

P

P wave
14.2: Cardiac Muscle and Electrical Activity

pacemaker
14.2: Cardiac Muscle and Electrical Activity

pain
10.4: Review Questions

palatine bone
19.4.1: The Skull

palatine process
19.4.1: The Skull

palatoglossus
19.5.1: Axial Muscles of the Head, Neck, and Back

palmar interossei
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs

palmaris longus
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs

pancreas
12: The Endocrine System
12.6: Endocrine Pancreas
16.5: Accessory Organs in Digestion- The Liver, Pancreas, and Gallbladder
16.6: Review Questions

pancreatic islets
12.6: Endocrine Pancreas

papillary muscle
14.1: Heart Anatomy

paranasal sinuses
19.4.1: The Skull

parasympathetic division
11: The Autonomic Nervous System
11.1: Introduction to the Autonomic Nervous System (ANS)
11.3: The Parasympathetic Division of the ANS

parasympathetic nervous system
9.6: The Peripheral Nervous System

parenchyma
4.3: Connective Tissue

parietal bone
19.4.1: The Skull

passive transport
3.1: The Cell Membrane
3.4: Cell Transport and Osmosis

patella
19.4.7: Bones of the Lower Limb

patellar ligament
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs

patellar surface
19.4.7: Bones of the Lower Limb

pathologies
16.2: Digestive System Processes and Regulation

pathophysiology
14.5: Blood Flow, Blood Pressure, and Resistance

patient care
12.1: An Overview of the Endocrine System

pectinate line
16.4: Small and Large Intestines

pectinate muscles
14.1: Heart Anatomy

pectineus
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs

pectoral girdle
19.4.4: The Pectoral Girdle
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs

pectoralis major
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs

pectoralis minor
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs

pedicle
19.4.2: The Vertebral Column

pelvic cavity
18: The Reproductive System

pelvic diaphragm
19.5.2: Axial Muscles of the Abdominal Wall and Thorax

pelvic girdle
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs

perception
10.1: General and Special Senses

perfusion
14.4: Structure and Function of Blood Vessels

pericardial cavity
14.1: Heart Anatomy

pericardial sac
14.1: Heart Anatomy

pericardium
14.1: Heart Anatomy

perichondrium
19.3: Bone Formation and Development

perimysium
8.2: Skeletal Muscle Organ Structure

perineum
19.5.2: Axial Muscles of the Abdominal Wall and Thorax

periodic table
2.1: Elements and Atoms - The Building Blocks of Matter

periosteum
6.3: Bone Structure
6.4: Bone Remodeling and Calcium Homeostasis

peripheral nervous system
9: Overview of the Nervous System

peripheral nervous system (PNS)
9.1: Organization and Functions of the Nervous System

peripheralnervoussystem
9.7: Review Questions

peristalsis
16.2: Digestive System Processes and Regulation

perpendicular plate of the ethmoid bone
19.4.1: The Skull

petrous ridge
19.4.1: The Skull

pH
2.3: Inorganic Compounds Essential to Human Functioning

phalanx bone of the foot
19.4.7: Bones of the Lower Limb

phalanx bone of the hand
19.4.5: Bones of the Upper Limb

phospholipid bilayer
3.1: The Cell Membrane
3.4: Cell Transport and Osmosis

photoreceptors
10.2: Special Senses - Eyes

phototransduction
10.2: Special Senses - Eyes

physical science
1.2: Overview of the Scientific Method

physiological changes
11.2: The Sympathetic Division of the ANS
11.4: Review Questions

physiological parameters
1.4: Homeostasis

physiology
1: An Introduction to Anatomy and Physiology
1.1: Overview of Anatomy and Physiology
1.3: Structural Organization of the Human Body
1.6: Review Questions
6.2: Bone Classification
8: Muscle Tissue
8.5: Review Questions
11: The Autonomic Nervous System
12.1: An Overview of the Endocrine System
12.7: Review Questions
17: The Urinary System
18: The Reproductive System

piercings
19.2: Functions of the Integumentary System

piriformis
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs

pisiform
19.4.5: Bones of the Upper Limb

pituitary
12.7: Review Questions

pituitary gland
12: The Endocrine System
12.3: The Pituitary Gland and Hypothalamus

plagiarism
1.2: Overview of the Scientific Method

plantar aponeurosis
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs

plantar group
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs

plantaris
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs

plasma
13: The Cardiovascular System - Blood

plasma membrane
3: Cell Structure

plasma proteins
13.5: Review Questions

platelets
13: The Cardiovascular System - Blood
13.1: An Overview of Blood

PNS
9.6: The Peripheral Nervous System

pollex
19.4.5: Bones of the Upper Limb

polycythemia
13.2: Erythrocytes

polymorphonuclear
13.3: Leukocytes and Platelets

polyuria
17.7: Review Questions

popliteal fossa
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs

popliteus
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs

positive chemotaxis
13.3: Leukocytes and Platelets

positive feedback
1.4: Homeostasis

posterior (dorsal) sacral foramen
19.4.2: The Vertebral Column
posterior arch
19.4.2: The Vertebral Column
posterior cardiac vein
14.1: Heart Anatomy
posterior compartment of the leg
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
posterior compartment of the thigh
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
posterior interventricular artery
14.1: Heart Anatomy
posterior interventricular sulcus
14.1: Heart Anatomy
posterior longitudinal ligament
19.4.2: The Vertebral Column
posterior scalene
19.5.1: Axial Muscles of the Head, Neck, and Back
postganglionic fibers
11.3: The Parasympathetic Division of the ANS
postsynaptic cell
9.3: Synapses
PP cell
12.6: Endocrine Pancreas
precapillary sphincters
14.4: Structure and Function of Blood Vessels
preganglionic neurons
11.3: The Parasympathetic Division of the ANS
preload
14.6: Review Questions
19.7: Coronary Circulation
prepotential depolarization
14.2: Cardiac Muscle and Electrical Activity
pressure
17.6: Endocrine Regulation of Kidney Function
presynaptic cell
9.3: Synapses
primary curve
19.4.2: The Vertebral Column
primary ossification center
19.3: Bone Formation and Development
process
9.1: Organization and Functions of the Nervous System
prolactin
12.3: The Pituitary Gland and Hypothalamus
proliferative zone
19.3: Bone Formation and Development
pronator quadratus
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
pronator teres
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
propagation
9.3: Synapses
properties
2.3: Inorganic Compounds Essential to Human Functioning
Proprioception
10.1: General and Special Senses
protection
19.2: Functions of the Integumentary System
protein synthesis
3.2: The Cytoplasm and Cellular Organelles
proteins
2.4: Review Questions
3.3: The Nucleus and DNA
proximal radioulnar joint
19.4.5: Bones of the Upper Limb
proximal tibiofibular joint
19.4.7: Bones of the Lower Limb
pseudostratified columnar epithelium
4.2: Epithelial Tissue
psoas major
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
pterion
19.4.1: The Skull
puberty
18: The Reproductive System
pubococcygeus
19.5.2: Axial Muscles of the Abdominal Wall and Thorax
pulmonary
15.3: The Process of Breathing
pulmonary arteries
14.1: Heart Anatomy
pulmonary capillaries
14.1: Heart Anatomy
pulmonary circuit
14.1: Heart Anatomy
pulmonary circulation
15.5: Review Questions
pulmonary trunk
14.1: Heart Anatomy
pulmonary valve
14.1: Heart Anatomy
pulmonary veins
14.1: Heart Anatomy
pulmonary ventilation
15: The Respiratory System
15.4: Gas Exchange
pulse pressure
19.8: Mean Arterial Pressure and Pulse Pressure
Purkinje fibers
14.2: Cardiac Muscle and Electrical Activity

Q

QRS complex
14.2: Cardiac Muscle and Electrical Activity
quadratus femoris
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
quadratus lumborum
19.5.2: Axial Muscles of the Abdominal Wall and Thorax
quadriceps femoris group
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
quadriceps tendon
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs

R

radial fossa
19.4.5: Bones of the Upper Limb
radial notch of the ulna
19.4.5: Bones of the Upper Limb
radial tuberosity
19.4.5: Bones of the Upper Limb
radiocarpal joint
19.4.5: Bones of the Upper Limb
radius
19.4.5: Bones of the Upper Limb
ramus of the mandible
19.4.1: The Skull
reabsorption
17.3: Microscopic Anatomy of the Kidney
17.4: Urine Formation and Glomerular Filtration Rate (GFR)
17.5: Tubular Reabsorption and Secretion
reactions
2.4: Review Questions
receptor
9.7: Review Questions
10.4: Review Questions
rectal valve
16.4: Small and Large Intestines
rectum
16.4: Small and Large Intestines
rectus abdominis
19.5.2: Axial Muscles of the Abdominal Wall and Thorax
rectus femoris
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
rectus sheaths
19.5.2: Axial Muscles of the Abdominal Wall and Thorax
red blood cells
13.2: Erythrocytes
red marrow
6.1: Functions of the Skeletal System
reflex
10.4: Review Questions
regional anatomy
1.1: Overview of Anatomy and Physiology
relaxation
8.5: Review Questions
remodeling
6.5: Fractures - Bone Repair
19.3: Bone Formation and Development
renal
17.3: Microscopic Anatomy of the Kidney
renal anatomy
17.4: Urine Formation and Glomerular Filtration Rate (GFR)
renal corpuscle
17.3: Microscopic Anatomy of the Kidney
renal physiology
17.4: Urine Formation and Glomerular Filtration Rate (GFR)
17.5: Tubular Reabsorption and Secretion
renin
17.6: Endocrine Regulation of Kidney Function
replication
3.3: The Nucleus and DNA
reproductive
18.2: Anatomy and Physiology of the Female Reproductive System
reproductive anatomy
18.1: Anatomy and Physiology of the Male Reproductive System
reproductive health
18.2: Anatomy and Physiology of the Female Reproductive System
reproductive hormones
18: The Reproductive System
reserve zone
19.3: Bone Formation and Development

respiratory
15.3: The Process of Breathing
respiratory infections
15.2: The Lungs
respiratory rate
15.3: The Process of Breathing
respiratory system
15: The Respiratory System
15.2: The Lungs
15.4: Gas Exchange
respiratory zones
15: The Respiratory System
respiratorysystem
15.1: Organs and Structures of the Respiratory System
response
9.1: Organization and Functions of the Nervous System
rest and digest
11.1: Introduction to the Autonomic Nervous System (ANS)
results
1.2: Overview of the Scientific Method
reticular fiber
4.3: Connective Tissue
reticular lamina
4.2: Epithelial Tissue
reticular tissue
4.3: Connective Tissue
retinacula
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
retinal structure
10.2: Special Senses - Eyes
review article
1.2: Overview of the Scientific Method
review questions
2: A Brief Overview of Chemistry
11: The Autonomic Nervous System
RhoGAM
13.4: Blood Typing
rhomboid major
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
rhomboid minor
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
ribs
19.4: Divisions of the Skeletal System
right atrioventricular valve
14.1: Heart Anatomy
right colic flexure
16.4: Small and Large Intestines
RNA
3.3: The Nucleus and DNA
rotation
7.3: Types of Body Movements
rotator cuff
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
roughER
3.5: Review Questions

S

saccharolytic fermentation
16.4: Small and Large Intestines
sacral canal
19.4.2: The Vertebral Column
sacral foramina
19.4.2: The Vertebral Column
sacral hiatus
19.4.2: The Vertebral Column
sacral promontory
19.4.2: The Vertebral Column
sacrococcygeal curve
19.4.2: The Vertebral Column
sacrum
19.4: Divisions of the Skeletal System
sagittal suture
19.4.1: The Skull
saltatory conduction
9.3: Synapses
sarcolemma
8.2: Skeletal Muscle Organ Structure
sarcomere
8.2: Skeletal Muscle Organ Structure
8.3: Muscle Fiber Contraction and Relaxation
sarcoplasm
8.2: Skeletal Muscle Organ Structure
sarcoplasmic reticulum (SR)
8.2: Skeletal Muscle Organ Structure
sartorius
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
satellite cell
9.2: Anatomy of Nervous Tissue
scalene muscles
19.5.1: Axial Muscles of the Head, Neck, and Back
scaphoid
19.4.5: Bones of the Upper Limb
scapula
19.4.4: The Pectoral Girdle
Schwann cell
9.2: Anatomy of Nervous Tissue
science
1.2: Overview of the Scientific Method
scientific method
1: An Introduction to Anatomy and Physiology
1.2: Overview of the Scientific Method
scoliosis
19.4.2: The Vertebral Column
sebaceous glands
19.1: Accessory Structures of the Skin
secondary curve
19.4.2: The Vertebral Column
secondary ossification center
19.3: Bone Formation and Development
secretion
16.3: The Stomach and the Upper Digestive Organs
17: The Urinary System
17.3: Microscopic Anatomy of the Kidney
17.4: Urine Formation and Glomerular Filtration Rate (GFR)
17.5: Tubular Reabsorption and Secretion
segmental muscle group
19.5.1: Axial Muscles of the Head, Neck, and Back
selective permeability
3.1: The Cell Membrane
3.4: Cell Transport and Osmosis
sella turcica
19.4.1: The Skull
semilunar valves
14.1: Heart Anatomy
semimembranosus
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
semispinalis capitis
19.5.1: Axial Muscles of the Head, Neck, and Back
semispinalis cervicis
19.5.1: Axial Muscles of the Head, Neck, and Back
semispinalis thoracis
19.5.1: Axial Muscles of the Head, Neck, and Back
semitendinosus
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
sensation
9.1: Organization and Functions of the Nervous System
10.1: General and Special Senses
sensory input
11.4: Review Questions
sensory modalities
10.1: General and Special Senses
sensory modality
10.4: Review Questions
sensory neuron
9.2: Anatomy of Nervous Tissue
sensory neurons
9.6: The Peripheral Nervous System
sensory receptors
9.4: The Function of Nervous Tissue
septal cartilage
19.4.1: The Skull
septum
14.1: Heart Anatomy
septum primum
14.1: Heart Anatomy
serendipity
1.2: Overview of the Scientific Method
serous gland
4.2: Epithelial Tissue
serratus anterior
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
sesamoid bones
6.2: Bone Classification
sex organs
18: The Reproductive System
shaft of the femur
19.4.7: Bones of the Lower Limb
shaft of the fibula
19.4.7: Bones of the Lower Limb
shaft of the humerus
19.4.5: Bones of the Upper Limb
shaft of the radius
19.4.5: Bones of the Upper Limb
shaft of the tibia
19.4.7: Bones of the Lower Limb
shaft of the ulna
19.4.5: Bones of the Upper Limb
short bones
6.2: Bone Classification
6.6: Review Questions
sigmoid colon
16.4: Small and Large Intestines
signaling
12.1: An Overview of the Endocrine System
12.7: Review Questions
signaling pathways
12.2: Hormones
simple columnar epithelium
4.2: Epithelial Tissue
simple cuboidal epithelium
4.2: Epithelial Tissue

simple squamous epithelium
4.2: Epithelial Tissue
sinoatrial (SA) node
14.2: Cardiac Muscle and Electrical Activity
sinus rhythm
14.2: Cardiac Muscle and Electrical Activity
sinusoid capillary
14.4: Structure and Function of Blood Vessels
skeletal
8.4: Types of Muscle Fibers and Exercise
skeletal development
6.4: Bone Remodeling and Calcium Homeostasis
skeletal muscle
4.4: Review Questions
8: Muscle Tissue
8.1: Muscle Tissues
11.2: The Sympathetic Division of the ANS
skeletal system
6: Bone Tissue and the Skeletal System
6.1: Functions of the Skeletal System
6.2: Bone Classification
6.6: Review Questions
19: Optional Reading
skeleton
19.4: Divisions of the Skeletal System
skin
5.1: Introduction
5.2: Layers of the Skin
19: Optional Reading
19.1: Accessory Structures of the Skin
19.2: Functions of the Integumentary System
skin disorders
5.2: Layers of the Skin
skin health
5.2: Layers of the Skin
skin layers
5.1: Introduction
skin pigmentation
5.2: Layers of the Skin
skull
19.4: Divisions of the Skeletal System
sliding filament model
8.3: Muscle Fiber Contraction and Relaxation
slow
8.4: Types of Muscle Fibers and Exercise
small cardiac vein
14.1: Heart Anatomy
small intestine
16: The Digestive System
16.4: Small and Large Intestines
smoking
15.2: The Lungs
smooth muscle
8: Muscle Tissue
8.1: Muscle Tissues
sodium
17.5: Tubular Reabsorption and Secretion
soleal line
19.4.7: Bones of the Lower Limb
soleus
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
soma
9.1: Organization and Functions of the Nervous System
somatic nervous system (SNS)
9.1: Organization and Functions of the Nervous System
somatosensation
9.1: Organization and Functions of the Nervous System
sound waves
10.3: Special Senses - Ears
special sense
9.1: Organization and Functions of the Nervous System
special senses
19.4.4: The Pectoral Girdle
sperm cell
18.1: Anatomy and Physiology of the Male Reproductive System
sperm maturation
18.1: Anatomy and Physiology of the Male Reproductive System
spermatogenesis
18.1: Anatomy and Physiology of the Male Reproductive System
sphenoid bone
19.4.1: The Skull
sphenoid sinus
19.4.1: The Skull
sphincter urethrovaginalis
19.5.2: Axial Muscles of the Abdominal Wall and Thorax
spinal cord
9: Overview of the Nervous System
9.1: Organization and Functions of the Nervous System
9.4: The Function of Nervous Tissue
9.5: The Central Nervous System
10.4: Review Questions
spinal nerve
9.1: Organization and Functions of the Nervous System
spinal nerves
9.6: The Peripheral Nervous System
spinalis capitis
19.5.1: Axial Muscles of the Head, Neck, and Back
spinalis cervicis
19.5.1: Axial Muscles of the Head, Neck, and Back
spinalis group
19.5.1: Axial Muscles of the Head, Neck, and Back
spinalis thoracis
19.5.1: Axial Muscles of the Head, Neck, and Back
spine of the scapula
19.4.4: The Pectoral Girdle
spinous process
19.4.2: The Vertebral Column
splenius
19.5.1: Axial Muscles of the Head, Neck, and Back
splenius capitis
19.5.1: Axial Muscles of the Head, Neck, and Back
splenius cervicis
19.5.1: Axial Muscles of the Head, Neck, and Back
spongy bone
6.3: Bone Structure
spontaneous depolarizationv
14.2: Cardiac Muscle and Electrical Activity
squamous suture
19.4.1: The Skull
stability
7: Joints
stage of exhaustion
12.5: Adrenal Glands
stage of resistance
12.5: Adrenal Glands
sternal angle
19.4.3: The Thoracic Cage
sternal end of the clavicle
19.4.4: The Pectoral Girdle
sternoclavicular joint
19.4.4: The Pectoral Girdle
sternocleidomastoid
19.5.1: Axial Muscles of the Head, Neck, and Back
sternohyoid
19.5.1: Axial Muscles of the Head, Neck, and Back
sternothyroid
19.5.1: Axial Muscles of the Head, Neck, and Back
sternum
19.4: Divisions of the Skeletal System
stimulus
9.1: Organization and Functions of the Nervous System
stomach
16: The Digestive System
16.6: Review Questions
stratified columnar epithelium
4.2: Epithelial Tissue
stratified cuboidal epithelium
4.2: Epithelial Tissue
stratified squamous epithelium
4.2: Epithelial Tissue
stratum corneum
5.2: Layers of the Skin
stress response
12: The Endocrine System
stroke volume
19.8: Mean Arterial Pressure and Pulse Pressure
stroke_volume
14.3: Cardiac Cycle
structural classification
7: Joints
structural framework
4: Tissue Organization
structural organization
1: An Introduction to Anatomy and Physiology
styloglossus
19.5.1: Axial Muscles of the Head, Neck, and Back
stylohyoid
19.5.1: Axial Muscles of the Head, Neck, and Back
styloid process
19.4.1: The Skull
styloid process of the radius
19.4.5: Bones of the Upper Limb
styloid process of the ulna
19.4.5: Bones of the Upper Limb
stylomastoid foramen
19.4.1: The Skull
subscapular fossa
19.4.4: The Pectoral Girdle
subscapularis
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
sulcus
14.1: Heart Anatomy
superficial anterior compartment of the forearm
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
superficial posterior compartment of the forearm
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs

superior angle of the scapula
19.4.4: The Pectoral Girdle
superior articular process
19.4.2: The Vertebral Column
superior articular process of the sacrum
19.4.2: The Vertebral Column
superior border of the scapula
19.4.4: The Pectoral Girdle
superior extensor retinaculum
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
superior gemellus
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
superior nuchal line
19.4.1: The Skull
superior orbital fissure
19.4.1: The Skull
superior vena cava
14.1: Heart Anatomy
supinator
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
supportive connective tissue
4.3: Connective Tissue
supraglenoid tubercle
19.4.4: The Pectoral Girdle
suprahyoid muscles
19.5.1: Axial Muscles of the Head, Neck, and Back
supraorbital foramen
19.4.1: The Skull
supraorbital margin
19.4.1: The Skull
suprascapular notch
19.4.4: The Pectoral Girdle
supraspinatus
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
supraspinous fossa
19.4.4: The Pectoral Girdle
supraspinous ligament
19.4.2: The Vertebral Column
surgical neck
19.4.5: Bones of the Upper Limb
sustentaculum tali
19.4.7: Bones of the Lower Limb
suture
19.4.1: The Skull
sweat glands
19.1: Accessory Structures of the Skin
sweating
11.4: Review Questions
sympathetic division
11: The Autonomic Nervous System
11.1: Introduction to the Autonomic Nervous System (ANS)
11.2: The Sympathetic Division of the ANS
11.3: The Parasympathetic Division of the ANS
sympathetic nervous system
9.6: The Peripheral Nervous System
sympathetic response
11.4: Review Questions
synapse
9.2: Anatomy of Nervous Tissue
synaptic
9.7: Review Questions
synaptic cleft
8.2: Skeletal Muscle Organ Structure
9.3: Synapses
synaptic end bulb
9.2: Anatomy of Nervous Tissue
synarthrosis
7.2: Classification of Joints
synovial joint
7.2: Classification of Joints
synovialjoints
7.3: Types of Body Movements
system
18.2: Anatomy and Physiology of the Female Reproductive System
Systemic Anatomy
1.1: Overview of Anatomy and Physiology
systemic circuit
14.1: Heart Anatomy
systole
14.6: Review Questions
19.7: Coronary Circulation
systolic pressure
14.5: Blood Flow, Blood Pressure, and Resistance
19.8: Mean Arterial Pressure and Pulse Pressure

T

T lymphocytes
13.3: Leukocytes and Platelets
13.5: Review Questions
T wave
14.2: Cardiac Muscle and Electrical Activity
talus
19.4.7: Bones of the Lower Limb
target organs
11.3: The Parasympathetic Division of the ANS
tarsal bone
19.4.7: Bones of the Lower Limb
taste
10.1: General and Special Senses
tattoos
5.1: Introduction
19.2: Functions of the Integumentary System
temporal bone
19.4.1: The Skull
temporal fossa
19.4.1: The Skull
temporal process of the zygomatic bone
19.4.1: The Skull
temporalis
19.5.1: Axial Muscles of the Head, Neck, and Back
tendinous intersections
19.5.2: Axial Muscles of the Abdominal Wall and Thorax
tenia coli
16.4: Small and Large Intestines
tensor fascia lata
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
teres major
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
teres minor
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
testicular reproductive system
18.1: Anatomy and Physiology of the Male Reproductive System
testosterone
18: The Reproductive System
18.1: Anatomy and Physiology of the Male Reproductive System
textbooks
InfoPage
thalamus
9.4: The Function of Nervous Tissue
10.4: Review Questions
theory
1.2: Overview of the Scientific Method
thermoregulation
19.1: Accessory Structures of the Skin
19.2: Functions of the Integumentary System
thick filament
8.2: Skeletal Muscle Organ Structure
thigh
19.4.7: Bones of the Lower Limb
thin filament
8.2: Skeletal Muscle Organ Structure
thoracic cage
19.4: Divisions of the Skeletal System
thoracic cavity
1.5: Anatomical Terminology
thoracic curve
19.4.2: The Vertebral Column
thoracic vertebrae
19.4.2: The Vertebral Column
thoroughfare channel
14.4: Structure and Function of Blood Vessels
threshold
9.3: Synapses
thrombocytes
13.3: Leukocytes and Platelets
thrombocytopenia
13.3: Leukocytes and Platelets
thrombocytosis
13.3: Leukocytes and Platelets
thyrohyoid
19.5.1: Axial Muscles of the Head, Neck, and Back
thyroid
12.7: Review Questions
thyroid gland
12: The Endocrine System
12.4: Thyroid Gland and Parathyroid Glands
thyroid hormones
12.2: Hormones
thyroxine
12.4: Thyroid Gland and Parathyroid Glands
tibia
19.4.7: Bones of the Lower Limb
tibialis anterior
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
tibialis posterior
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
tight junction
4.2: Epithelial Tissue
tissue
4.1: Types of Tissues
4.4: Review Questions
6: Bone Tissue and the Skeletal System
8.5: Review Questions
tissues
1.3: Structural Organization of the Human Body
1.6: Review Questions
4: Tissue Organization

trabeculae carneae
14.1: Heart Anatomy
trabecular bone
6.4: Bone Remodeling and Calcium Homeostasis
trachea
15.1: Organs and Structures of the Respiratory System
15.5: Review Questions
tract
9.1: Organization and Functions of the Nervous System
transcription
3.5: Review Questions
transfusion
13.4: Blood Typing
transitional epithelium
4.2: Epithelial Tissue
transverse colon
16.4: Small and Large Intestines
transverse foramen
19.4.2: The Vertebral Column
transverse process
19.4.2: The Vertebral Column
transversus abdominis
19.5.2: Axial Muscles of the Abdominal Wall and Thorax
trapezium
19.4.5: Bones of the Upper Limb
trapezius
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
trapezoid
19.4.5: Bones of the Upper Limb
treatments
5.1: Introduction
triad
8.2: Skeletal Muscle Organ Structure
triceps brachii
19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs
tricuspid valve
14.1: Heart Anatomy
triiodothyronine
12.4: Thyroid Gland and Parathyroid Glands
triquetrum
19.4.5: Bones of the Upper Limb
trochlea
19.4.5: Bones of the Upper Limb
trochlear notch
19.4.5: Bones of the Upper Limb
tropomyosin
8.2: Skeletal Muscle Organ Structure
8.3: Muscle Fiber Contraction and Relaxation
troponin
8.2: Skeletal Muscle Organ Structure
8.3: Muscle Fiber Contraction and Relaxation
true ribs
19.4.3: The Thoracic Cage
tubercle of the rib
19.4.3: The Thoracic Cage
tubular reabsorption
17: The Urinary System
tunica externa
14.4: Structure and Function of Blood Vessels
tunica intima
14.4: Structure and Function of Blood Vessels
tunica media
14.4: Structure and Function of Blood Vessels
types of fractures
6.5: Fractures - Bone Repair
types of tissues
4: Tissue Organization

U

ulna
19.4.5: Bones of the Upper Limb
ulnar notch of the radius
19.4.5: Bones of the Upper Limb
ulnar tuberosity
19.4.5: Bones of the Upper Limb
uniaxial joint
7.2: Classification of Joints
unipolar
9.2: Anatomy of Nervous Tissue
unmyelinated
9.2: Anatomy of Nervous Tissue
urinary system
17: The Urinary System
urine concentration
17.5: Tubular Reabsorption and Secretion
urine formation
17: The Urinary System
17.3: Microscopic Anatomy of the Kidney
urine production
17.4: Urine Formation and Glomerular Filtration Rate (GFR)
urine_color
17.7: Review Questions
urogenital triangle
19.5.2: Axial Muscles of the Abdominal Wall and Thorax

V

Valsalva’s maneuver
16.4: Small and Large Intestines
valve
14.1: Heart Anatomy
valves
14.6: Review Questions
variable
1.2: Overview of the Scientific Method
vasa vasorum
14.4: Structure and Function of Blood Vessels
vascular resistance
14.5: Blood Flow, Blood Pressure, and Resistance
vascular shunt
14.4: Structure and Function of Blood Vessels
vasoconstriction
14.4: Structure and Function of Blood Vessels
vasodilation
14.4: Structure and Function of Blood Vessels
vasomotion
14.4: Structure and Function of Blood Vessels
vastus lateralis
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
vastus medialis
19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs
vein
14.4: Structure and Function of Blood Vessels
venous reserve
14.4: Structure and Function of Blood Vessels
ventilation
15.3: The Process of Breathing
15.4: Gas Exchange
ventricle
9.2: Anatomy of Nervous Tissue
14.1: Heart Anatomy
ventricular ejection phase
19.7: Coronary Circulation
venule
14.4: Structure and Function of Blood Vessels
vertebra
19.4: Divisions of the Skeletal System
vertebral (spinal) canal
19.4.2: The Vertebral Column
vertebral arch
19.4.2: The Vertebral Column
vertebral column
19.4: Divisions of the Skeletal System
vertebral foramen
19.4.2: The Vertebral Column
vestibulocochlear nerve
10.3: Special Senses - Ears
villus
16.4: Small and Large Intestines
visceral sense
9.1: Organization and Functions of the Nervous System
vision
10.1: General and Special Senses
10.2: Special Senses - Eyes
visual acuity
10.2: Special Senses - Eyes
visual cortex
10.4: Review Questions
vitamin D synthesis
19.2: Functions of the Integumentary System
vomer bone
19.4.1: The Skull

W

white matter
9.1: Organization and Functions of the Nervous System
9.5: The Central Nervous System

Y

yellow marrow
6.1: Functions of the Skeletal System

Z

zona fasciculata
12.5: Adrenal Glands
zona glomerulosa
12.5: Adrenal Glands
zona reticularis
12.5: Adrenal Glands
zone of calcified matrix
19.3: Bone Formation and Development
zone of maturation and hypertrophy
19.3: Bone Formation and Development
zygomatic arch
19.4.1: The Skull
zygomatic bone
19.4.1: The Skull
zygomatic process of the temporal bone
19.4.1: The Skull

Glossary

Sample Word 1 | Sample Definition 1

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    - 1.4: Homeostasis - *CC BY 4.0*
    - 1.5: Anatomical Terminology - *CC BY 4.0*
    - 1.6: Review Questions - *Undeclared*
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  - 3: Cell Structure - *Undeclared*
    - 3.1: The Cell Membrane - *CC BY 4.0*
    - 3.2: The Cytoplasm and Cellular Organelles - *CC BY 4.0*
    - 3.3: The Nucleus and DNA - *CC BY 4.0*
    - 3.4: Cell Transport and Osmosis - *CC BY 4.0*
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  - 4: Tissue Organization - *Undeclared*
    - 4.1: Types of Tissues - *CC BY 4.0*
    - 4.2: Epithelial Tissue - *CC BY-NC-SA 4.0*
    - 4.3: Connective Tissue - *CC BY-NC-SA 4.0*
    - 4.4: Review Questions - *Undeclared*
  - 5: The Integumentary System - *Undeclared*
    - 5.1: Introduction - *CC BY 4.0*
    - 5.2: Layers of the Skin - *CC BY 4.0*
  - 6: Bone Tissue and the Skeletal System - *Undeclared*
    - 6.1: Functions of the Skeletal System - *CC BY-NC-SA 4.0*
    - 6.2: Bone Classification - *CC BY 4.0*
    - 6.3: Bone Structure - *CC BY 4.0*
    - 6.4: Bone Remodeling and Calcium Homeostasis - *CC BY 4.0*
    - 6.5: Fractures - Bone Repair - *CC BY 4.0*
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    - 7.1: Introduction - *CC BY-NC-SA 4.0*
    - 7.2: Classification of Joints - *CC BY-NC-SA 4.0*
    - 7.3: Types of Body Movements - *CC BY 4.0*
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    - 8.1: Muscle Tissues - *CC BY-NC-SA 4.0*
    - 8.2: Skeletal Muscle Organ Structure - *CC BY-NC-SA 4.0*
    - 8.3: Muscle Fiber Contraction and Relaxation - *CC BY 4.0*
    - 8.4: Types of Muscle Fibers and Exercise - *CC BY 4.0*
    - 8.5: Review Questions - *Undeclared*
  - 9: Overview of the Nervous System - *Undeclared*
    - 9.1: Organization and Functions of the Nervous System - *CC BY-NC-SA 4.0*
    - 9.2: Anatomy of Nervous Tissue - *CC BY-NC-SA 4.0*
    - 9.3: Synapses - *CC BY-NC-SA 4.0*
    - 9.4: The Function of Nervous Tissue - *CC BY 4.0*
    - 9.5: The Central Nervous System - *CC BY 4.0*
    - 9.6: The Peripheral Nervous System - *CC BY 4.0*

- 9.7: Review Questions - *Undeclared*
- 10: Sensory Perception - *Undeclared*
  - 10.1: General and Special Senses - *CC BY 4.0*
  - 10.2: Special Senses - Eyes - *Undeclared*
  - 10.3: Special Senses - Ears - *Undeclared*
  - 10.4: Review Questions - *Undeclared*
- 11: The Autonomic Nervous System - *Undeclared*
  - 11.1: Introduction to the Autonomic Nervous System (ANS) - *Undeclared*
  - 11.2: The Sympathetic Division of the ANS - *Undeclared*
  - 11.3: The Parasympathetic Division of the ANS - *Undeclared*
  - 11.4: Review Questions - *Undeclared*
- 12: The Endocrine System - *Undeclared*
  - 12.1: An Overview of the Endocrine System - *CC BY 4.0*
  - 12.2: Hormones - *CC BY 4.0*
  - 12.3: The Pituitary Gland and Hypothalamus - *CC BY 4.0*
  - 12.4: Thyroid Gland and Parathyroid Glands - *CC BY-NC-SA 4.0*
  - 12.5: Adrenal Glands - *CC BY-NC-SA 4.0*
  - 12.6: Endocrine Pancreas - *CC BY-NC-SA 4.0*
  - 12.7: Review Questions - *Undeclared*
- 13: The Cardiovascular System - Blood - *CC BY 4.0*
  - 13.1: An Overview of Blood - *CC BY 4.0*
  - 13.2: Erythrocytes - *CC BY 4.0*
  - 13.3: Leukocytes and Platelets - *CC BY-NC-SA 4.0*
  - 13.4: Blood Typing - *CC BY 4.0*
  - 13.5: Review Questions - *CC BY-NC-SA 4.0*
- 14: The Cardiovascular System - Heart and Blood Vessels - *Undeclared*
  - 14.1: Heart Anatomy - *CC BY-NC-SA 4.0*
  - 14.2: Cardiac Muscle and Electrical Activity - *CC BY-NC-SA 4.0*
  - 14.3: Cardiac Cycle - *CC BY 4.0*
  - 14.4: Structure and Function of Blood Vessels - *CC BY-NC-SA 4.0*
  - 14.5: Blood Flow, Blood Pressure, and Resistance - *CC BY 4.0*
  - 14.6: Review Questions - *CC BY-NC-SA 4.0*
- 15: The Respiratory System - *Undeclared*
  - 15.1: Organs and Structures of the Respiratory System - *CC BY 4.0*
  - 15.2: The Lungs - *CC BY 4.0*
  - 15.3: The Process of Breathing - *CC BY 4.0*
  - 15.4: Gas Exchange - *CC BY 4.0*
  - 15.5: Review Questions - *Undeclared*
- 16: The Digestive System - *Undeclared*
  - 16.1: Overview of the Digestive System - *CC BY 4.0*
  - 16.2: Digestive System Processes and Regulation - *CC BY 4.0*
  - 16.3: The Stomach and the Upper Digestive Organs - *CC BY 4.0*
  - 16.4: Small and Large Intestines - *CC BY-NC-SA 4.0*
  - 16.5: Accessory Organs in Digestion- The Liver, Pancreas, and Gallbladder - *CC BY 4.0*
  - 16.6: Review Questions - *Undeclared*
- 17: The Urinary System - *Undeclared*
  - 17.1: Introduction to the Urinary System - *CC BY-NC-SA 4.0*
  - 17.2: Overview of the Kidney - *CC BY-NC-SA 4.0*
  - 17.3: Microscopic Anatomy of the Kidney - *CC BY 4.0*
  - 17.4: Urine Formation and Glomerular Filtration Rate (GFR) - *CC BY 4.0*
  - 17.5: Tubular Reabsorption and Secretion - *CC BY 4.0*
  - 17.6: Endocrine Regulation of Kidney Function - *CC BY 4.0*
  - 17.7: Review Questions - *Undeclared*
- 18: The Reproductive System - *Undeclared*
  - 18.1: Anatomy and Physiology of the Male Reproductive System - *CC BY 4.0*
  - 18.2: Anatomy and Physiology of the Female Reproductive System - *CC BY 4.0*
- 19: Optional Reading - *Undeclared*
  - 19.1: Accessory Structures of the Skin - *CC BY 4.0*
  - 19.2: Functions of the Integumentary System - *CC BY 4.0*
  - 19.3: Bone Formation and Development - *CC BY-NC-SA 4.0*
  - 19.4: Divisions of the Skeletal System - *CC BY-NC-SA 4.0*
    - 19.4.1: The Skull - *CC BY-NC-SA 4.0*
    - 19.4.2: The Vertebral Column - *CC BY-NC-SA 4.0*
    - 19.4.3: The Thoracic Cage - *CC BY-NC-SA 4.0*
    - 19.4.4: The Pectoral Girdle - *CC BY-NC-SA 4.0*
    - 19.4.5: Bones of the Upper Limb - *CC BY-NC-SA 4.0*
    - 19.4.6: The Pelvic Girdle and Pelvis - *CC BY-NC-SA 4.0*
    - 19.4.7: Bones of the Lower Limb - *CC BY-NC-SA 4.0*
  - 19.5: Introduction to the Muscular System - *CC BY-NC-SA 4.0*
    - 19.5.1: Axial Muscles of the Head, Neck, and Back - *CC BY-NC-SA 4.0*
    - 19.5.2: Axial Muscles of the Abdominal Wall and Thorax - *CC BY-NC-SA 4.0*

        - 19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs - *CC BY-NC-SA 4.0*
        - 19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs - *CC BY-NC-SA 4.0*
    - 19.6: Special Senses - Others - *Undeclared*
    - 19.7: Coronary Circulation - *CC BY-NC-SA 4.0*
    - 19.8: Mean Arterial Pressure and Pulse Pressure - *Undeclared*
- Back Matter - *Undeclared*
    - Index - *Undeclared*
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    - Detailed Licensing - *Undeclared*
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  - Front Matter - *Undeclared*
    - TitlePage - *Undeclared*
    - InfoPage - *Undeclared*
    - Table of Contents - *Undeclared*
    - Acknowledgements - *Undeclared*
    - Licensing - *Undeclared*
    - About the Author - *Undeclared*
    - Licensing - *Undeclared*
  - 1: An Introduction to Anatomy and Physiology - *Undeclared*
    - 1.1: Overview of Anatomy and Physiology - *CC BY 4.0*
    - 1.2: Overview of the Scientific Method - *CC BY 4.0*
    - 1.3: Structural Organization of the Human Body - *CC BY 4.0*
    - 1.4: Homeostasis - *CC BY 4.0*
    - 1.5: Anatomical Terminology - *CC BY 4.0*
    - 1.6: Review Questions - *Undeclared*
  - 2: A Brief Overview of Chemistry - *Undeclared*
    - 2.1: Elements and Atoms - The Building Blocks of Matter - *CC BY 4.0*
    - 2.2: Chemical Bonds - *CC BY 4.0*
    - 2.3: Inorganic Compounds Essential to Human Functioning - *CC BY 4.0*
    - 2.4: Review Questions - *Undeclared*
  - 3: Cell Structure - *Undeclared*
    - 3.1: The Cell Membrane - *CC BY 4.0*
    - 3.2: The Cytoplasm and Cellular Organelles - *CC BY 4.0*
    - 3.3: The Nucleus and DNA - *CC BY 4.0*
    - 3.4: Cell Transport and Osmosis - *CC BY 4.0*
    - 3.5: Review Questions - *Undeclared*
  - 4: Tissue Organization - *Undeclared*
    - 4.1: Types of Tissues - *CC BY 4.0*
    - 4.2: Epithelial Tissue - *CC BY-NC-SA 4.0*
    - 4.3: Connective Tissue - *CC BY-NC-SA 4.0*
    - 4.4: Review Questions - *Undeclared*
  - 5: The Integumentary System - *Undeclared*
    - 5.1: Introduction - *CC BY 4.0*
    - 5.2: Layers of the Skin - *CC BY 4.0*
  - 6: Bone Tissue and the Skeletal System - *Undeclared*
    - 6.1: Functions of the Skeletal System - *CC BY-NC-SA 4.0*
    - 6.2: Bone Classification - *CC BY 4.0*
    - 6.3: Bone Structure - *CC BY 4.0*
    - 6.4: Bone Remodeling and Calcium Homeostasis - *CC BY 4.0*
    - 6.5: Fractures - Bone Repair - *CC BY 4.0*
    - 6.6: Review Questions - *Undeclared*
  - 7: Joints - *Undeclared*
    - 7.1: Introduction - *CC BY-NC-SA 4.0*
    - 7.2: Classification of Joints - *CC BY-NC-SA 4.0*
    - 7.3: Types of Body Movements - *CC BY 4.0*
  - 8: Muscle Tissue - *Undeclared*
    - 8.1: Muscle Tissues - *CC BY-NC-SA 4.0*
    - 8.2: Skeletal Muscle Organ Structure - *CC BY-NC-SA 4.0*
    - 8.3: Muscle Fiber Contraction and Relaxation - *CC BY 4.0*
    - 8.4: Types of Muscle Fibers and Exercise - *CC BY 4.0*
    - 8.5: Review Questions - *Undeclared*
  - 9: Overview of the Nervous System - *Undeclared*
    - 9.1: Organization and Functions of the Nervous System - *CC BY-NC-SA 4.0*
    - 9.2: Anatomy of Nervous Tissue - *CC BY-NC-SA 4.0*
    - 9.3: Synapses - *CC BY-NC-SA 4.0*
    - 9.4: The Function of Nervous Tissue - *CC BY 4.0*
    - 9.5: The Central Nervous System - *CC BY 4.0*
    - 9.6: The Peripheral Nervous System - *CC BY 4.0*

- 9.7: Review Questions - *Undeclared*
- 10: Sensory Perception - *Undeclared*
  - 10.1: General and Special Senses - *CC BY 4.0*
  - 10.2: Special Senses - Eyes - *Undeclared*
  - 10.3: Special Senses - Ears - *Undeclared*
  - 10.4: Review Questions - *Undeclared*
- 11: The Autonomic Nervous System - *Undeclared*
  - 11.1: Introduction to the Autonomic Nervous System (ANS) - *Undeclared*
  - 11.2: The Sympathetic Division of the ANS - *Undeclared*
  - 11.3: The Parasympathetic Division of the ANS - *Undeclared*
  - 11.4: Review Questions - *Undeclared*
- 12: The Endocrine System - *Undeclared*
  - 12.1: An Overview of the Endocrine System - *CC BY 4.0*
  - 12.2: Hormones - *CC BY 4.0*
  - 12.3: The Pituitary Gland and Hypothalamus - *CC BY 4.0*
  - 12.4: Thyroid Gland and Parathyroid Glands - *CC BY-NC-SA 4.0*
  - 12.5: Adrenal Glands - *CC BY-NC-SA 4.0*
  - 12.6: Endocrine Pancreas - *CC BY-NC-SA 4.0*
  - 12.7: Review Questions - *Undeclared*
- 13: The Cardiovascular System - Blood - *CC BY 4.0*
  - 13.1: An Overview of Blood - *CC BY 4.0*
  - 13.2: Erythrocytes - *CC BY 4.0*
  - 13.3: Leukocytes and Platelets - *CC BY-NC-SA 4.0*
  - 13.4: Blood Typing - *CC BY 4.0*
  - 13.5: Review Questions - *CC BY-NC-SA 4.0*
- 14: The Cardiovascular System - Heart and Blood Vessels - *Undeclared*
  - 14.1: Heart Anatomy - *CC BY-NC-SA 4.0*
  - 14.2: Cardiac Muscle and Electrical Activity - *CC BY-NC-SA 4.0*
  - 14.3: Cardiac Cycle - *CC BY 4.0*
  - 14.4: Structure and Function of Blood Vessels - *CC BY-NC-SA 4.0*
  - 14.5: Blood Flow, Blood Pressure, and Resistance - *CC BY 4.0*
  - 14.6: Review Questions - *CC BY-NC-SA 4.0*
- 15: The Respiratory System - *Undeclared*
  - 15.1: Organs and Structures of the Respiratory System - *CC BY 4.0*
  - 15.2: The Lungs - *CC BY 4.0*
  - 15.3: The Process of Breathing - *CC BY 4.0*
  - 15.4: Gas Exchange - *CC BY 4.0*
  - 15.5: Review Questions - *Undeclared*
- 16: The Digestive System - *Undeclared*
  - 16.1: Overview of the Digestive System - *CC BY 4.0*
  - 16.2: Digestive System Processes and Regulation - *CC BY 4.0*
  - 16.3: The Stomach and the Upper Digestive Organs - *CC BY 4.0*
  - 16.4: Small and Large Intestines - *CC BY-NC-SA 4.0*
  - 16.5: Accessory Organs in Digestion- The Liver, Pancreas, and Gallbladder - *CC BY 4.0*
  - 16.6: Review Questions - *Undeclared*
- 17: The Urinary System - *Undeclared*
  - 17.1: Introduction to the Urinary System - *CC BY-NC-SA 4.0*
  - 17.2: Overview of the Kidney - *CC BY-NC-SA 4.0*
  - 17.3: Microscopic Anatomy of the Kidney - *CC BY 4.0*
  - 17.4: Urine Formation and Glomerular Filtration Rate (GFR) - *CC BY 4.0*
  - 17.5: Tubular Reabsorption and Secretion - *CC BY 4.0*
  - 17.6: Endocrine Regulation of Kidney Function - *CC BY 4.0*
  - 17.7: Review Questions - *Undeclared*
- 18: The Reproductive System - *Undeclared*
  - 18.1: Anatomy and Physiology of the Male Reproductive System - *CC BY 4.0*
  - 18.2: Anatomy and Physiology of the Female Reproductive System - *CC BY 4.0*
- 19: Optional Reading - *Undeclared*
  - 19.1: Accessory Structures of the Skin - *CC BY 4.0*
  - 19.2: Functions of the Integumentary System - *CC BY 4.0*
  - 19.3: Bone Formation and Development - *CC BY-NC-SA 4.0*
  - 19.4: Divisions of the Skeletal System - *CC BY-NC-SA 4.0*
    - 19.4.1: The Skull - *CC BY-NC-SA 4.0*
    - 19.4.2: The Vertebral Column - *CC BY-NC-SA 4.0*
    - 19.4.3: The Thoracic Cage - *CC BY-NC-SA 4.0*
    - 19.4.4: The Pectoral Girdle - *CC BY-NC-SA 4.0*
    - 19.4.5: Bones of the Upper Limb - *CC BY-NC-SA 4.0*
    - 19.4.6: The Pelvic Girdle and Pelvis - *CC BY-NC-SA 4.0*
    - 19.4.7: Bones of the Lower Limb - *CC BY-NC-SA 4.0*
  - 19.5: Introduction to the Muscular System - *CC BY-NC-SA 4.0*
    - 19.5.1: Axial Muscles of the Head, Neck, and Back - *CC BY-NC-SA 4.0*
    - 19.5.2: Axial Muscles of the Abdominal Wall and Thorax - *CC BY-NC-SA 4.0*

        - 19.5.3: Appendicular Muscles of the Pectoral Girdle and Upper Limbs - *CC BY-NC-SA 4.0*
        - 19.5.4: Appendicular Muscles of the Pelvic Girdle and Lower Limbs - *CC BY-NC-SA 4.0*
    - 19.6: Special Senses - Others - *Undeclared*
    - 19.7: Coronary Circulation - *CC BY-NC-SA 4.0*
    - 19.8: Mean Arterial Pressure and Pulse Pressure - *Undeclared*
- Back Matter - *Undeclared*
    - Index - *Undeclared*
    - Glossary - *Undeclared*
    - Detailed Licensing - *Undeclared*
    - Detailed Licensing - *Undeclared*